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Skeletal and polycyclic sterically hindered alkenes

B M Lerman

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Abstract. Data on the chemistry of strained tetrasubstituted alkenes with skeletal and polycyclic fragments are surveyed. A systematic account is given of information concerning the methods of their synthesis and data are presented on the deformation of their molecular geometry relative to the usual geometry. The characteristic features of the reactivity of skeletal compounds of this type are considered — the formation of unusual adducts and substitution products in reactions with electrophiles. The oxidation reactions of the alkenes are discussed and their value as starting materials for the synthesis of stable dioxetanes, which have found practical application as chemiluminescent labels and probes in immunology and molecular biology, is demonstrated. The bibliography includes 152 references.

I. Introduction

Effective routes to the synthesis of many organic substances proceed via reactions involving addition to alkenes, and this has been a permanent stimulus for the expansion of the available range of the latter. Each year there is a growth in the number of new and saturated compounds involved in practical organic synthesis; apart from the usual, unstrained alkenes, strained compounds are beginning to be used with increasing frequency in synthesis, including sterically hindered alkenes (SHA). The atoms involved in the SHA double bond have substituents comprising bulky groups or strained fragments shielding the bond. The presence of such substituents induces a steric strain in the molecule and can lead to definite structural deformations. The group of SHA includes substituted ethenes with branched alkyl substituents, polycyclanes, and skeletal compounds with an exocyclic double bond incorporated in a rigid polycyclic system as well as alkylidenepolycyclanes with bulky substituents in the side chain, and α-octamethyl-substituted cycloalkylidenecyclanes.

SHA occupy a special place in the chemistry of unsaturated compounds. They are less readily available than the usual alkenes and their synthesis therefore constitutes an independent synthetic problem. The reactivity of the shielded double bond in SHA differs significantly from that of the corresponding bond in the usual alkenes; the specificity of the reactions involving it is also different, especially in the case of skeletal SHA.

The unusual chemical properties of skeletal SHA have attracted considerable attention by investigators during the last decade. Nevertheless, the chemistry of SHA was not duly described in the review[1] devoted to strained organic molecules; its individual aspects (as regards the state in 1977) have been examined by Tidwell[2] in a review of sterically hindered molecules. Even in the familiar review of the chemistry of alkenes[3] as well as monographs[4,5] and reviews[6–8] devoted to the chemistry of skeletal compounds, very little attention has been devoted to the chemistry of SHA.

In the present review, an attempt is made to survey data on the synthesis, structure, and chemical properties of polycyclic and skeletal SHA with a tetra-substituted double bond and also the applications of the dioxetanes obtained from these compounds (in the discussion of the limits of the applicability of synthetic methods, of the degree of deformation of the molecules, and of the relative strain in SHA, data on aliphatic and aromatic compounds are quoted).

II. Methods of synthesis of sterically hindered alkenes

Only a few of the synthetic approaches known for the usual alkenes are used to obtain SHA. These are mainly methods which lead to the creation of the carbon skeleton with simultaneous introduction of the double bond; they are based on the dimerisation (coupling) of ketones or their derivatives. Numerous modifications of these methods, involving a transition to increasingly more reactive synthons, have expanded their possibilities and have made many SHA available.

Another route to strained alkenes of this type is via the Diels–Alder synthesis. Novel methods of synthesis, involving elimination, the use of sulfur-containing synthons, the participation of organometallic reagents, etc. have been proposed for individual SHA.

1. Synthesis of sterically hindered alkenes by the reductive coupling of ketones (the McMurry method)

Certain steric SHA with a symmetrical structure can be obtained in one stage by the McMurry reaction via the intermolecular reductive coupling of ketones under the influence of low-valence titanium reagents.[9–12] The latter are obtained in situ from $TiCl_3$ or $TiCl_4$ on treatment with reductants and are used in the

B M Lerman Fine Organic Synthesis Laboratory, Institute of Organic Chemistry, Ufa Scientific Centre of the Russian Academy of Sciences, prosp. Oktyabrya 71, 450054 Ufa. Fax (7-347) 235 60 66.
Tel. (7-347) 235 61 44. E-mail: AAhCZrk8k1@chemorg.bashkiria.su

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Table 1. Syntheses of sterically hindered alkenes by McMurry's method.

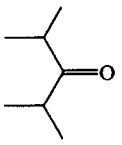
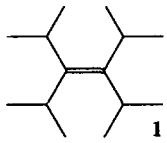
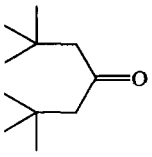
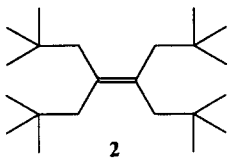
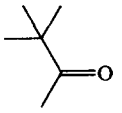
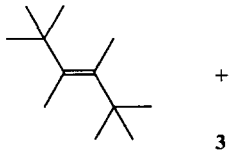
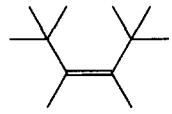
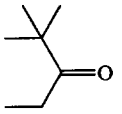
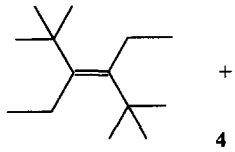
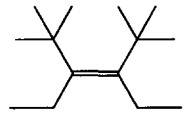
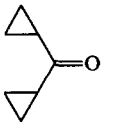
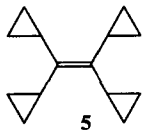
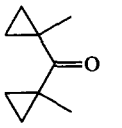
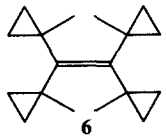
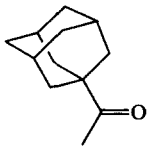
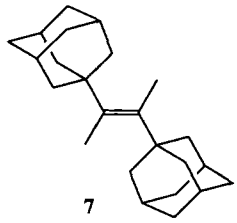
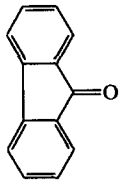
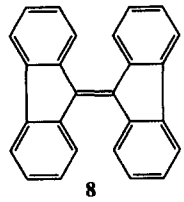
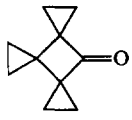
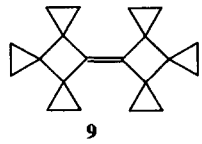
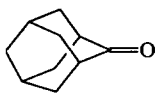
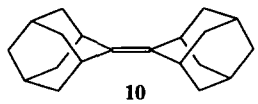
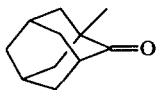
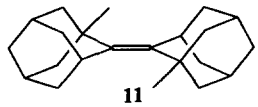
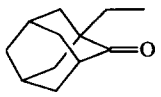
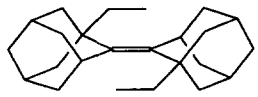
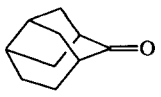
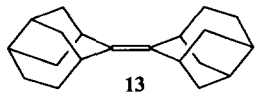
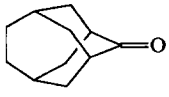
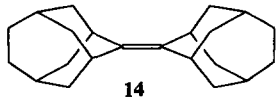
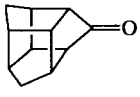
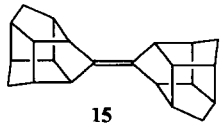
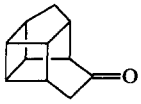
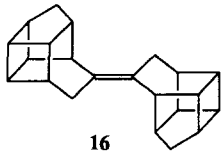
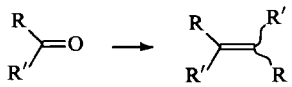
Initial ketone	Reaction product	Titanium reagent	Yield (%)	Ref.
	 **1**	$TiCl_3-K$	37	11, 14
		$TiCl_3-LiAlH_4$	12	15
		$TiCl_3-Zn-Cu$	87	12
	 **2**	$TiCl_3-LiAlH_4$	40	16
	 +  **3**	$TiCl_3-Zn$	68[a]	17
		$TiCl_4-LiAlH_4$	70[b]	18
	 +  **4**	$TiCl_3-LiAlH_4$	8[c]	19
	 **5**	$TiCl_4-Zn$	25	20
		$TiCl_3-LiAlH_4$	15	21
	 **6**	$TiCl_3-LiAlH_4$	13	22
	 **7**	$TiCl_4-Zn$	15	20
	 **8**	$TiCl_3-K$	85	11
		$TiCl_3-Mg-Hg$	-	23
	 **9**	$TiCl_3-LiAlH_4$	8	24

Table 1 (continued)

Initial ketone	Reaction product	Titanium reagent	Yield (%)	Ref.
	 **10**	$TiCl_3-LiAlH_4$	85	9
		$TiCl_3-K$	82	11
		$TiCl_3-Li$	91	11
		$TiCl_4-Zn$	98	25
	 **11**	$TiCl_3-K$	52	26
	 **12**	$TiCl_3-K$	40	27
	 **13**	$TiCl_3-K$	45	20, 28
	 **14**	$TiCl_3-K$	40	29
	 **15**	$TiCl_4-Zn$	51	30
	 **16**	$TiCl_3-LiAlH_4$	32	30

[a] The yield of the (*E*)-isomer is quoted; [b] *E* : *Z* is 1 : 1; [c] *E* : *Z* is 12 : 1.

form of $TiCl_4-Zn$, $TiCl_3-K$, $TiCl_3-Li$, $TiCl_3-LiAlH_4$, etc. systems.†

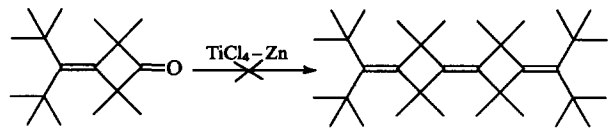


The tetraalkylethenes **1**–**7** and the polycyclic and skeletal alkenes **8**–**16** have been synthesised in this way. The reagents employed for the synthesis of the alkenes and the yield of the latter are presented in Table 1. It is seen from the table that the method is particularly effective for the synthesis of adamantylideneadamantane (2,2′-bisadamantylidene) **10**, for which an almost quantitative yield has been achieved. The yield of other SHA depends significantly on the extent to which the double bond is sterically hindered, diminishing with increasing branching of the substituents at the bond itself (tetrasubstituted ethenes) or following the introduction of alkyl substituents in the α-position relative to the bond (dialkyladamantylideneadamantanes). The choice of the system as a whole — the nature of the reductant and the solvent — has a significant influence on the yield of the SHA. This can be seen in relation to 1,1,2,2-tetraisopropylethene **1** and adamantylideneadamantane **10**. High stereoselectivity — the formation of only the *trans*-isomer — is characteristic of reactions leading to dimethyladamantylideneadamantane **11** and diethyladamantylideneadamantane **12**. The ratio of the (*E*)- and (*Z*)-isomers of 1,2,-di-*tert*-butyl-1,2 dimethylene **3** depends on the nature of the reductant.

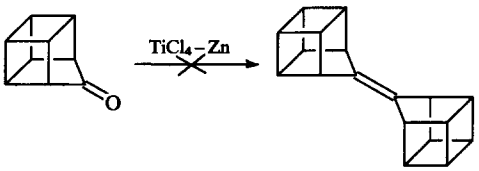
The limitations of the method are associated mainly with the difficulty of the introduction into the reductive coupling reaction of ketones with branched alkyl substituents — *tert*-butyl isopropyl ketone, di-*tert*-butyl ketone, *tert*-butyl neopentyl ketone,[16] and also 3-(di-*tert*-butylmethylene)-2,2,4,4-tetramethylcyclobutanone **17**.[31]

The attempt to achieve the single-stage synthesis of the diskeletal alkene **18** from homocubanone was unsuccessful.[32]

† Various aspects of the preparation of these reagents, the mechanisms of their action, and their applications in organic synthesis have been described in Lenoir's review.[13]

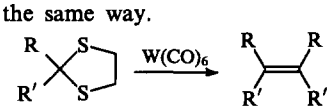


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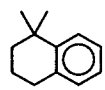
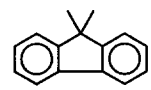


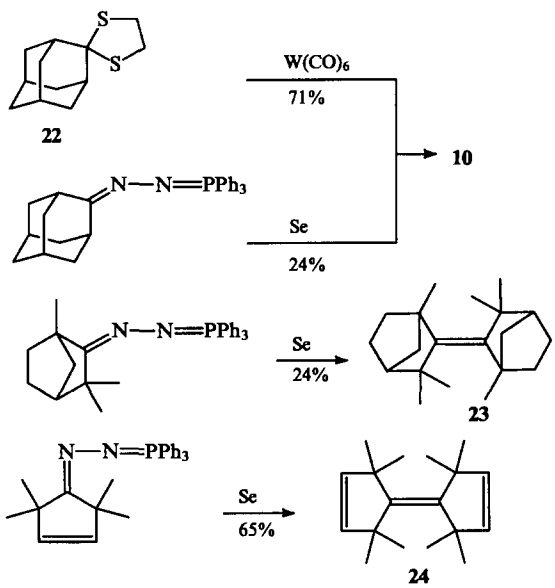
18

Together with the reductive coupling of the ketones themselves, examples of similar reactions have been described for the thio- and seleno-derivatives. Thus the desulfurisation of aromatic dithioketals by $W(CO)_6$ leads to the corresponding alkenes **19–21**, while the analogous reaction of the adamantanone dithioketal **22** affords adamantylideneadamantane **10**.[33] The latter has also been obtained in the reaction of adamantanone triphenylphosphorylidenehydrazone with selenium. Fenchylidenefenchane **23** [34] and 1,1′-bis(2,2,5,5-tetramethylcyclopent-3-enylidene) **24** [35,36] have been synthesised in the same way.



19–21

R, R′ = Ph, Me (**19**);  (**20**);  (**21**)



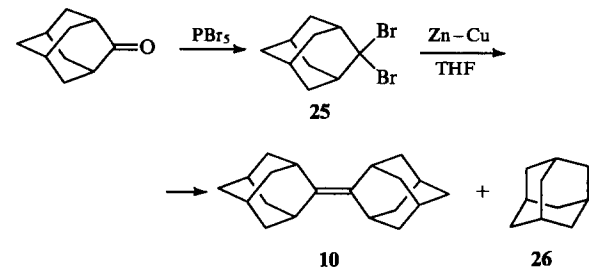
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23

24

2. The 'carbenoid' method of synthesis of sterically hindered alkenes

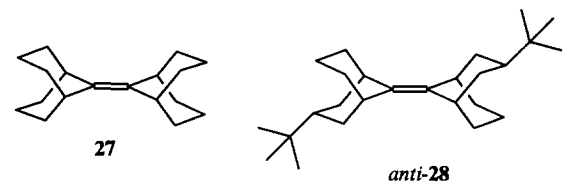
The synthesis of one of the best known SHA—the alkene **10**—from adamantanone via 2,2-dibromoadamantane **25** with subsequent debromination of the latter by the zinc–copper couple has been proposed by Geluk.[37] This method was used widely for a long time as a preparative procedure. The low yield of adamantylideneadamantane (60%–75%) owing to the side reaction **25**→**26** in the second stage and the need for the numerous repetitions of this stage must be regarded as its disadvantages. The yield of the target product depends on the quality of the zinc and the activity of the zinc–copper couple. Subsequently this method came to be called the 'carbenoid' method.



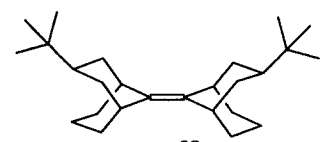
25

10 26

Bis(bicyclo[3.3.1]non-9-ylidene) **27** as well as its di-*tert*-butyl derivative **28** have been synthesised similarly in the form of a mixture of two stereoisomers.[39]

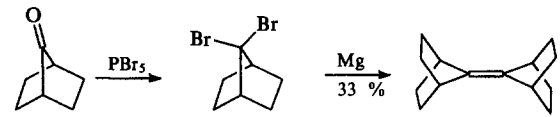


27 *anti*-**28**

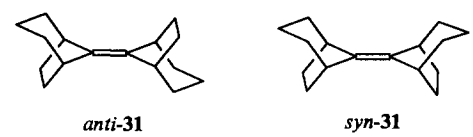


syn-**28**

The use of magnesium instead of the zinc–copper couple made it possible to increase the yield of the alkene **10** to 83%.[40] Bis(bicyclo[2.2.1]hept-7-ylidene) **30** [40] and bis(bicyclo[3.2.1]oct-8-ylidene) **31** have been synthesised in the same way in the form of a mixture of the *syn*- and *anti*-isomers.[41]

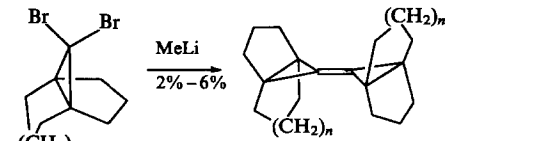


29 30

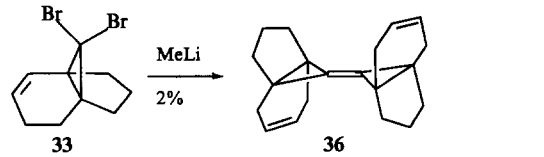


anti-**31** *syn*-**31**

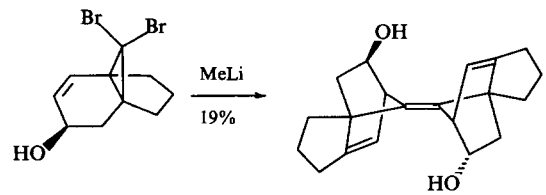
The SHA **35–37** are formed as side products (2%–19%) in the reactions of MeLi with *gem*-dibromo-substituted tricyclanes and tricyclenes with the propellane structure. The carbene dimers **35a, b** and **36** with fragments of the initial propellane structure have been obtained from the corresponding dibromo-derivatives **32a, b** and **33**, while the dimer **37** with a rearranged structure has been synthesised from the dibromo-derivative **34**. The structure of the dimer **37** has been confirmed by X-ray diffraction.[42,43]



32a, b **35a, b** *n* = 1 (**a**), 2 (**b**)



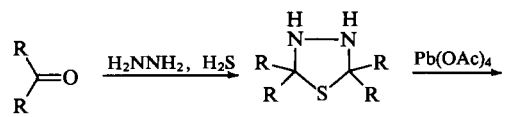
33 36



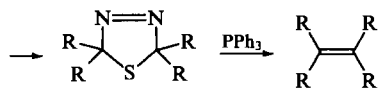
34 37

3. Double elimination (the thia- and selena-diazoline method) in the synthesis of sterically hindered alkenes

The thiadiazoline method has been used to obtain a series of asymmetric and strained symmetrical SHA. The method is based on the double elimination principle proposed by Barton and Willis[44] — the elimination of nitrogen and sulfur from synthons having the general formula **B**.[44]

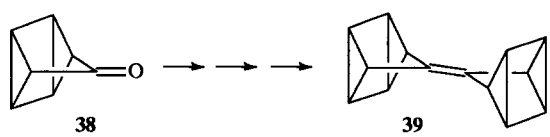


A



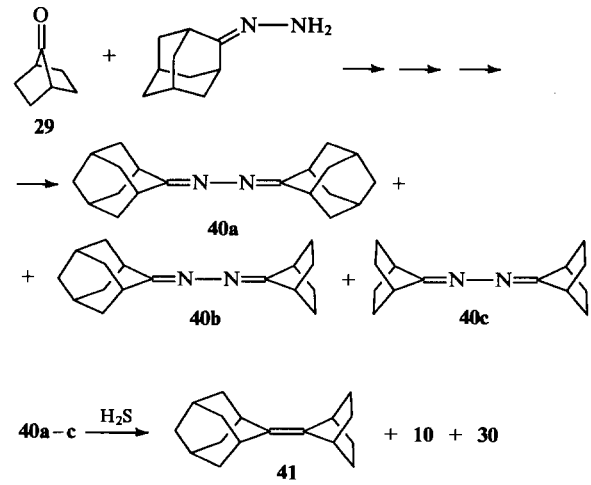
B

In the version proposed initially, the thiadiazolidine **A** was obtained from the corresponding ketone by treatment with hydrazine or H_2S (or as a result of the treatment of an azine by the latter). The oxidation of compound **A** by $Pb(OAc)_4$ led to Δ^3-1,3,4-thiadiazoline **B** and the latter was converted by treatment with PPh_3 into the alkene. Bisquadricyclene **39** has been synthesised[45] by this procedure from the ketone **38** as well as a series of symmetrical alkenes: the yield of the alkene **10**, obtained by the thiadiazoline method, is then the same as that of the products synthesised by the carbenoid method,[46] while the yield of the alkenes **27**, **28**, and **30** is significantly lower.[39]



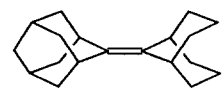
38 **39**

The use of the thiadiazoline method in order to obtain asymmetric alkenes has been demonstrated in relation to bicyclo[2.2.1]heptylideneadamantane.[41] The mixture of the azines **40a–c** formed on interaction of the ketone **29** with adamantanone hydrazone was treated with hydrogen sulfide and then oxidised and subjected to the elimination reaction. The alkene **41** was isolated by preparative gas–liquid chromatography (GLC) from its mixture with the alkenes **10** and **30**.



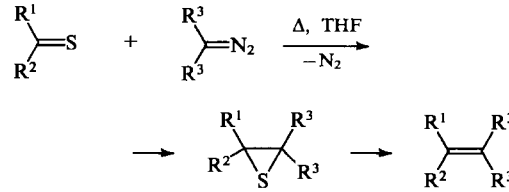
41

Bicyclo[3.3.1]nonylideneadamantane **42** has been obtained similarly.[39]

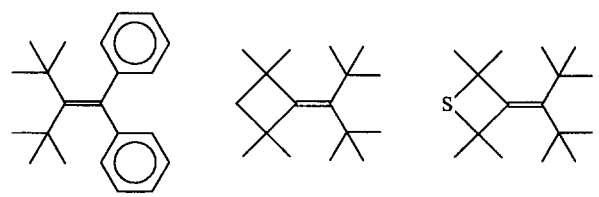


42

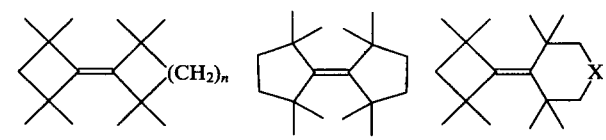
Certain more hindered asymmetric alkenes, which could not be obtained in accordance with the scheme indicated above, have been synthesised via a two-stage version in which a thione and a diazo-compound were used as synthons.[47]



The strained di-*tert*-butyldiphenylethene **43** has been obtained by this procedure from di-*tert*-butyl thioketone and diphenyldiazomethane (or from thiobenzophenone and di-*tert*-butyldiazomethane).[48] This route proved to be effective also for the synthesis of strained SHA such as 1,1,2,2-tetra(methylcyclopropyl)ethene **6**,[49] 2-(di-*tert*-butylmethylene)-1,1,3,3-tetramethylcyclobutane **44** and its thia-analogue **45**,[50] the keto-alkene **17**,[31] the octamethylbicycloalkylidenes **46–50** and their hetero-analogues **51–53**, the cycloalkylideneindans **54** and **55**, the triene **24**,[52,53] cyclobutylidene-Δ^1-pyrazoline **56**, and di(Δ^1-pyrazolylidene) **57**.[54,55]



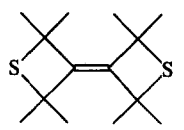
43 **44** **45**



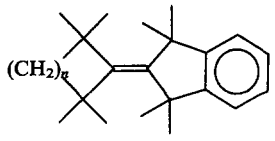
46–49 **50** **51, 52**

n = 1 (**46**), 2(**47**), 3(**48**), 4(**49**)

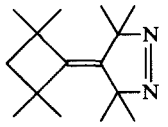
51: X = S,
52: X = O



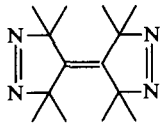
53



54, 55
54: n = 1,
55: n = 2

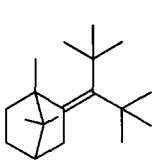


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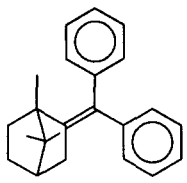


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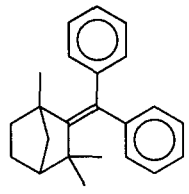
Di-*tert*-butylmethylenecamphane **58** has been obtained by means of this two-stage scheme from (±)-thiocamphor and di-*tert*-butyldiazomethane, while (±)-diphenylmethylenecamphane **59** has been obtained from the same thione and diphenyldiazomethane.[47] (±)-2-Diphenylmethylenefenchane **60**[48] and its individual (+)- and (−)-forms[47] as well as camphenylidenetetramethylcyclobutane **61**, camphenylideneadamantane **62**, adamantylidenecamphane **63**, camphenylidenecamphenylene **64**,[56] and the alkene **23**[52,53] have been synthesised similarly.



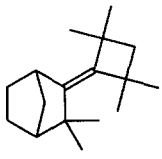
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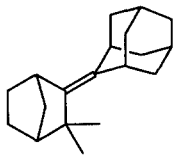
59



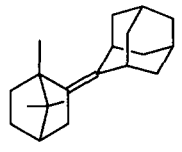
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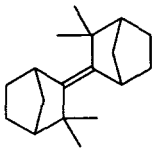
61



62



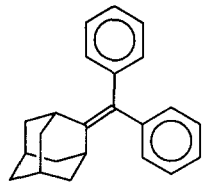
63



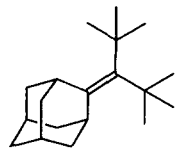
64

A series of methyleneadamantanes such as diphenylmethyleneadamantane **65**[57] and di(*tert*-butylmethylene)adamantane **66**,[58] adamantylidenefluorene **67**,[58] and adamantylidene-*N*-methylacridine **68** have been synthesised in accordance with the same scheme.[59]

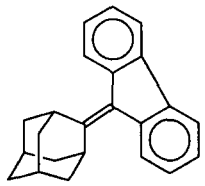
The preparation of the adamantane **66** in the thiadiazoline decomposition stage is complicated by the formation of adamantylideneadamantane **10**, the content of which in a mixture with the adamantane **66** reaches 53%.



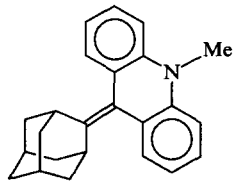
65



66

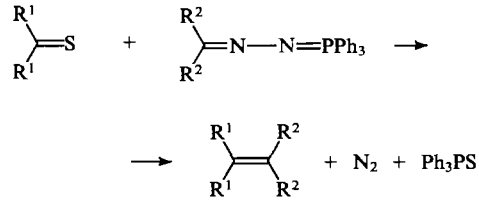


67

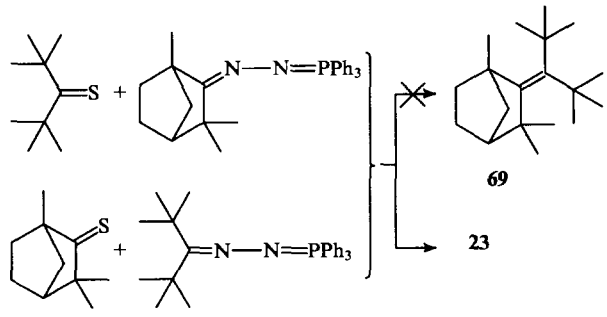


68

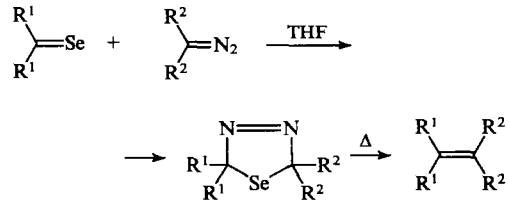
The possibility of using phosphorylidenehydrazones instead of diazo-compounds in the reactions considered has been demonstrated in the synthesis of the alkenes **58**–**60**. This version makes it possible to obtain the alkenes **58**–**60** in one stage but the yield of the product is then lower than in the two stage synthesis via diazo-compounds.[47]



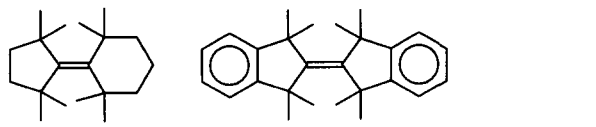
The attempts to obtain the strained di-*tert*-butylmethylenefenchane **69** in this way were unsuccessful and only the alkene **23** was isolated.[47]



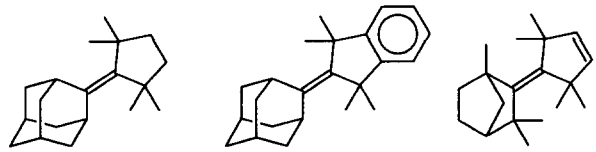
The selenadiazoline method proved to be effective for the synthesis of a series of SHA which could not be obtained by the thiadiazoline procedure. The corresponding thia- and selenadiazolines are formed under the same conditions. More severe conditions are necessary for the synthesis of the alkene **42** from the thiadiazoline than for its synthesis from the selena-analogue.[60]



The alkene **24**,[36] the octamethylbicycloalkylidenes **70** and **71**,[51] and the adamantane-containing alkenes **72** and **73**[39] have been synthesised by means of the selenadiazoline method. The preparation of 1,1'-bis(2,2,5,5-tetramethylcyclopent-3-enylidene)fenchane **74** by the procedure indicated is complicated by the formation of side products (60%) — the alkene **23** and the triene **24**.[36]

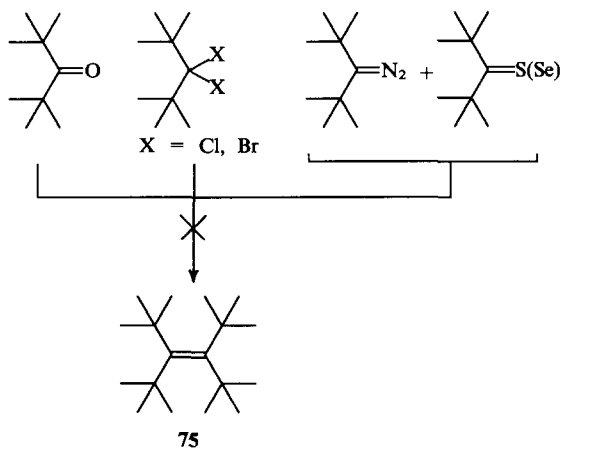


70 **71**



72 **73** **74**

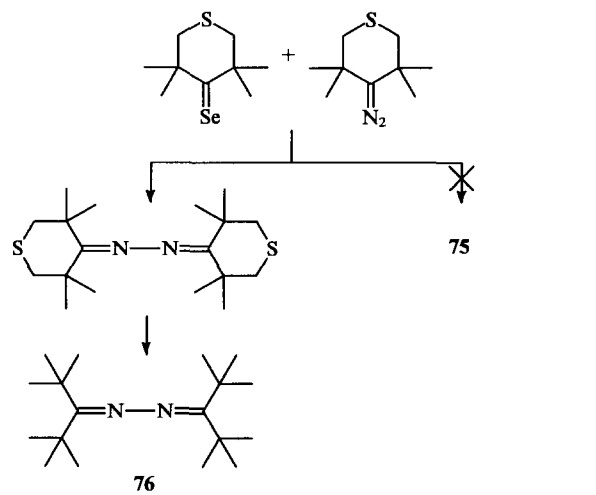
However, the attempt to obtain strained tetra-*tert*-butylethene **75** by the methods indicated above proved unsuccessful.[36,47,48,51,52] The alkene **75** could not be synthesised by the photolytic decomposition of di-*tert*-butyldiazomethane either.[61]



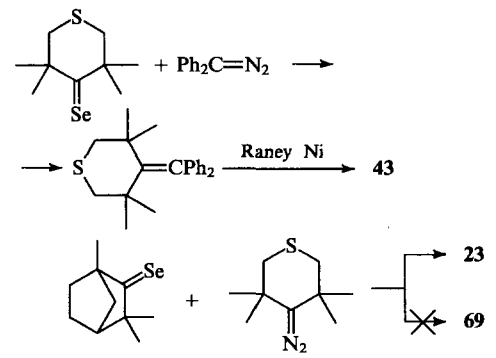
75

The unusual strategy combining the selenadiazoline method and the use of sulfur-containing synthons (synthons bound 'from the rear') also failed to afford the alkene **75**: instead of alkene **75**, the di-*tert*-butyl ketone azine **76** was isolated. This approach had been used successfully in a previous synthesis of the alkene **43**.

The sterically hindered alkene **69** could not be synthesised by this procedure either and the alkene **23** was obtained instead.[62]



76

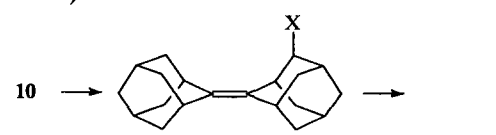


Thus the synthesis of compound **75** still remains an attractive and hitherto unattained aim.

4. Syntheses as a result of the modification of sterically hindered alkenes

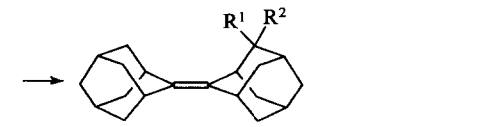
Certain alkenes, which can be obtained by the methods examined above, served in their turn as precursors in the synthesis of more strained SHA. Thus a series of 4-substituted adamantylideneadamantanes have been obtained from adamantylideneadamantane **10** in accordance with schemes involving the halogenation of the alkene **10** with formation of 4*e*-haloketenes **77** and **78**[63,64–67] and further synthetic transformations in the side chains. The ketoalkene **79**[63] and the maleimido-derivatives **80**, **81a–c**, and **82** have been obtained in this way (see Scheme 1).[68]

Scheme 1



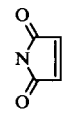
77–78

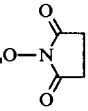
X = Cl (**77**), Br (**78**)



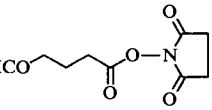
79–82

79: $R^1 + R^2 = O$;

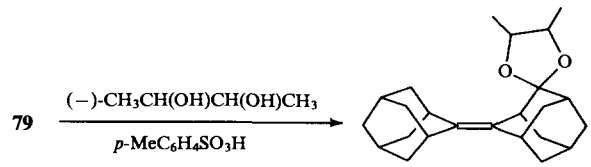
80: R^1 =  , R^2 = H;

81a–c: $R^1 = OCO(CH_2)_nO-$  , R^2 = H;

n = 2 (**a**), 3 (**b**), 4 (**c**)

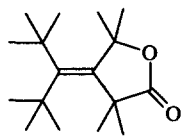
82: R^1 = NHCO  , R^2 = H.

A mixture of the diastereoisomeric ketals (+)-**83** and (−)-**83** has been synthesised from the ketalkene **79** and the optically active pure (−)-butane-2,3-diol. The ketal (−)-**83** was isolated from this mixture with 95% purity.[69]

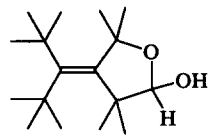


(+)-**83**, (−)-**83**

Highly strained di-*tert*-butylalkenes with lactone (compound **84**) and lactol (compound **85**) fragments have been obtained from the ketoalkene **17** via ring expansion reactions.[31]



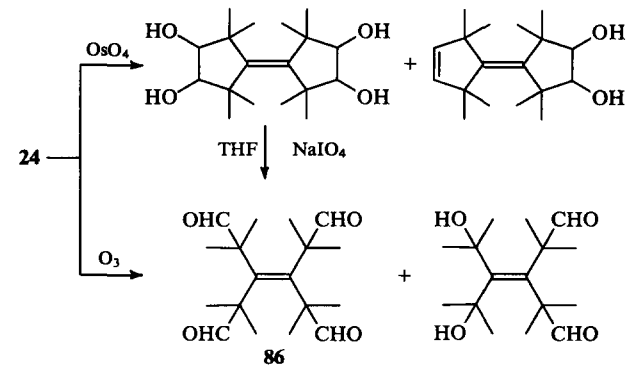
84



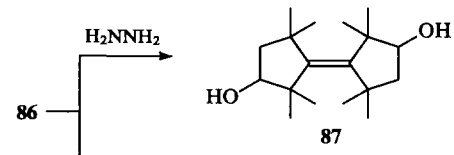
85

In the search for approaches to the hypothetical alkene **75**, the triene **24** has been used as the synthon. The triene was converted into the tetraaldehyde **86** by ozonolysis or hydroxylation with subsequent oxidative ring opening. The attempts to convert the tetraaldehyde **86** into the alkene **75** were unsuccessful and only the dilactol **87** and the diol **88** were obtained.[52,53]

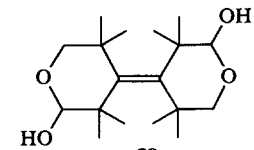
A series of SHA without quadricyclane fragments have been obtained from bisquadricyclylidene **39**. The transformation of one or both quadricyclane fragments into methylenenorbornene fragments was achieved via the diene synthesis reaction employing dienophiles such as dimethyl ethynedicarboxylate [acetylenedicarboxylate (DEAC)], dicyanoethyne, maleic anhydride, vinylidene carbonate, and dimethyl azodicarboxylate (see Scheme 2). The 1:1 adducts **89–92** and the 2:1 adducts **93–98** obtained constitute two new structural types of SHA. In addition, SHA of a third structural type (compound **99**) can be obtained from the 1 : 1 adducts as a result of the isomerisation of the quadricyclane fragment to the norbornadiene fragment.[70]



86

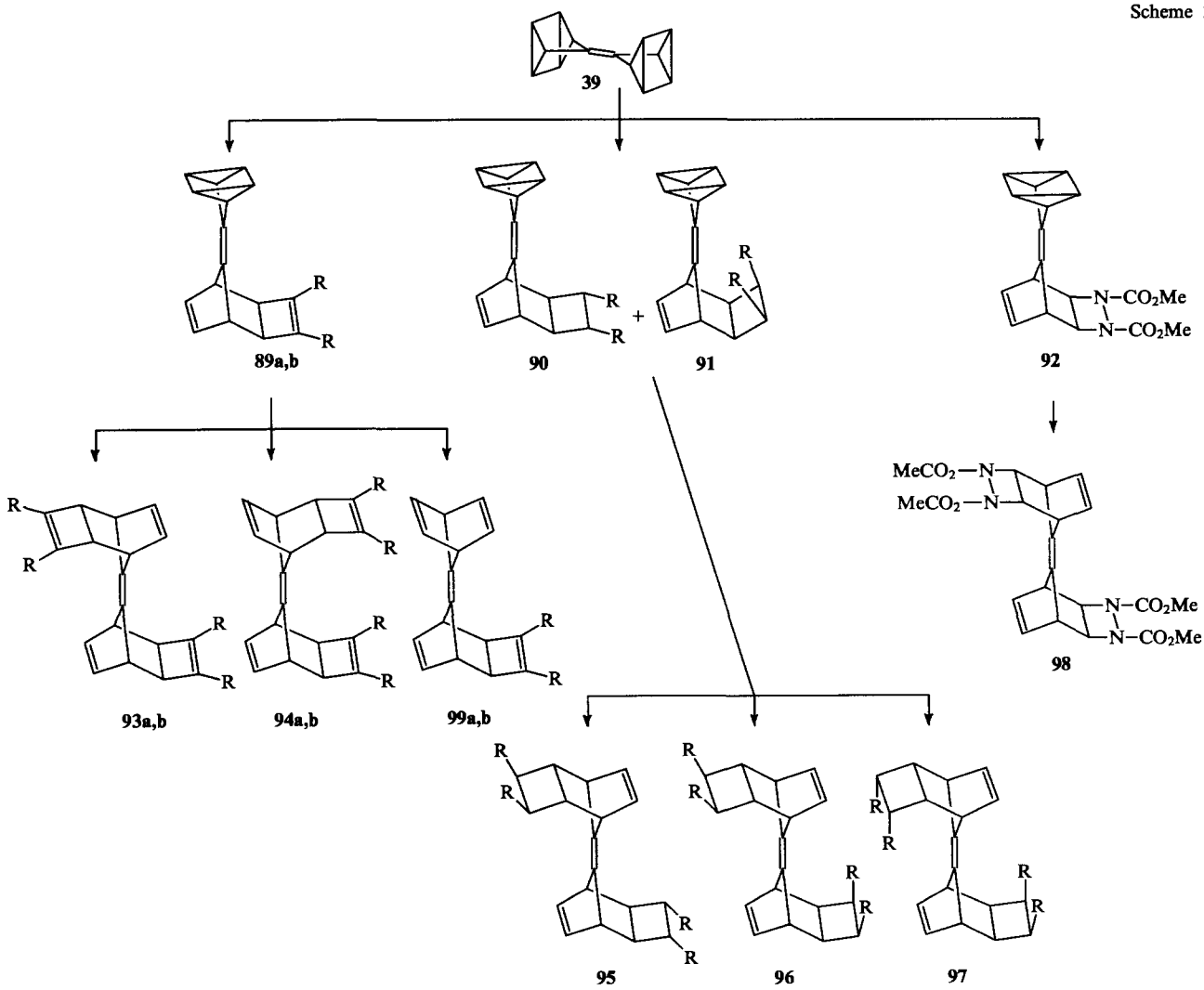


87



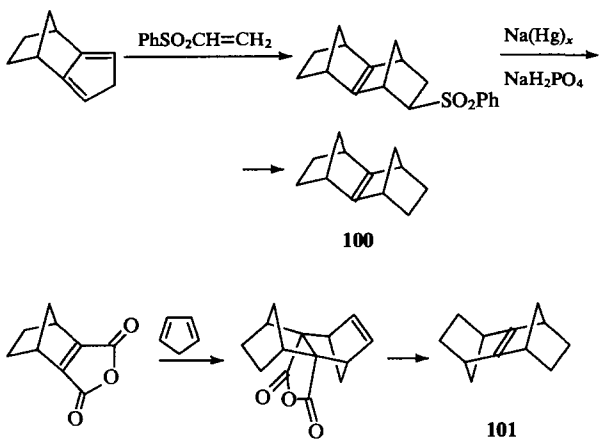
88

Scheme 2



5. Sterically hindered alkenes obtained by diene synthesis with participation of 1,3-dienes and fulvenes

The syntheses of SHA based on the diene synthesis reactions of cyclo-1,3-dienes and skeletal fulvenes with various dienophiles are considered in this subsection. *syn*-Sesquinorbornene **100** and *anti*-sesquinorbornene **101** have been obtained in this way. The scheme for the synthesis of the norbornene **100** includes the stereospecific cycloaddition of phenyl vinyl sulfone to isobicyclopentadiene and the subsequent reductive desulfonation of the adduct.[71,72] The alkene **101** was synthesised by the cycloaddition of cyclopentadiene to the anhydride of norbornenedicarboxylic acid and the subsequent hydrogenation and decarboxylation of the adduct.[73]



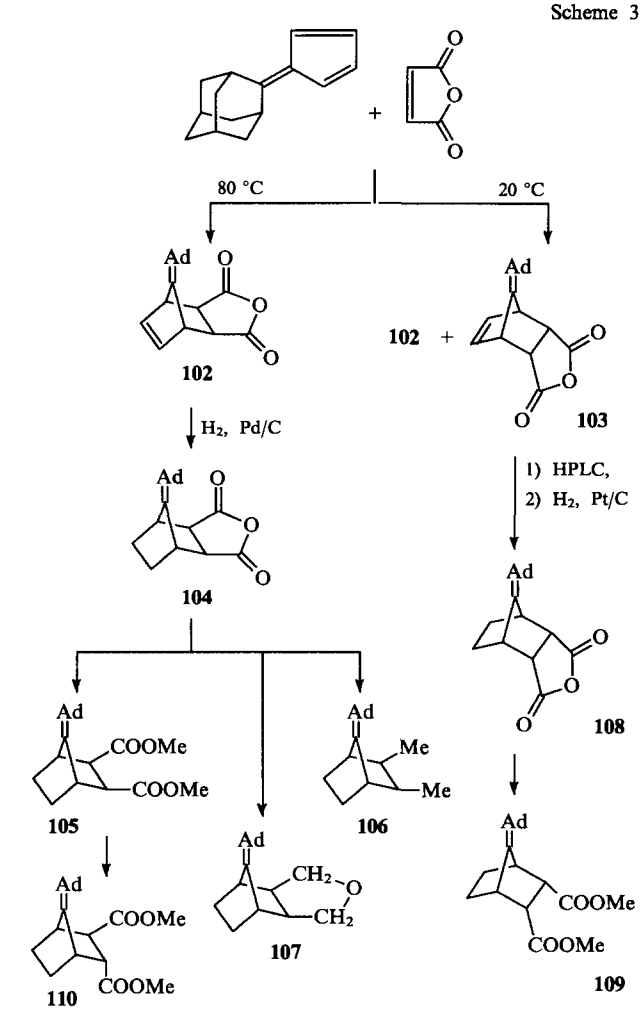
The second group of SHA which can be obtained by diene synthesis comprises asymmetric alkenes with functional-group substituents and an exocyclic double bond incorporated in the polycyclic and skeletal fragments. These compounds are obtained from skeletal fulvenes. When maleic anhydride is used as the dienophile, the monocyclic fragment in the above fulvenes is built up to the norbornene fragment and when the dienophile is DEAC or hexafluorodimethylethyne, it is built up to the norbornadiene fragment. Further synthetic transformations of the adducts (hydrogenation, photocyclisation) make it possible to achieve a transition to SHA with norbornane and quadricyclane fragments respectively.

A series of isomeric 2,3-disubstituted 7-adamantylidenenorbornanes have been obtained in accordance with the scheme involving the diene synthesis reaction of cyclopentadienylideneadamantane with maleic anhydride (Scheme 3). The *exo, exo*-adduct **102** is formed at 80 °C, while a mixture of the *exo, exo*- and *endo, endo*-isomers **102** and **103** in proportions of 1 : 1 is produced at 20 °C. Subsequently, the *endo, endo*-isomer is isolated from the mixture. The alkenes **104**–**107** can be obtained from the *exo, exo*-adducts as a result of appropriate synthetic transformations, while the alkenes **108** and **109** can be formed from the *endo, endo*-adducts. The isomerisation of the *exo, exo*-diester **105** leads to the formation of the *exo, endo*-diester **110**.[74]

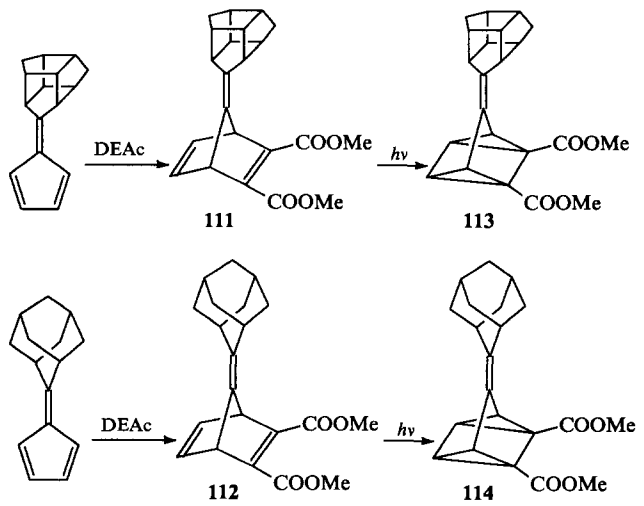
The biskeletal trienes **111** and **112** have been obtained by the diene synthesis reaction of DEAC with the corresponding skeletal fulvenes. The subsequent photocyclisation of the trienes **111** and **112** leads to the SHA **113** and **114** with a quadricyclane fragment.[75]

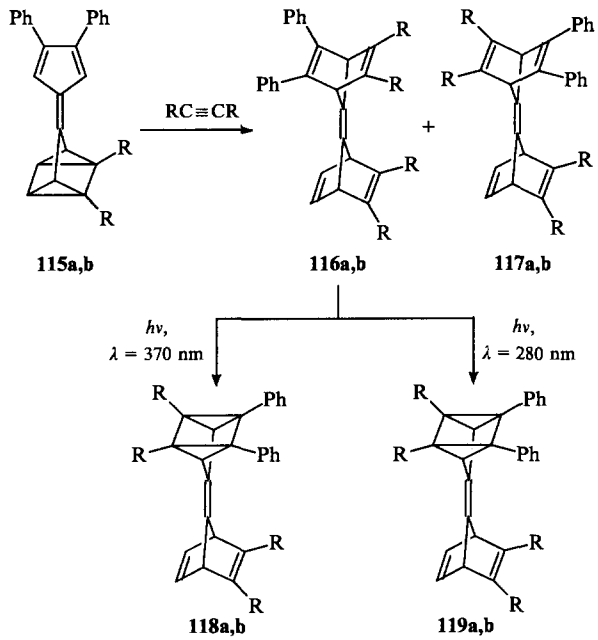
The reactions of tetrasubstituted cyclopentadienylidenequadricyclanes **115a, b** with DEAC or hexafluorodimethylethyne are accompanied by the isomerisation of the quadricyclane fragment and lead to mixtures of the corresponding isomeric SHA (**116a, b** + **117a, b**) with the bisnorbornadiene structure. The subsequent photocyclisation in one or both norbornadiene fragments leads to polysubstituted derivatives of quadricyclylidenenorbornadiene (**118a, b**) and bisquadricyclylidene (**119a, b**) respectively.[46] We have already spoken above about the involvement of similar adducts in diene synthesis with formation of new SHA.

Scheme 3



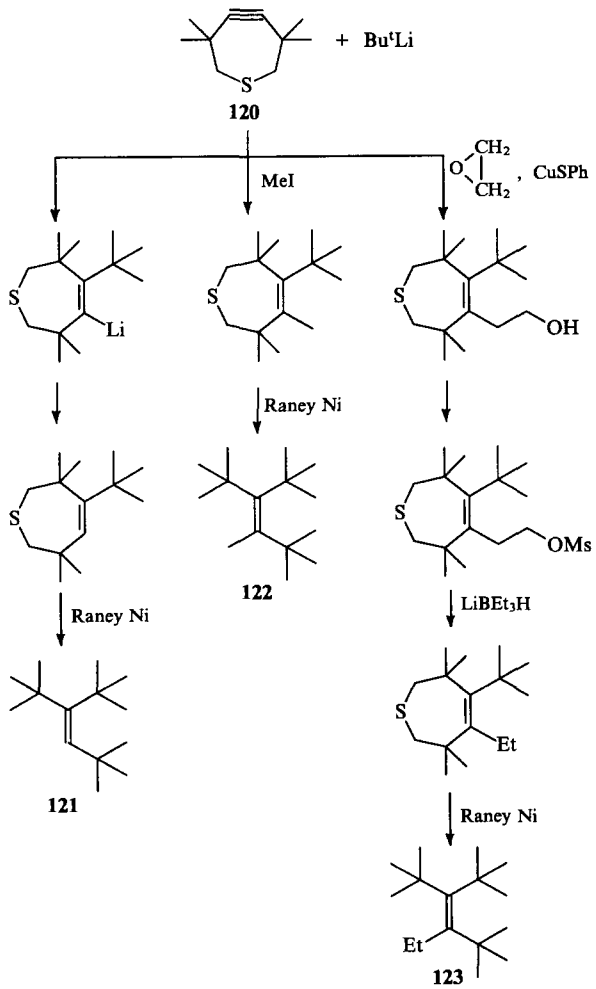
Here and henceforth the designation Ad has been retained for adamantylidene



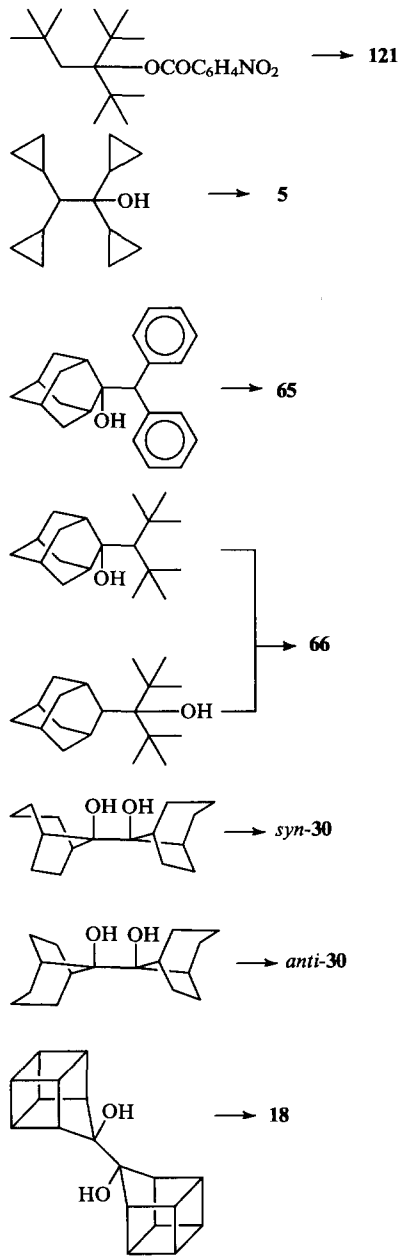


6. Other syntheses

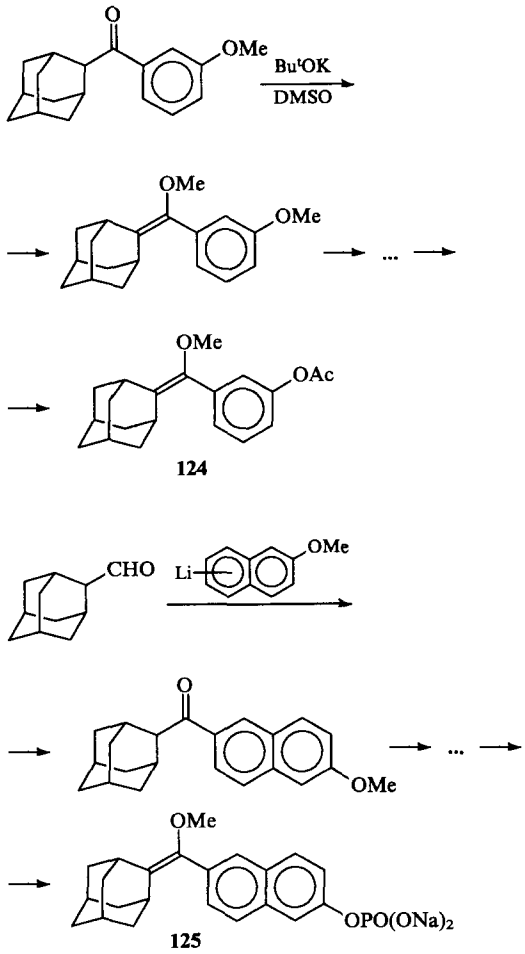
Other synthetic approaches, different from those examined above, have been proposed for certain types of SHA or their individual representatives. Thus tri-*tert*-butylethene **121** and its homologues **122** and **123** have been synthesised from the sulfur-containing synthon **120** in accordance with the schemes below:[52,53]



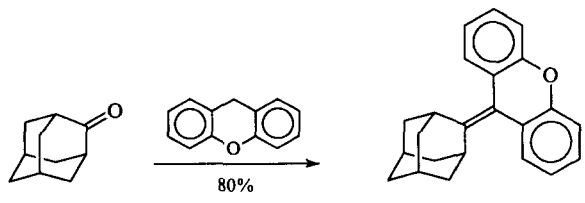
The syntheses of a series of SHA, including reactions involving the elimination of hydroxylated intermediates or their derivatives, have been described. Thus the alkene **121** has been obtained by the pyrolysis of the branched tetradecyl *p*-nitrobenzoate,[76,77] the alkenes **5**, **65**, and **66** have been synthesised by the dehydration of the corresponding carbinols,[78,79] and the *syn*- and *anti*-alkenes **30** and the biskeletal alkene **18** have been prepared by the dehydroxylation of diols.[32,41]



The synthesis of methoxyarylmethylideneadamantanes (enol ethers), based on the *O*-alkylation reaction of adamantyl allyl ketone, is presented below in relation to 2-[methoxy-(3′-acetoxyphenyl)methylidene]adamantane **124**[80] and the disodium salt of 2-[methoxy-(6′-phosphoryloxy)-2-naphthylmethylidene]adamantane **125**.[81]

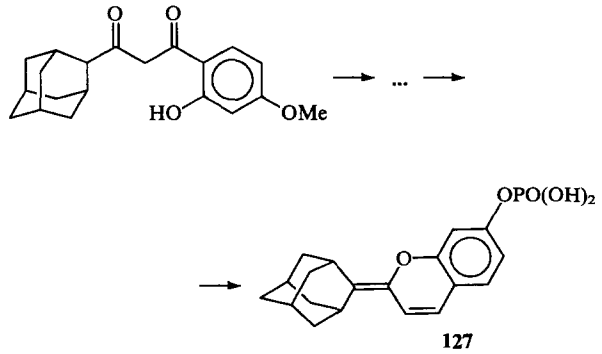


9-Xanthylideneadamantane **126** has been obtained in one stage from adamantanone and xanthene by the Peterson reaction involving conversion into an alkene.[82]



126

The scheme for the synthesis of adamantylidenechromene phosphate **127** includes intramolecular cyclisation in the corresponding diketone as the key stage.[83]



127

III. Geometrical and thermodynamic parameters of sterically hindered alkenes

The presence in SHA of bulky substituents at the double bond or the incorporation of the latter in a rigid polycyclic system lead to appreciable intramolecular repulsive interactions and hence to a significant steric strain. The study of the influence of this factor on the structural parameters and thermodynamic characteristics of SHA is of considerable theoretical interest.

X-Ray diffraction data for strained SHA are presented in Table 2 (see next page). These compounds have a distorted (compared with the usual alkenes) molecular geometry primarily in the geometry of the double bond, the bond itself being extended up to 1.358 Å (in ethene, the bond length is 1.313 Å). Furthermore, the C–C bonds adjoining the double bond are lengthened and the angles are distorted. In the most strained SHA the double bond is twisted and the largest values of the torsional angle (24.0° – 37.5°) are characteristic of alkenes with *tert*-butyl substituents and of compound **86** — a structural analogue of the hypothetical tetra-*tert*-butylethene (for the latter, this value can be 44° according to calculated data). According to the same data, the structural analogues of the alkene **75** — the polysubstituted cycloalkylidenecycloalkanes **46** – **57** — are significantly less strained (Table 3, see p. 14). Evidently, the degree of structural deformations in this series depends on the structure of the cyclic fragments in which the double bond has been included.

There are considerable synthetic difficulties which must be overcome on the way to individual representatives of SHA. The failure of the attempts to synthesise the alkane **75** aroused considerable interest in the thermodynamic parameters of SHA. Calculations have been made of the strain energies and enthalpies of formation of a series of polyalkyl-substituted ethenes, adamantanes, and adamantylideneadamantanes (Table 4, see page 15). As can be seen, in the series of skeletal alkenes it is possible to trace clearly an increase in the energy of the double bond due to the increase in the degree of substitution in the admantane ring.

IV. Reactions of sterically hindered alkenes

The structural characteristics of SHA are responsible for the significant differences in the chemical behaviour of these compounds compared with the usual alkenes. Thus the successful hydrogenation of the double bond in SHA has been described only in relation to the alkene **121**.[95] Many alkenes of this type are inert to electrophiles; skeletal SHA are an exception, but their reactions lead as a rule to products other than those of the analogous reactions of the usual alkenes. Thus SHA with a highly shielded double bond are inert to oxidising agents; the ozonisation of skeletal SHA leads to epoxides instead of ozonides.

1. Reactions of skeletal sterically hindered alkenes with electrophiles

In most of the studies of the reactions of SHA with electrophiles, the synthetically available adamantylideneadamantane **10** was used as the model compound. Only individual examples of the involvement of other skeletal SHA in the reaction under discussion have been described.

Table 2. Torsional angles and bond lengths in sterically hindered alkenes (X-ray diffraction data).

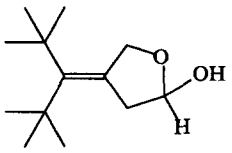
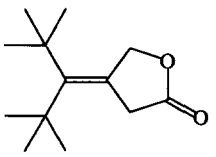
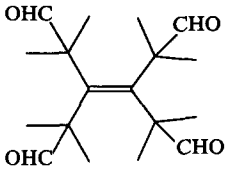
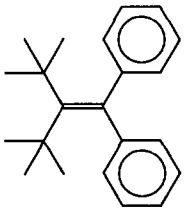
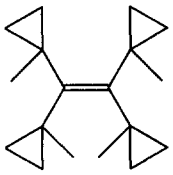
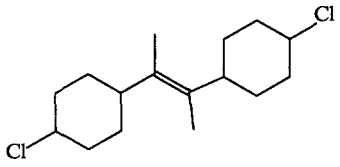
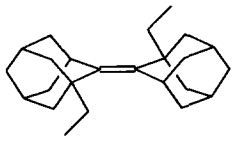
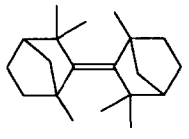
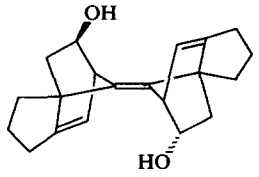
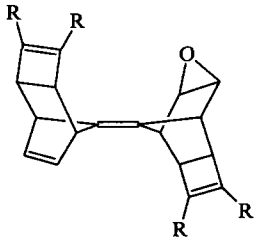
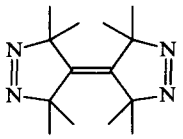
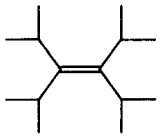
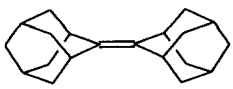
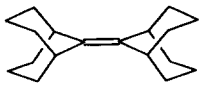
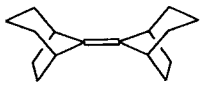
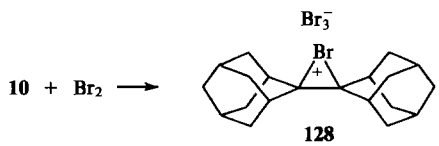
Compound	C=C torsional angle/deg	C=C bond length/A	Ref.
	37.5	1.367	31
	33.8	1.357	31
	28.6	1.357	53, 84
	24.0	1.357	85
	19.7	1.353	86
	16.0	1.353	87
	12.3	1.358	27
 **23**	11.8	1.349	88
	8.3	1.302	42

Table 2 (continued)

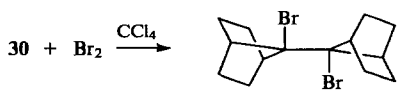
Compound	C=C torsional angle/deg	C=C bond length/A	Ref.
	5.4	1.314	70
	0.0	1.356	54
	0.0	1.347	89
	0.0	1.336	90
	0.0	1.324	91
	0.0	1.307	43

The reaction of the alkene **10** with bromine leads to the formation of an unusual adduct — the stable bromonium salt **128**.[96] The structure of the latter has been confirmed by X-ray diffraction data.[97] The structure found became a true scientific sensation because it had been postulated for many years that the reactions of the usual alkenes with bromine proceed precisely via intermediates of this kind.[98,99] The complex behaviour of the **10** + Br_2 system in solution has been investigated.[100]



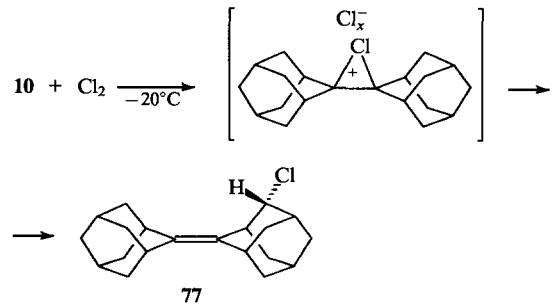
128

A bromonium salt — the adduct $C_{22}H_{33}Br_4$ insoluble in ether and hexane[26] — was also obtained in the reaction of *trans*-1,1′-dimethyladamantylideneadamantane **11** with bromine. In contrast to the alkenes **10** and **11**, the alkene **30** reacts with bromine to form the usual 1,2-adduct — the dibromo-derivative **129**.[40]



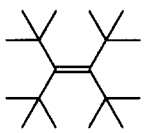
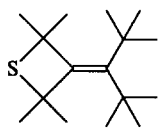
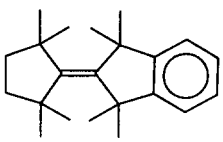
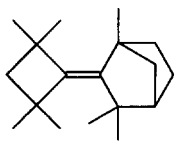
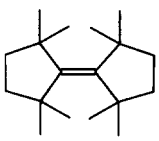
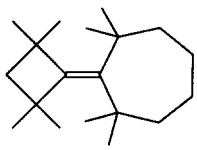
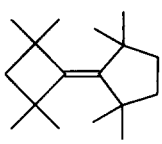
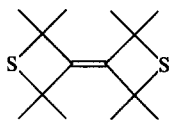
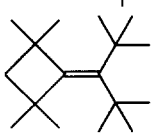
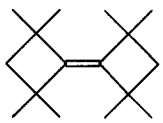
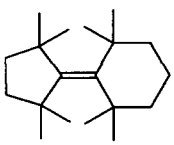
129

A substitution product — the chloroalkene **77** — has been obtained in a quantitative yield in the interaction of the alkene **10** with chlorine. In the initial stage of the chlorination reaction, the precipitation of the chloronium salt was observed visually. It was not possible to isolate it from the reaction mixture in view of its instability.[63]

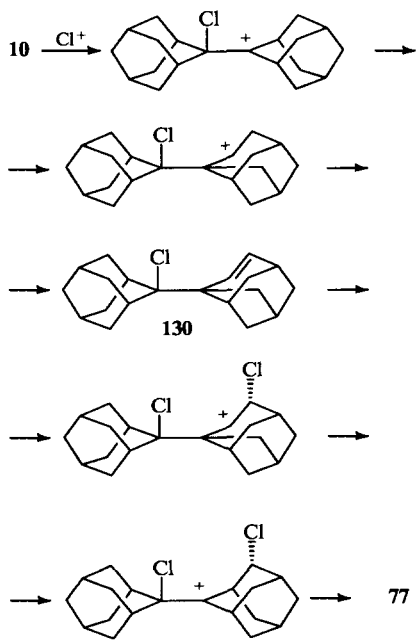


77

Table 3. Torsional angles and bond lengths in sterically hindered alkenes (calculated data[92]).

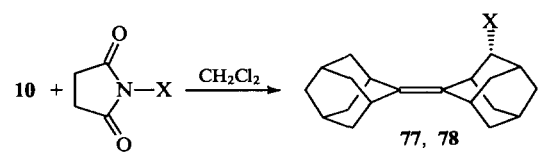
Compound	C=C torsional angle/deg	C=C bond length/A	Compound	C=C torsional angle/deg	C=C bond length/A
	44.0	1.379		4.2	1.373
	12.1	1.369		3.5	1.347
	5.5	1.371		1.0	1.370
	5.1	1.351		0.1	1.344
	5.0	1.366		0.05	1.330
	4.9	1.379			

A mechanism, the key stage of which is the formation of the protoadamantene-like intermediate **130**, has been proposed for this reaction.

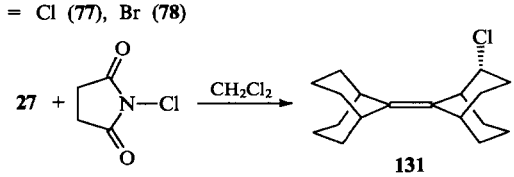


The formation of an iodonium salt in the reaction of the alkene **10** with the ICN–SbF_5 (1:1) system in SO_2 has been detected spectroscopically.[101]

The radical-chain type of halogenation of the alkenes **10** and **27** has been described. The reaction of the alkene **10** with *N*-chlorosuccinimide leads quantitatively to the halo-derivatives **77** and **78**; this reaction constitutes the simplest and preparatively the most convenient method of synthesis of the chloroalkene **77**. Similar haloalkenes are formed on chlorination with *tert*-butyl hypochlorite or the NaOCl–MeCOOH system. The reaction of the alkene **27** with *N*-chlorosuccinimide leads to the chloroalkene **131**.[64–67]

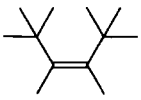
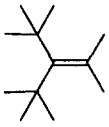
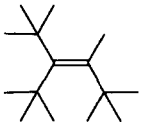
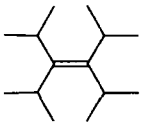
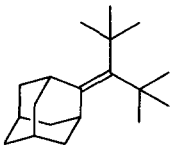
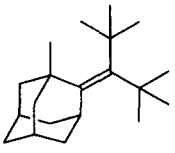
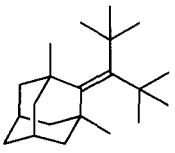
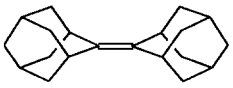
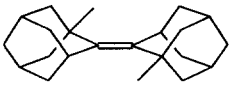
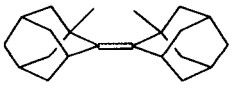
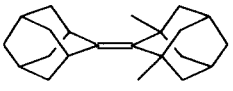
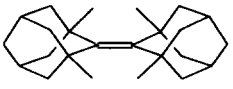


X = Cl (**77**), Br (**78**)

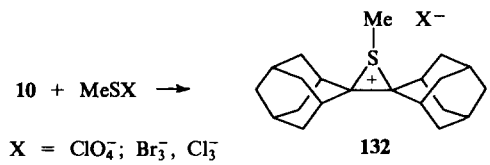


The reactions considered take place as selective homoallyl halogenation, whereas the usual alkenes afford the products of allyl halogenation on treatment with the same reagents.

Table 4. Thermodynamic parameters of sterically hindered alkenes (calculated data).

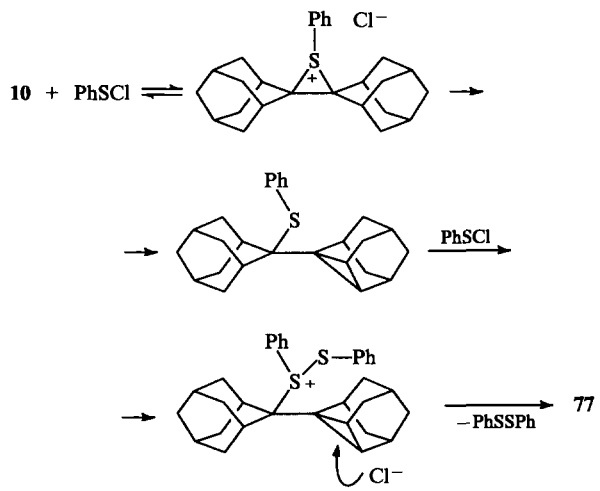
Compound	Standard enthalpy of formation/kcal mol^{-1}	Strain energy/kcal mol^{-1}	Ref.
	—	11.1	93, 94
	—	12.0	93, 94
	—	32	93, 94
	—	18	93, 94
	−28.92	46.14	58
	−17.73	66.20	58
	−6.16	86.64	58
	−30.36	13.54	26, 37, 58
	−26.10 (26.49)	35.54	27
	−18.20	43.44	26, 27
	−24.34	37.30	26, 27
	−61.07	75.31	26, 27

The reactions of adamantylideneadamantane **10** with electrophiles containing both a halogen and sulfur or both a halogen and selenium take place in an unusual manner. Thus the reactions of the above alkene with methanesulfenyl halides lead to the formation of the stable episulfonium salt **132**.[102] The formation of such compounds as intermediates was postulated previously in reactions involving the addition of alkanesulfenyl halides to the usual alkenes.



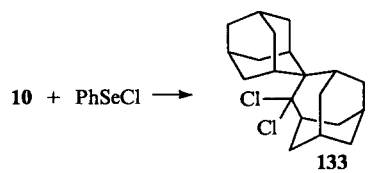
132

The reaction of the alkene **10** with 2 equiv. of PhSCl leads to the chloroalkene **77**.[103]



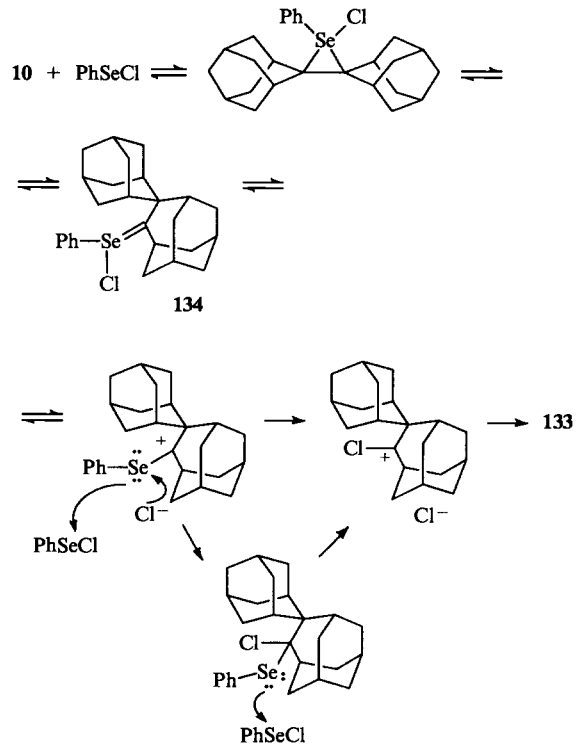
As in the interaction with chlorine, a substitution product is formed in this reaction instead of the 1,2-adduct.

The reaction of the alkene **10** with PhSeCl leads to an unexpected product — 3,3′-dichlorospiro(adamantane-2,2-homoadamantane) **133**.[104]



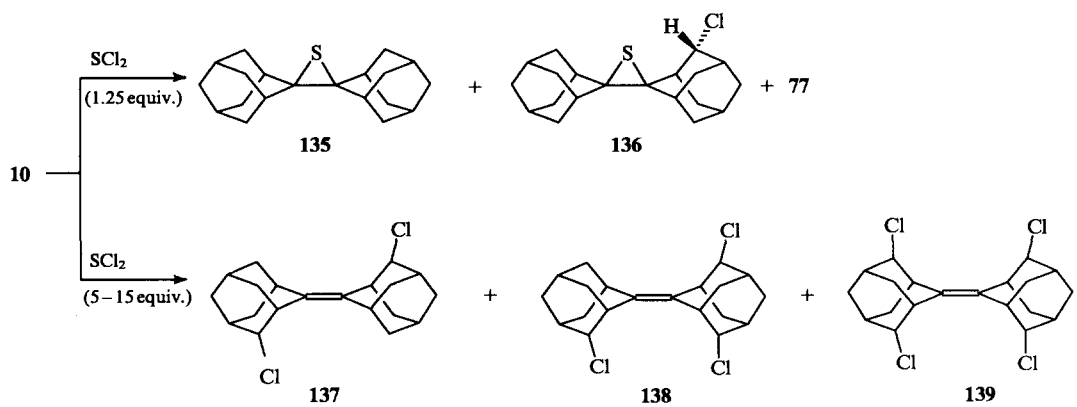
133

The proposed mechanism for this reaction includes a skeletal rearrangement in the intermediate **134**, the interaction of the rearranged derivative with a second molecule of the reagent, and cleavage of the salt formed.

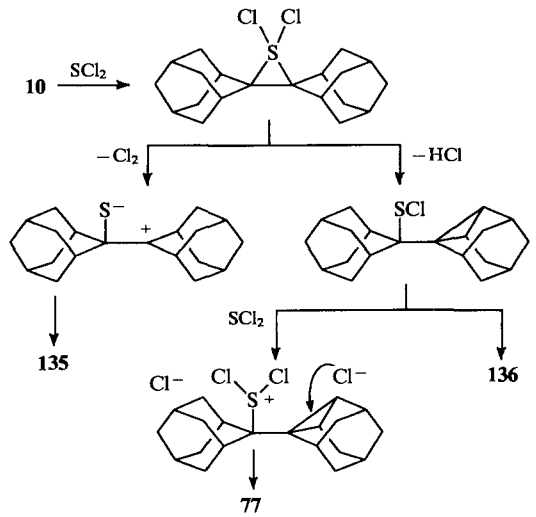


The reaction of the alkene **10** with SCl_2 leads to the epithio-compounds **135** and **136** and the (poly)chloroalkenes **77** and **137**–**139** (Scheme 4). Compounds **77**, **135**, and **136** are formed for an alkene : reagent ratio of 1 : 1, when the thiirane **135** is obtained predominantly in $CHCl_3$, the chlorothiirane **136** in CH_2Cl_2, and the chloro-derivative **77** in hexane. The specific synthesis of (poly)chloroalkenes **137**–**139** has been achieved in CH_2Cl_2 in the presence of a fivefold, sevenfold, and 15-fold excess of the reagent respectively.[105–106] The reaction of the alkene **10** with S_2Cl_2, in which the same epithio-compounds and chloroalkenes are obtained, is distinguished by a lower selectivity relative to the epi-compounds and by the formation of less chlorinated products than the reaction with SCl_2 occurring under the same conditions.[107] The structure of the chlorothiirane **136** has been confirmed by X-ray diffraction data.

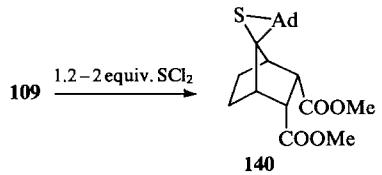
Scheme 4

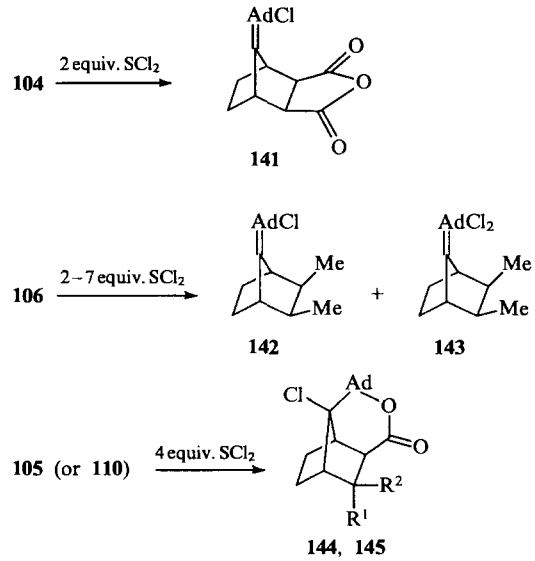


The diversity of the products formed in the reactions of the alkene **10** with SCl_2 and S_2Cl_2 may be explained by the existence of several versions of the stabilisation of the key intermediates — the primary sulfurane and sulfenyl chloride — and also by the successive chlorination of the unsaturated reaction products.

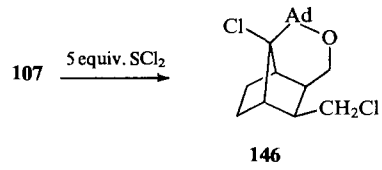


In the reactions of a series of disubstituted adamantylidenenorbornanes with SCl_2, the nature of the products depends significantly on the nature and the steric disposition of the substituents. Thus the reaction of SCl_2 with the *endo,endo*-diester **109** in $CHCl_3$ leads only to the thiirane **140**, while the reaction in CH_2Cl_2 leads to a complex mixture of products containing 17% of the latter. The chloroalkenes **141** and **142** have been obtained by the reactions of the *exo, exo*-adducts **104** and **106** respectively with 1.2–2 equiv. of SCl_2 in solution in CH_2Cl_2, while a mixture of five isomeric dichloroalkenes **143a–e** has been synthesised by the reaction of the alkene **106** with 7 equiv. of SCl_2.[74] The reactions of the *exo, exo*-diester **105** and the *exo, endo*-diester **110** with four equivalents of SCl_2 are accompanied by lactonisation, as a result of which the chlorolactones **144** and **145** respectively have been isolated in high yields. The dichloroether **146** has been obtained from the cyclic ether **107** as the product of the cleavage of the tetrahydrofuran fragment in the latter and subsequent etherification.[74]

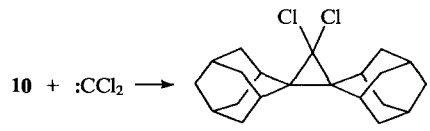




105, **144**: R^1 = H, R^2 = COOMe;
110, **145**: R^1 = COOMe, R^2 = H

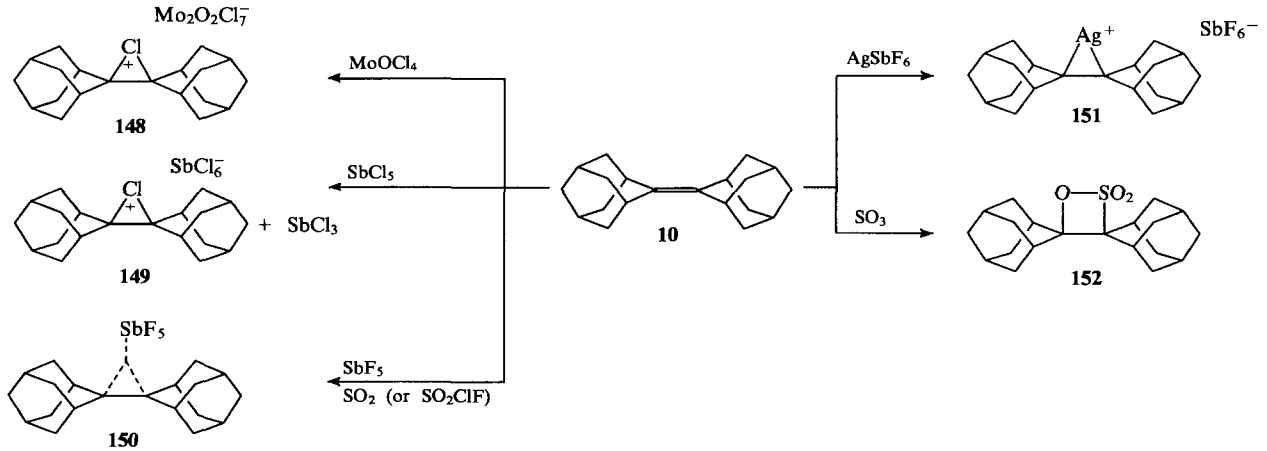


The normal cycloaddition product, the adduct **147**, is formed in the reaction of the alkene **10** with dichlorocarbene; this addition reaction takes place more slowly than with the usual alkenes, such as 2-methyladamantane (by a factor of 20) and 2-isopropylideneadamantane (by a factor of 200).[108]



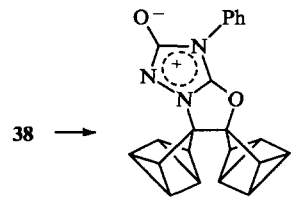
The reactions of the alkene **10** with $MoOCl_4$ and $SbCl_5$ in the presence of Lewis acids (Scheme 5) lead to the stable adamantylideneadamantanechloronium salts **148** and **149** respectively.[109]

Scheme 5



The adducts of the alkene **10** with SbF_5 and $AgSbF_6$—compounds **150** and **151** respectively[101]—as well as the β-sultone **152**[110] were detected in the reaction mixtures by ^1H and ^{13}C NMR.

The 1 : 1 adduct **153** has been obtained from the alkene **38** and *N*-phenyl-1,2,4-triazolinedione.[70]

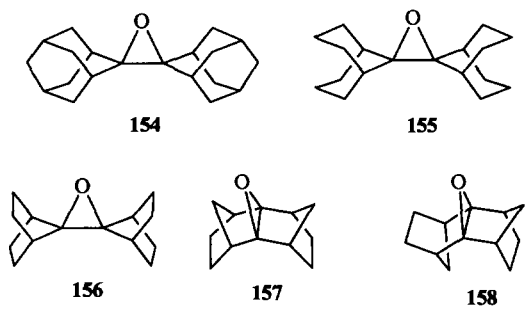


153

2. Oxidation reactions of sterically hindered alkenes

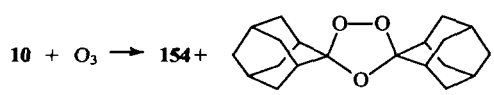
The behaviour of SHA in oxidation processes has been investigated on model reactions such as epoxidation, ozonisation, and 1,2-cycloaddition with participation of singlet or triplet oxygen.

The formation of epoxides from SHA on treatment with *m*-chloroperbenzoic acid has been described for the alkenes **9**,[24] **23**,[48] **42**,[48] and **50**.[90] The epoxides **154**,[111] **155**,[38] **156**,[40] **157**,[72] and **158**[73] have been obtained in the same way from the corresponding alkenes in satisfactory yields.



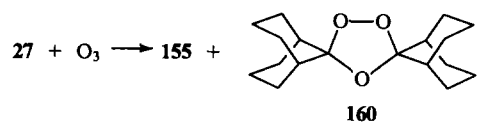
154 **155** **156** **157** **158**

The ozonisation of SHA in most cases does not lead to ozonides—the normal products of the usual alkenes with ozone. The alkene **121** is an exception. Its ozonisation proceeds normally and affords (after the appropriate treatment of the reaction products) di-*tert*-butyl ketone and pivalic aldehyde.[95] The reactions of other SHA with ozone proceed differently. Thus the reaction of the alkene **10** with ozone in nonpolar solvents leads to a mixture of the epoxide **154** and the ozonide **159** in proportions which depend on the nature of the solvent: the epoxide is formed exclusively in polar solvents. The reaction of O_3 with the alkene **27** proceeds similarly, leading to a mixture of the epoxide **155** and the ozonide **160** or only the former.[38,72] The thermal decomposition of the ozonide **159** results in the formation of a 1 : 1 mixture of adamantanone and a lactone.[38]



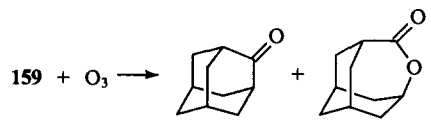
159

Solvent	Yield (%)	
	154	**159**
C_5H_{12}	60	33
C_5H_{12}–MeCOOEt	66	28
MeCOOEt	92	0

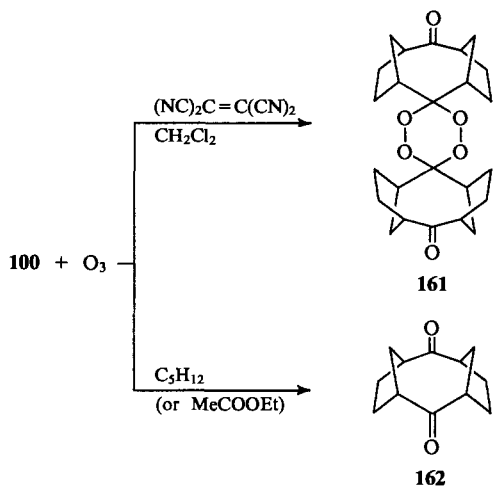


160

Solvent	Yield (%)	
	155	**160**
C_5H_{12}	77	18
MeCOOEt	100	0



Only the epoxide **156** has been obtained in the reaction of O_3 with the alkene **30**.[40] The ozonisation of the alkenes **23** and **100** is accompanied by the dissociation of the double bond; fenchone is formed from the first alkene,[48] while the peroxydiketone **161** or the diketone **162** is formed from the second (depending on the conditions).[72] The inertness of the alkenes **65** and **66** to O_3 has been noted.[112]



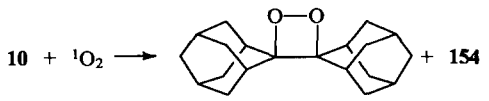
161 **162**

The oxidation of SHA of the 1,2-addition type leads to normal products—dioxetanes. The latter are more stable than the dioxetanes obtained from the usual alkenes. Thus the dioxetane **163**, synthesised from the alkene **10**, can be stored under the usual conditions. This feature of the dioxetanes obtained from SHA attracted considerable attention to them in connection with the problem of the strong chemiluminescence arising on thermal decomposition of compounds of this class.

Many SHA, especially adamantane-containing compounds, have been subjected to oxidation of the type of 1,2-addition. These alkenes have been involved in several types of reactions leading to dioxetanes: photosensitised oxidation by singlet oxygen and the radical-cation and electrochemical oxidation by oxygen. Mainly the synthetic possibilities and stereochemical characteristics of the above reactions are considered in the present review because the mechanisms of the latter and various aspects of the chemiluminescence of the dioxetanes on their decomposition have been described in detail in a monograph.[113] The synthesis and properties of various dioxetanes have been briefly considered in a review.[114]

Photochemical oxidation by singlet oxygen sensitised by dyes has been usually employed to obtain dioxetanes from SHA. The dioxetane **163** has been synthesised by precisely this method from the alkene **10**. Methylene Blue (MB) was used in this reaction as the sensitiser.[115] The structure of the above dioxetane was

confirmed by X-ray diffraction[116] (a method for the preparative synthesis of the dioxetane **163** has been described[117]).



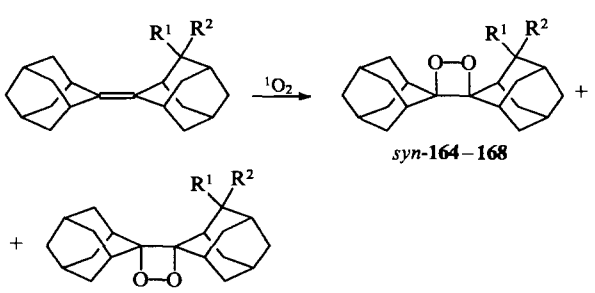
163

The above photochemical oxidation of the alkene **10** affords, together with the dioxetane **163**, also the epoxide **154**; the ratio of these products depends on the nature of the dye and the solvent (Table 5). Evidently, the dioxetane is formed selectively in the presence of MB or tetraphenylporphin (TPP).[118,119]

Table 5. Photochemical oxidation of adamantylideneadamantane **10** in acetone.[118,119]

Sensitiser	Yield of reaction products (%)	
	163	**154**
m-Tetraphenylporphin	95	traces
Methylene Blue	95	traces
Rhodamine B	95	5
Eosin	95	5
Fluorescein	90	10
Erythrosin	30	70
Rose Bengal	traces	95

The photochemical oxidation of 4-substituted adamantylideneadamantanes by singlet oxygen under the conditions of the selective synthesis of dioxetanes proceeds nonstereospecifically, affording a mixture of two isomeric dioxetanes. Thus a mixture of the *syn*- and *anti*-dioxetanes **164** in proportions of 3.1:1 has been obtained from the chloroalkene **77**.[120] Oxidation of the alkenes **80**–**82** with functional group substituents leads to the corresponding dioxetanes **165**–**167** in the form of mixtures of two isomers.[68] The analogous oxidation of the ketoalkene **79** gives rise to a 1:2 mixture of the *syn*- and *anti*-dioxetanes **168**,[121,122] while the optically active 1,2-dioxetane **169** has been obtained from the ketal (−)-**83** as the sole isomer.[69]



syn-**164**–**168**

anti-**164**–**168**

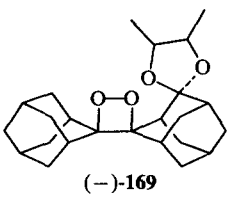
164: R^1 = Cl, R^2 = H;

165: R^1 = $NHCOCH_2CH_2COO-N$ (succinimide), R^2 = H;

166: R^1 = $O(CH_2)_nCOO-N$ (succinimide), R^2 = H;

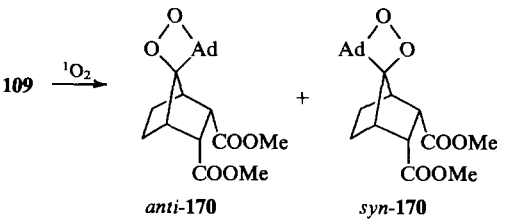
167: R^1 = $-N$ (succinimide), R^2 = H;

168: $R^1 + R^2$ = O

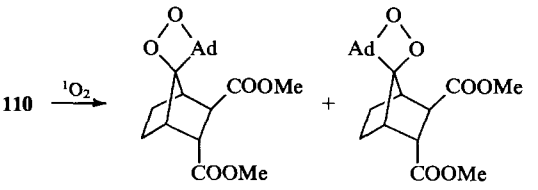


(−)-**169**

The photochemical oxidation of a series of isomeric 2,3-disubstituted 7-adamantylidenenorbornanes on treatment with $^1O_2$ was carried out in CH_2Cl_2 in the presence of MB. A 2:1 mixture of the dioxetanes *anti*-**170** and *syn*-**170** was obtained from the *endo,endo*-diester **109** in 90% yield, while the *exo,endo*-diester **110** afforded a 92% yield of 1.4:1 mixture of the dioxetanes *anti*-**171** and *syn*-**171**. The individual dioxetanes were isolated from the corresponding mixtures with the aid of high performance liquid chromatography (HPLC). The compounds of the *exo,exo*-series (**104**–**106**) are inert to singlet oxygen.[121–124]

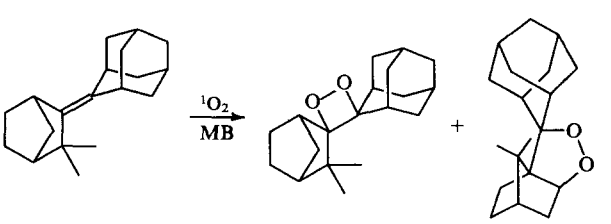


109 → *anti*-**170** + *syn*-**170**



110 → *anti*-**171** + *syn*-**171**

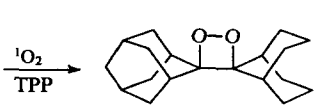
The photochemical oxidation of the alkene **62** in the presence of MB leads to the formation of the dioxetane **172** and the dioxolane **173** in proportions which depend on the nature of the solvent.[56,125]



172 **173**

Solvent	172 : 173 ratio
CH_2Cl_2	7 : 3
MeCN	3 : 7
Me_2CO	1 : 9

The photochemical oxidation of the alkene **42** in CH_2Cl_2 in the presence of TPP affords a high yield of the dioxetane **174**.[126]



174

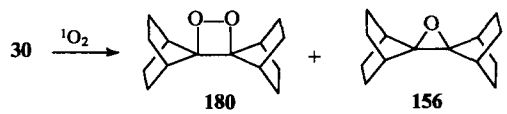
The adamantane series dioxetanes **175**–**179**, containing the phenyl (compounds **175a**–**d**), naphthyl (compounds **175e**–**k**),[81] fluorene (compound **176**),[127,128] methylacridine (compound

177),[129-131] and xanthene (compound **178**)[82] fragments as well as the methoxy-group have been synthesised similarly from the corresponding alkenes. The phosphate derivative of the dioxetane **178** (compound **179**)[132] as well as the dioxetanes **175b**, **c**, **g**–**j**[80,133,134] have been obtained in the presence of Rose Bengal (RB) bound to a polymer.

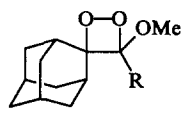
Table 6. Photosensitised oxidation of alkene **30** (see Ref. 40).

Sensitiser	Solvent	Yield of reaction products (%)	
		180	**156**
m-Tetraphenylporphin	CH_2Cl_2	60.3	39.7
	$t\text{-}C_4H_9COCH_3$	25.9	74.1
	1,4-dioxetane	24.8	75.2
	C_6H_6	18.2	81.8
	CH_3COCH_3	16.4	83.6
Methylene Blue	CH_3CN	54.0	46.0
	CH_2Cl_2	46.4	53.6
Rose Bengal	CH_3OH	44.4	55.6

The photochemical oxidation of the alkene **30** by singlet oxygen in various solvents and with the aid of different dyes leads in all cases to a mixture of the dioxetane **180** and the epoxide **156** [the content of the dioxetane **180** varies from 16% to 60% (Table 6)].[40] The dioxetane **181** has been obtained from the alkene **27** in the presence of TPP in CH_2Cl_2 (in the presence of MB, the yield of the dioxetane was 83%,[135] while according to other data[38] it was 51%).

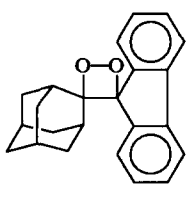


180 **156**

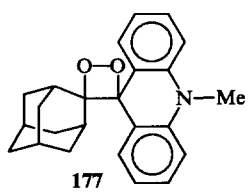


175a–l

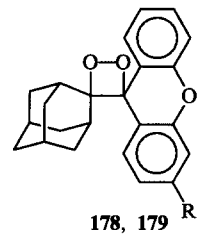
R = (**175a**), (**175b**), OAc; (**175c**), $OSi(Bu^t)Me_2$; (**175d**), $OPO(ONa)_2$; (**175e**), (**175f**), $OPO(ONa)_2$; (**175g**), (**175h**), OH; (**175i**), OAc; (**175j**), $OSi(Bu^t)Me_2$; (**175k**), $OPO(ONa)_2$; (**175l**).



176

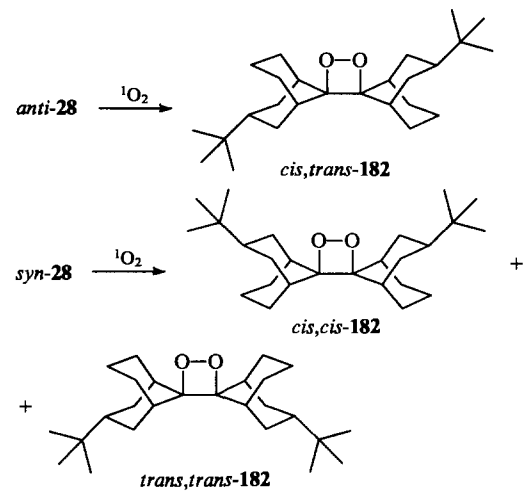


177



178, **179** R = H (**178**), $OPO_3^-H \cdot Py^+H$ (**179**)

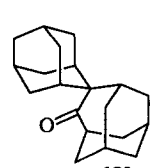
The oxidation of the *anti*-alkene **28** by singlet oxygen (with TPP as the sensitiser) afforded only the *cis,trans*-dioxetane **182**, whilst the oxidation of the alkene *syn*-**28** gave rise to a 2:1 mixture of the dioxetanes *trans,trans*-**182** and *cis,cis*-**182**.[39,126] The structure of the latter was established by X-ray diffraction.[51]



The alkenes inert to $^1O_2$ include the alkenes **23**, **64**, and **104**–**106**.[56] The attempts to obtain dioxetanes by the photochemical oxidation of the alkenes **100** and **101** were also unsuccessful. Only the epoxide **157** is formed from the alkene **100** in benzene in the presence of RB, while in acetonitrile in the presence of MB and in 1,2-dichloroethane in the presence of TPP the product is the diketone **162**.[77] Only the epoxide **158** has been obtained from the alkene **101** in benzene (with diacetyl as the sensitiser).[73]

The oxidation of SHA by oxygen under the conditions of a radical-cation chain process initiated by one-electron oxidants also leads to the formation of dioxetanes together with photochemical oxidation by singlet oxygen. Such oxidants are hexahaloantimonates of stable radical-cations: $(4\text{-}BrC_6H_4)_3N^{\cdot+}.SbCl_6^-$, $(2,4\text{-}Br_2C_6H_3)_3N^{\cdot+}.SbCl_6^-$, $(2,4\text{-}Br_2.C_6H_3)_3N^{\cdot+}.SbF_6^-$, and $NO^+PF_6^-$, $NO_2^+PF_6^-$, as well as sensitisers capable of generating radical-cations from the alkene on photoirradiation, such as, for example, 9,10-dicyanoanthracene (DCA) The radical-cations are also generated on electrochemical oxidation by oxygen.

The oxidation of the alkene **10** by oxygen in the presence of $(2,4\text{-}Br_2C_6H_3)_3N^{\cdot+}.SbCl_6^-$ results in the selective formation of the dioxetane **163**,[135] while in the presence of other oxidants the product is a mixture of the dioxetane **163** with the epoxide **154** and the spiroketone **183** in proportions which depend on the nature of the oxidant and the conditions (Table 7).[136]



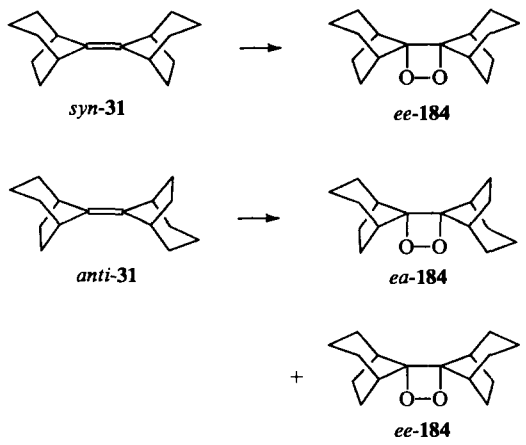
183

Table 7. Oxidation of adamantylideneadamantane **10** by oxygen in CH_2Cl_2 in the presence of oxidants.[136]

Oxidant	Content of oxidant (mol.%)	Time/min	Yield of reaction products (%)			
			163	**154**	**183**	**26**
MBPA.$SbCl_6$[a]	11.1	260	42	—	—	57
$NO^+PF_6^-$	103	2.5	6	86	—	—
$NO^+PF_6^-$	12.5	30	21	55	—	—
$NO_2^+PF_6^-$	3.5	180	40	7	—	40
$NO^+PF_6^-$	1.6	80	15	—	—	84
$NO_2^+PF_6^-$	95	2	—	—	73	—
$NO_2^+PF_6^-$	2.7	30	24	33	—	38

[a] MBPA = tris(*p*-bromophenyl)amine.

The oxidation of a series of enol ethers by the above procedure [in the presence of $(4\text{-}BrC_6H_4)_3N^{\cdot+}.SbCl_6^-$] leads to quantitative yields of the corresponding dioxetanes **175a** and **175g**.[137] A 25:1 mixture of the *syn*- and *anti*-dioxetanes **164** has been obtained similarly from the chloroalkene **77** in the presence of $(2,4\text{-}Br_2C_6H_3)_3N^{\cdot+}.SbF_6^-$.[118] A higher selectivity is attained in this reaction than in the photochemical oxidation of the above alkene by singlet oxygen. The oxidation of the isomers of the alkene **31** by oxygen in the presence of $(2,4\text{-}Br_2C_6H_3)_3N^{\cdot+}.SbCl_6^-$ resulted in the formation of only the *ee*-dioxetane **184** from the *syn*-isomer and a 4:1 mixture of the *ea*- and *ee*-dioxetanes from the *anti*-isomer.[138]

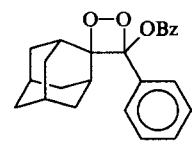


syn-**31** → *ee*-**184**

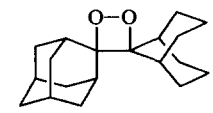
anti-**31** → *ea*-**184** + *ee*-**184**

The synthesis of dioxetanes from SHA via the DCA-sensitised photochemical oxidation by oxygen has been described in relation to the alkenes **10**, **27**, **28**, and **42**. The oxidation of the alkene **28** stereoisomers by this procedure afforded the same products as their oxidation by $^1O_2$, but the ratio of the *cis,cis*- and *trans,trans*-dioxetanes is in this case 27:22. A dioxetane is not formed from the alkene **30** under these conditions.[39,126] The sensitised photochemical oxidation of a series of enol ethers afforded high yields of the corresponding dioxetanes **175a**, **e**, **g**, **l** and **185**.[139]

The electrochemical oxidation by oxygen is also used together with the oxidation method described above for the synthesis of dioxetanes from the alkenes **10**, **27**, **28**, and **42**; the ratios of the relative reactivities of the alkenes **10**, **27**, and **42** are then 1:0.74:0.06. The formation of mixtures of *cis,trans*-, *cis,cis*-, and *trans,trans*-dioxetanes **182** in proportions of 34:24:21 (from the *anti*-isomer) and 23:51:11 (from the *syn*-isomer) from the *syn*- and *anti*-stereoisomers of the alkene **28** is evidence in support of a different reaction mechanism than in other types of oxidation. The dioxetane **186** has been obtained in the same way from the alkene **41**, while the alkene **30** is inert to oxygen under the conditions indicated.[39,126,140]



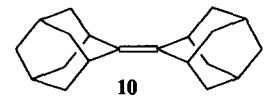
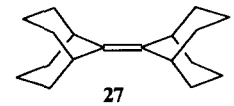
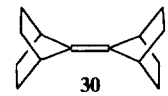
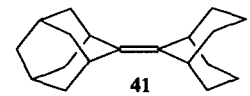
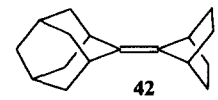
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Comparison of three oxidation methods (singlet, DCA-sensitised, and electrochemical) in relation to the alkenes **10**, **27**, **30**, **41**, and **47** showed that oxidation by singlet oxygen is most effective for the preparation of dioxetanes from the above alkenes (Table 8). Among all the alkenes examined, the alkene **30**, is the most reactive.[126]

Table 8. Singlet, DCA-sensitised, and electrochemical oxidation of a series of alkenes.[39,126]

Alkene	Yield of dioxetane (%)		
	$^1O_2$	DCA	$^3O_2$
 **10**	98	66	87
 **27**	100	21	80
 **30**	15	does not react	does not react
 **41**	—	—	69
 **42**	92	59	72

The higher relative thermal stability of the dioxetanes based on SHA compared with those based on the usual alkenes is illustrated by the data in Table 9, which lists the activation energies E_a for the thermolysis of a series of dioxetanes (this is one of the characteristics of the stability of compounds of this type). The table shows that the adamantane and bridging bicyclic fragments increase the stability of dioxetanes and that, of the two stereoisomers, the *anti*-isomers are more stable than the *syn*-isomers.

Table 9. Activation energies for thermal decomposition in the chemiluminescent thermolysis of dioxetanes.

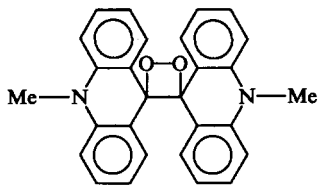
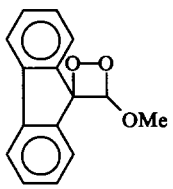
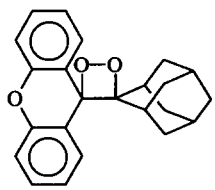
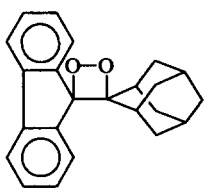
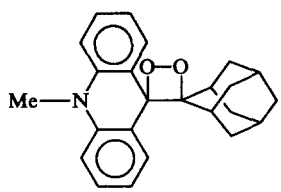
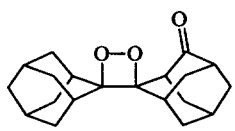
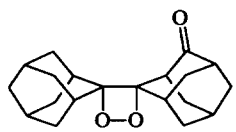
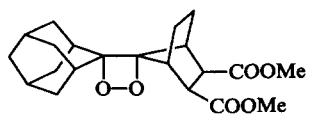
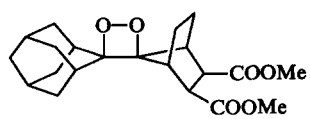
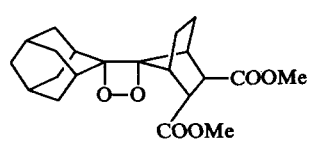
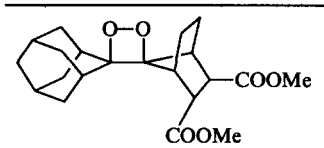
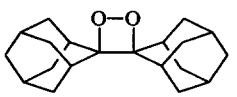
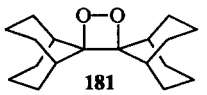
Dioxetane	E_a/kcal mol^{-1}	Ref.
	18.7	141, 142
	21.0	143
	23.8	82
	25.8	127
	26.3	131
	33.2	122
	33.5	122
	29.5	122
	33.0	122
	33.5	122

Table 9 (continued)

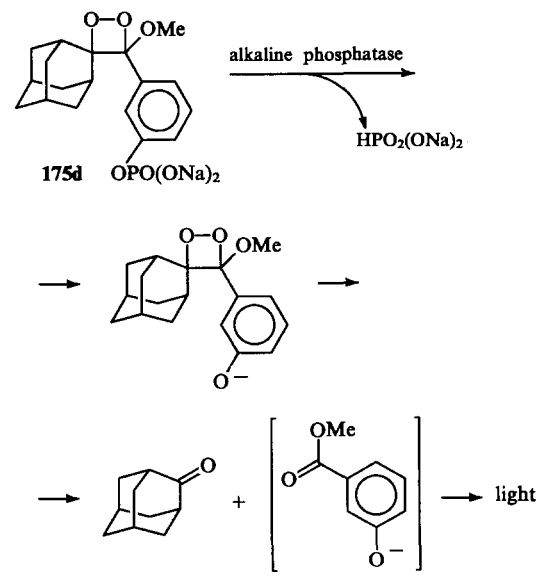
Dioxetane	E_a/kcal mol^{-1}	Ref.
	36.3	122
	34.6	144
 **181**	35.6	145

V. Applications of dioxetanes based on sterically hindered alkenes

It has been discovered in the last decade that adamantane-containing dioxetanes with functional group substituents are likely to find applications as chemiluminescent labels and probes in labelling systems and in the determination of DNA, hormones, and other biological substances. Different aspects of the use of dioxetanes in molecular biology, immunology, and biotechnology have been described in detail in reviews[146,147] and patents.[80,83,148–152]

The glow in the systems under discussion is generated under the influence of enzymes — alkaline phosphatase (in the presence of disodium phosphates), aryl esterase (in the presence of acetates) — and of the fluoride ion (in the presence of trialkylsilyl ethers). The glow is excited as a result of the splitting off of the corresponding functional group, which leads to an unstable intermediate. The latter undergoes in its turn spontaneous decomposition in the dioxetane ring accompanied by chemiluminescence.[132,134] These transformations are illustrated below in relation to the dioxetane **175d** — 3-(2′-spiroadamantane)-4-methoxy-4-(3″-phosphoryloxy)phenyl-1,2-dioxetane (AMPD) (Scheme 6).

Scheme 6



It has been suggested that dioxetanes based on 4-substituted adamantylideneadamantanes **165** and **166**,[68] adamantylidene-(hetero)tricyclanes **176–179**,[82,127–132] compounds of the methoxyarylmethylideneadamantane series **175d–i**,[80,81,83,148] and others be employed as chemiluminescent labels. A system incorporating AMPD and alkaline phosphatase has found nowadays a real practical application. This system is manufactured by the Tropix Company. An advantage of systems of this kind is the combination of a high rate of assay with a high sensitivity (an order of magnitude higher than in the case where the usual luminescent reagents are employed), safety (compared with radioactive labelling), and diversity of applications.

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Silicon-containing alka-1,3-dienes and their functional derivatives in organic synthesis

M D Stadnichuk, T I Voropaeva

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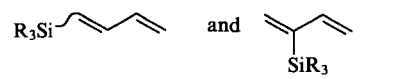
Abstract. Data on the synthesis and chemical reactions of silicon-containing 1,3-dienes are surveyed for the first time in the present review. It is shown that the addition reactions of 1- and 2-triorganosilylalka-1,3-dienes and their derivatives are the most interesting and promising in fine organic synthesis. The application of the trialkylsilyl group as a protecting group and as a new reaction centre, which makes it possible to obtain carbon—carbon or carbon–heteroatom bonds, is examined. It has been found that the double bonds remote from the silicon atom are the most reactive in addition reactions and that regardless of the nature of the reagent the attacking species always binds to the terminal carbon atom of the buta-1,3-diene fragment. The bibliography includes 329 references.

I. Introduction

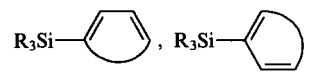
1,3-Diene hydrocarbons and their derivatives have long served as convenient and readily available intermediates in the synthesis of complex aliphatic, carbocyclic, and heterocyclic compounds as well as polymers with useful properties. Silicon-containing derivatives of 1,3-diene hydrocarbons were first obtained in 1954.[1] The authors suggested that the product of the catalytic hydrogenation of 1-trimethylsilylbut-3-en-1-yne is 1-trimethylsilylbuta-1,3-diene. However, it was later established that the product is a mixture of 1-trimethylsilylbut-1-yne and the isomeric 1-trimethylsilylbuta-1,2-diene and 1-trimethylsilylbuta-1,3-diene.[2–4] Judging from gas–liquid chromatographic (GLC) data, the fraction of the 1,3-diene isomer in the mixture does not exceed 36%.[4]

2-Trialkylsilylbuta-1,3-dienes[5] and 1-trialkylsilylbuta-1,3-dienes[6] were first obtained in a pure state as late as 1956 to 1957 by the dehydration of the corresponding alcohols. Subsequently the chemistry of unsaturated organosilicon compounds began to develop in two directions. The first is associated with the development of the methods of synthesis of silicon-containing hydrocarbons — model compounds for the investigation of the relation between structure and reactivity and also of the delocalisation of the π-electrons of the multiple bonds with participation of unoccupied *d* orbitals of silicon ($d_\pi - p_\pi$ interaction); the second direction is associated with the development of methods of synthesis of carbofunctional derivatives of 1,3-diene silicon-containing hydrocarbons and with their application as synthetic units in the synthesis of natural products and their synthetic analogues, including silane analogues.[7,8]

Representatives of virtually all possible types of silylalka-1,3-dienes have now been synthesised, but the present review surveys the results of studies on only 1- and 2-organosilylalka-1,3-dienes containing the fragments



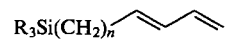
In view of the specificity of the methods of synthesis and of the characteristic features of their structure and reactivity, silylcyclo-1,3-dienes



silacyclo-1,3-dienes



and aliphatic compounds of the type



$n > 0$,

are not analysed in the present review.

Special reviews, including a full analysis of the chemistry of silicon-containing alkadienes and their functional derivatives, are lacking although compilatory[9–13] and narrow-profile[14–23] reviews, as well as certain monographs[24–26] include data also on the chemistry of 1,3-diene organosilicon compounds.

II. Synthesis of 1- and 2-triorganosilylalka-1,3-dienes and their functional derivatives

All the methods of synthesis of silicon-containing 1,3-dienes known at present can be divided into two groups. The first includes all the methods in which the initial compounds already contain the required carbon skeleton and the task of the investigator reduces either to the introduction of the organosilyl group into the organic molecule or to the creation of silyl-substituted 1,3-diene structures as a result of the chemical transformation of the corresponding unsaturated organosilicon compounds. The second group consists of methods involving the

M D Stadnichuk, T I Voropaeva Department of Organic Chemistry, St Petersburg State Technological Institute, Zagorodnyi proezd 49, 198013 St Petersburg, Russian Federation.
Fax (7-812) 110 62 85, Tel. (7-812) 316 33 77 (M D Stadnichuk)

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creation of silicon-substituted 1,3-diene structures from simpler synthetic units. The methods include the obligatory formation of new carbon–carbon bonds.

1. Synthesis of silicon-containing 1,3-dienes from the corresponding alkenynes

Catalytic hydrogenation of the available 1,3-enyne silicon-containing hydrocarbons and their derivatives is one of the promising methods of synthesis of the corresponding dienes.[26] According to Petrov et al.,[1] catalytic hydrogenation of 1-trimethylsilylbut-3-en-1-yne in the presence of palladium on barium sulfate actually takes place chemoselectively at the triple bond.

$$Me_3SiC{\equiv}C{-}CH{=}CH_2 + H_2 \xrightarrow{Pd/BaSO_4} Me_3SiCH{=}CH{-}CH{=}CH_2$$

Other workers who investigated the catalytic reduction of silicon-containing vinylethyne ethers[27] and glycols[28] arrived at a similar conclusion.

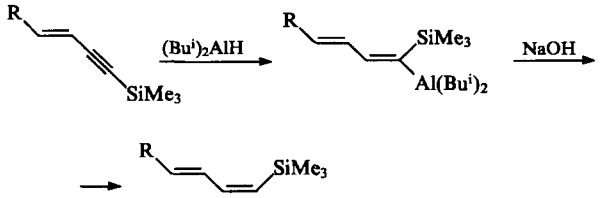
$$Me_3SiC{\equiv}C{-}CH{=}CHOR + H_2 \xrightarrow{Pd+Pt} Me_3SiCH{=}CH{-}CH{=}CHOR$$

$$Me_2C(OH)C{\equiv}C{-}CH{=}C(SiEt_3){-}C(OH)Me_2 \xrightarrow{Pd/BaSO_4} Me_2C(OH)CH{=}CH{-}CH{=}C(SiEt_3){-}C(OH)Me_2$$

It has been noted that the alkenyne ethers are not hydrogenated in the presence of palladium on calcium carbonate or platinum on charcoal, but readily combine with catalytically activated hydrogen when a mixture of these catalysts is employed.

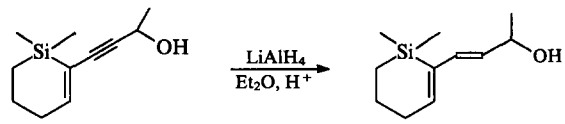
However, it was later shown[2–4] that the hydrogenation of silicon-containing alkenynes is a nonselective process: apart from the corresponding 1,3-diene, silicon-containing hydrocarbons and ethyne and allene products are formed. Since conclusions concerning the mode of hydrogenation were reached in the above investigations[1,27,28] on the basis of spectroscopic data (Raman or IR spectra) and the ability of the hydrogenation products to form cyclic adducts with maleic anhydride (which is possible also when the mixture contains 20%–30% of the 1,3-diene), the authors' conclusion[1,27,28] that catalytically activated hydrogen adds chemoselectively to the triple bond of silicon-containing 1,3-enyne hydrocarbons must be regarded as erroneous.

According to the available data, silicon-containing alk-1-en-3-ynes combine chemospecifically with diisobutylaluminium hydride at the triple bond. The corresponding (*Z*, *E*)-alkadienes were obtained by the protodemetallation of the adduct and the interaction with donors of the electrophilic halogens (chlorosuccinimide, bromocyanogen, and iodine) afforded the corresponding halo-derivatives of silicon-containing dienes.[29–33]

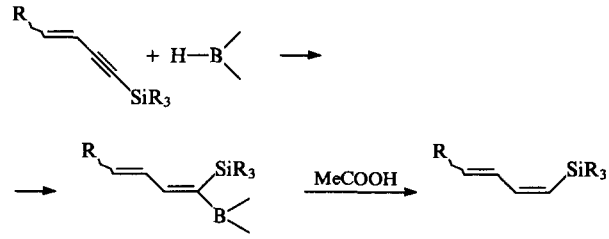


R = C_6H_{13}, C_6H_{11}, Bu^t, Me_3Si.

The reduction of the triple bond by lithium tetrahydroaluminate is known only for the corresponding alkenyne alcohols (a stereo-, regio-, and chemospecific reaction).[7]



The hydroboration of 1-trialkylsilylalk-3-en-1-ynes as well as their hydroalumination proceed chemo-, regio-, and stereo-specifically with formation of (*Z*)-adducts. The configuration of the 3,4-double bond is not altered.[32,34–37] Treatment of the adducts with acetic acid afforded the corresponding (1*Z*)-alkadienes.



The addition of hydrosilanes to 1,3-enyne compounds is nowadays one of the most important methods of synthesis of silicon-containing alka-1,3-dienes despite the fact that in many cases these reactions are characterised by a relatively low chemo- and regioselectivity. A 0.1 N solution of chloroplatinic acid in isopropyl alcohol (the Speier catalyst) is usually employed as the reaction catalyst; platinum on charcoal or other compounds of platinum group metals are more rarely employed.

It has been reported that conjugated alkenynes[38–47] and their functional derivatives[48,49] containing terminal ethyne groups combine with hydrosilanes exclusively at the triple bond with the silyl group becoming attached to the α-carbon atom. The nature of the R^1 and R^2 substituents does not affect the mode of the reaction and the yield of its products. In the interaction of trichlorosilane with vinylethyne, no individual adducts could be isolated.[43]

$$CH{\equiv}C{-}CR^1{=}CHR^2 + Cl_nR_{3-n}SiH \longrightarrow Cl_nR_{3-n}SiCH{=}CH{-}CR^1{=}CHR^2$$

R^1 = H, Me; R^2 = H, Me, OMe, NEt_2.

Judging from the yields, the reactivity of haloalkylhydrosilanes decreases in the sequence $Me_2ClSiH > MeCl_2SiH > Cl_3SiH$, which differs from that obtained previously in Greber's study.[45]

However, it was later established[50,51] that alkenynes with a terminal triple bond interact with hydrosilanes chemo- and regio-specifically: apart from 1-trialkylsilylalka-1,3-dienes, the products of the addition of hydrosilanes to the double bond also in the 1,4-positions as well as 2-trialkylsilylalka-1,3-dienes are formed. The yields of these compounds are low and they can be removed by fractionation.

Judging from the available data,[52–56] 1-trialkylsilyl alk-1-en-3-ynes also combine with hydrosilanes preferentially at the triple bond. However, considerable amounts of allene adducts are also formed in these reactions, their fraction in the mixture being determined by the structure of the enyne fragment and the hydrosilane.

$$Me_3SiC{\equiv}C{-}CR^2{=}CHR^3 + R^1_nCl_{3-n}SiH \longrightarrow$$

$$\longrightarrow Me_3SiCH{=}C(SiCl_{3-n}R^1_n){-}CR^2{=}CHR^3$$

$$\xrightarrow{H^+}$$

$$\longrightarrow Me_3SiCH{=}C{=}CR^2{-}CHR^3SiCl_{3-n}R^1_n$$

Trialkylhydrosilanes add to 1-trialkylsilylbut-3-en-1-ynes ($R^2 = R^3 = H$) exclusively in the 1,4-positions, while 3-methyl-1-trimethylsilylbut-3-en-1-yne ($R^2 = Me$) reacts with the same reagents to form almost exclusively the products of addition to the triple bond.

Alkylchlorohydrosilanes react with 1-trialkylsilylalk-3-en-1-ynes almost always at the triple bond regardless of the structure of the enyne fragment. It has been established that allene adducts readily isomerise in an acid medium to 1,3-diene adducts with migration of the trialkylsilyl group. These results enabled the authors [52,55] to postulate that the reactions proceed in all cases as 1,4-addition. The adducts obtained under these conditions isomerise to 1,3-dienes already under the conditions of the addition reaction. Chloroplatinic acid or hydrogen chloride, which is always present in chlorohydrosilanes, function as isomerisation catalysts. The isomerisation most probably proceeds via a quasi-cyclic transition state stage. [53]

It has been shown for the hydrosilylation of 1,2,4-tris-(trimethylsilyl)but-1-en-3-yne that the nature of the catalyst [H_2PtCl_6, $PtCl(PPh_3)_3$, $Pt(PPh)_4$, $PdCl_2(PPh_3)_2$, and $Pd(PPh_3)_4$] and the structure of the hydrosilane ($PhMeSiH_2$, Ph_2SiH_2, and Et_3SiH) affect the yield and structure of the adducts. [55]

The interaction of alkenes with trialkylhydrosilanes in the presence of chloroplatinic acid is optimal for the preparation of 1,3-dienes. [55]

Regardless of the structure of the reactants and the nature of the catalyst (chloroplatinic acid or platinum on charcoal), hydrosilanes add exclusively to the triple bond of vinylethyne alcohols [57-62] and their ethers [63-65] and esters [66] in the hydrosilylation reaction.

$$R^1R^2C(OR^3)C{\equiv}C{-}CH{=}CH_2,$$

R^3 = H, Me, CH_2CH_2CN, MeCO, $CH_2CH{-}CH_2$ (O).

On the grounds that the adducts did not undergo "β-cleavage" on heating, a type **A** structure was initially attributed to them, but later the structure **B** was proposed on the basis of ^1H NMR spectroscopic data.

$$R^1R^2C(OR^3){-}C(SiR_nCl_{3-n}){=}CH{-}CH{=}CH_2$$

A

$$R^1R^2C(OR^3){-}CH{=}C(SiR_nCl_{3-n}){-}CH{=}CH_2$$

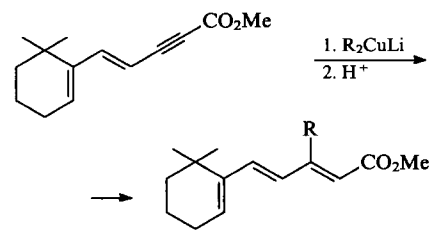
B

Ethyne and allene adducts have also been found in some investigations, [62,64] but the conclusions reached by the authors concerning the structure are open to doubt.

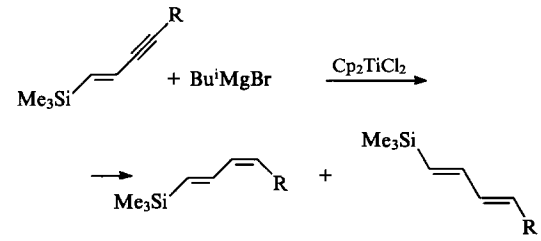
According to the data of Kakhniashvili and coworkers [67-69] and Shikhiev and coworkers, [70] alkenynes of the type *p*-$ROC_6H_4C(Me)_2C{\equiv}C{-}CH{=}CH_2$ give rise to a mixture of the corresponding 1,3-diene regioisomers, with type **B** adducts predominating (80%-90%), on interaction with trialkylhydrosilanes in the presence of chloroplatinic acid.

Analysis of the available data shows that hydrosilanes add to the triple bond of alkenynes with a high degree of selectivity and that in the case of terminal ethynes the silicon-containing group is attached predominantly to the α-carbon atom of the triple bond, while in reactions with internal triple bonds this group is attached to the β-carbon atom.

The addition of organometallic compounds to the double bond and in the 1,4-positions in alkenynes is of no interest as regards the synthesis of silicon-containing dienes with conjugated double bonds. [21] Only the reactions of silicon-containing lithium cuprates are an exception. Judging from the available data, these add chemo-, regio- and stereo-specifically to the triple bond of the methyl ester of the corresponding alkadienynoic acid. [71]

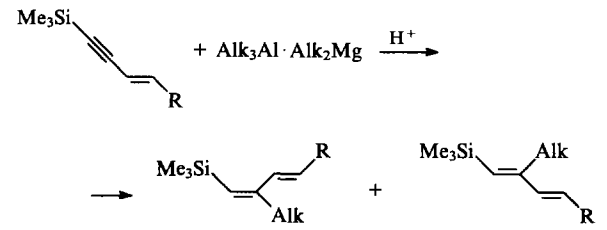


Under the usual conditions, Grignard reagents do not interact with silicon-containing alkenynes, but in the presence of catalytic amounts of dichloro(dicyclopentadienyl)titanium a reaction in which hydrogen and magnesium add to the unsaturated compound takes place. [32]



The overall yield of 1,3-diene silicon-containing hydrocarbons formed on demetallation with water does not exceed 30% and the isomer ratio is $E:Z = 42:58$.

Trialkylaluminium adds to 1-trialkylsilylalk-3-en-1-ynes only on heating. When a complex of trialkylaluminium with dialkylmagnesium is used as the reagent, the reaction takes place under milder conditions (the isomer ratio is $E,E:E,Z = 95:5$). [72,73]



The addition of mixed alkylaluminium chlorides in the presence of Cp_2TiCl_2 takes place similarly (the isomer ratio is $E,E:E,Z = 50:50$). [74]

The dealumination of the adducts formed can be carried out with iodine, whereupon one obtains 1-iodoalkadienes, which are difficult to obtain otherwise.

Judging from the data of Petrov et al., [1] the bromination of 1-trialkylsilylbut-3-en-1-ynes takes place exclusively at the triple bond and can be a convenient preparative method of synthesis of the corresponding 1,3-diene silicon-containing dibromo-derivatives. It was shown later that the 1,2-dibromo-derivatives are obtained as a result of the thermal isomerisation of the 1,4-dibromo-derivatives formed initially. [75]

$$R_3SiC{\equiv}C{-}CH{=}CH_2 + Br_2 \longrightarrow$$

$$\longrightarrow R_3SiCBr{=}C{=}CHCH_2Br \xrightarrow{\Delta}$$

$$\longrightarrow R_3SiCBr{=}CBr{-}CH{=}CH_2$$

The functional derivatives of the silylalkenynes $Me_3SiC{\equiv}C-CH{=}CRX$ (X = CN, COR, CO_2R) combine with bromine at the double and triple bonds. The ratio of the dibromo-derivatives formed is ~1:1.[76] The introduction of a methyl group in the α-position relative to the functional-group substituent promotes the formation of dibromo-1,3-dienes.[76]

In contrast to the halogens, sulfinic acid halides, and other electrophiles[21] which add to silicon-containing alkenes at the double bond and in the 1,4-positions, sulfenic acid chlorides and bromides and their selenium-containing analogues react exclusively[77] or preferentially[78-82] at the triple bond.

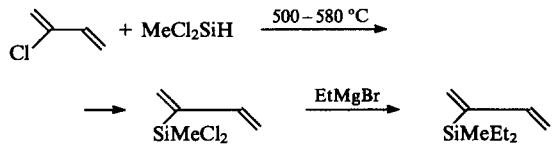
$$Me_3SiC{\equiv}C-CR^1{=}CHR^2 + R^3XY \longrightarrow$$
$$\longrightarrow Me_3SiC(XR^3){=}CY-CR^1{=}CHR^2$$
$$+ Me_3SiC{\equiv}C-CR^1YCHR^2XR^3$$

X = S, Se; Y = Cl, Br.

Other reagents (secondary amines[83] and thiols) add to the double bond and in the 1,4-positions under the conditions of free-radical initiation,[84,85] the content of 1,3-diene adducts not exceeding 5%. Therefore these reactions are of no interest as methods of synthesis of polyfunctional derivatives of silicon-containing 1,3-diene hydrocarbons.

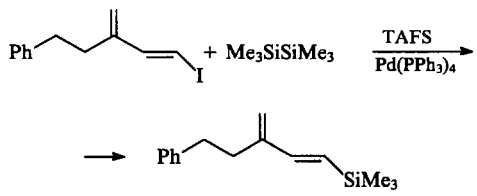
2. Silylation of derivatives of alka-1,3-dienes

Only two examples of the direct silylation of haloalkadienes, leading to the synthesis of the corresponding silicon-containing alka-1,3-dienes, are known. Thus 2-triorganosilylbuta-1,3-diene has been obtained in a low yield by the high-temperature (500–580 °C) condensation of dichloromethylsilane and chloroprene.[86]



Under milder conditions in the presence of a palladium catalyst and tris(diethylamino)sulfonium difluorotrimethylsilicate (TAFS), hexamethyldisilane interacts stereospecifically with 1-iodoalkadienes (Scheme 1).[87]

Scheme 1



The use of potassium or caesium fluoride as the fluoride anion donor is ineffective.[87]

Silicon-containing 1,3-diene ethers are formed readily and in satisfactory yields on condensation of lithium alkoxydienides with triorganosilanes.[14,88-92]

$$R^1OCH{=}CH-CH{=}CHR^2 \xrightarrow{BuLi}$$
$$\longrightarrow [R^1OC{=}CH-CH{=}CHR^2]^-Li^+ \xrightarrow{Me_3SiCl}$$
$$\longrightarrow R^1OC(SiMe_3){=}CH-CH{=}CHR^2$$

R^1 = Me, Et, $MeOCH_2$, $Me_3SiOCH_2CH_2CH_2$;

R^2 = H, Me, Pr^i.

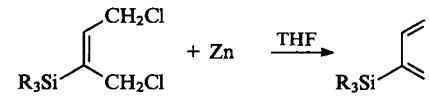
The lithium or sodium alkadienides interacting with Me_3SiCl can be obtained by metallating the corresponding halogen compounds[93] or as a result of the opening of the ring in furan derivatives[94] and cyclic acetals,[91] by transmetallation,[95,96] and by other procedures.[97-103]



TBS = Bu^tMe_2Si.

3. 1,2- and 1,4-Elimination reactions

Judging from the available data,[18,104-106] 1,4-dechlorination is the easiest method of synthesis of 2-triorganosilylbuta-1,3-dienes.



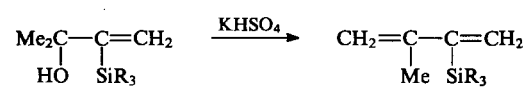
The initial 1,4-dichloro-2-triorganosilylbut-2-enes are obtained by hydrosilylating 1,4-dichlorobut-2-yne.

1,2-Dechlorination[107] can also be recommended as a convenient preparative method of synthesis of the corresponding derivatives of silicon-containing 1,3-dienes.

$$CF_2ClCFCl-CH{=}CHSiMe_3 + Zn \longrightarrow$$
$$\longrightarrow CF_2{=}CF-CH{=}CHSiMe_3$$

Another method of synthesis of 2-triorganosilylalka-1,3-dienes involves the 1,2- and 1,4-elimination of water from silicon-containing ethene alcohols. However, owing to the relatively low hydrolytic stability of the silicon–carbon bond towards strong inorganic acids and bases, the reaction must be carried out in the presence of acid potassium sulfate. It has been shown that tertiary and secondary alcohols are dehydrated under these conditions.[5,6,108-110]

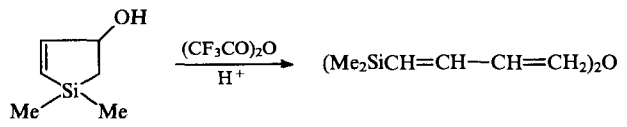
$$R_3SiCH_2\underset{OH}{C}H-CH{=}CHR^1 \xrightarrow{KHSO_4}$$
$$R^1 = H \longrightarrow R_3SiCH{=}CH-CH{=}CHR^1$$
$$R^1 = Me \longrightarrow R_3SiOSiR_3 + CH_2{=}CH-CH{=}CHR^1$$



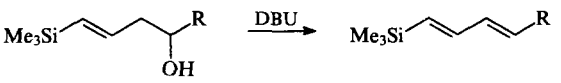
In all the cases investigated, tertiary alcohols are dehydrated under milder conditions than secondary alcohols. The dehydration of 1-trimethylsilylpent-3-en-2-ol takes place with almost complete desilylation. Heating the dihydric alcohols $R_2Si[CH_2CR^1(OH)-CH{=}CH_2]_2$ with $KHSO_4$ affords the corresponding bisbutadienylsilanes in low (~20%) yields.

Toluene-*p*-sulfonic acid began to be used later for the dehydration of secondary[111,112] and tertiary[113-116] silicon-containing alcohols.

The dehydration of 1,1-dimethyl-1-silacyclopent-2-en-4-ol by trifluoroacetic acid anhydride takes place with the opening of the ring and the formation of the corresponding siloxane.[117]

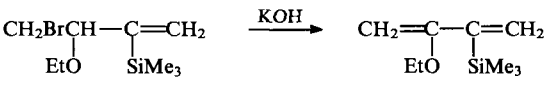


Examples of the dehydration of secondary silicon-containing alcohols on treatment with 1,8-diazabicyclo[5.4.0]undecane (DBU) are also known.[118]

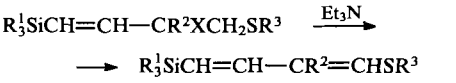


Thus, by varying the structure of the silicon-containing ethene alcohols and dehydrating agents synthesised by traditional methods, it is possible to obtain any silicon-containing conjugated alkadienes.

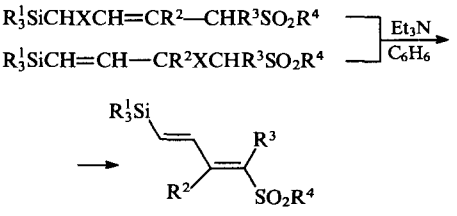
The 1,2- and 1,4-elimination of hydrogen halides and other acids proceeds as a rule only in a highly alkaline medium at high temperatures. This is apparently the reason why there are no data on the synthesis of silicon-containing 1,3-dienes by this procedure. However, it is known that, when carbonyl derivatives of silicon-containing ethene hydrocarbons contain a halogen and electron-accepting substituents, they readily split off hydrogen halides, the rate of reaction depending on the nature of the halogen (I > Br > Cl). Thus, according to the data of Shchukovskaya and coworkers,[119] β-bromoethers are dehydrobrominated by solid alkali at 90–120 °C.



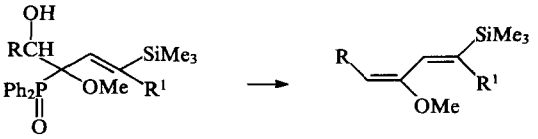
It was shown at the same time that silylchloro- and silylbromoalkyl sulfides containing a halogen in the allyl position readily split off the corresponding halogen halides even on treatment with triethylamine.[120] DBU was later used for similar purposes.[121–123]



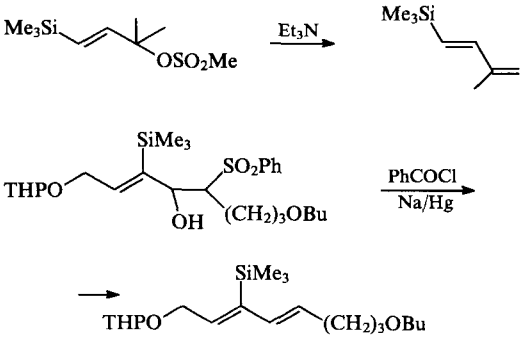
On treatment with triethylamine, the 1,2- and 1,4-dehydrohalogenation of unsaturated silicon-containing sulfones takes place at room temperature.[124–127] The 1,3-dienyl sulfones obtained under these conditions have the (*E*,*E*)-configuration.[128]



The 1,2-elimination of diphenylphosphonic acid takes place readily on treatment with butyllithium, lithium diisopropylamide,[129,130] or sodium hydride.[131]

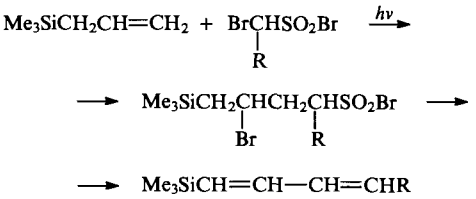


Examples of the synthesis of silicon-containing dienes as a result of the elimination of organic sulfonic acid from the corresponding esters[112] or sulfones[132] are known.



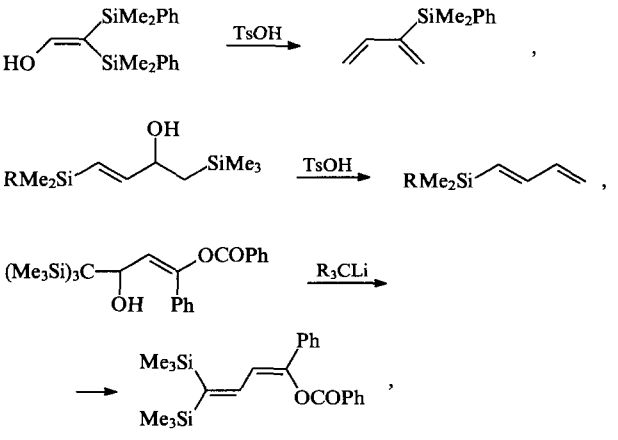
THP = 2-tetrahydropyranyl.

Block[133,134] proposed a novel method of synthesis of silicon-containing 1,3-diene hydrocarbons from readily available allylsilanes, which includes a stage in which hydrogen bromide and a sulfonic acid are eliminated.

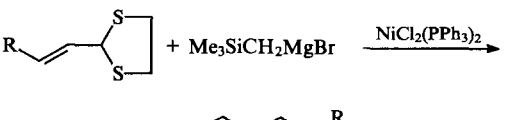


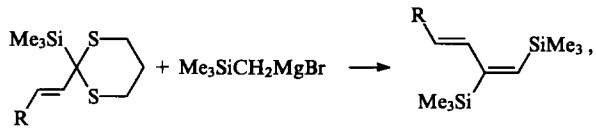
The replacement of triethylamine by 1,5-diazabicyclo [4.3.0]nonene does not affect the yields and the stereochemical result of the reaction. The employment of lithium or caesium *tert*-butoxide lowers somewhat the stereoselectivity of the reaction.[134]

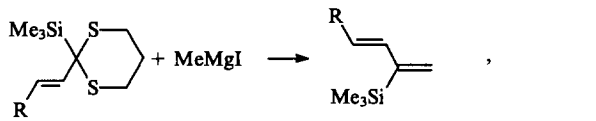
The synthesis of silicon-containing dienes as a result of the 1,2- or 1,4-elimination of silanols (on treatment with toluene-*p*-sulfonic acid[19,111,112,135] or bases[136])

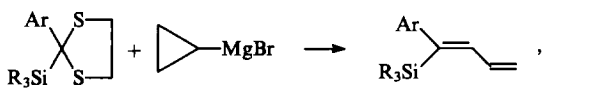


or of thiols from the products of the interaction of organomagnesium compounds with unsaturated dithioacetals[136,137]





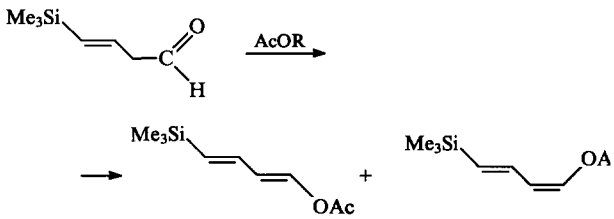




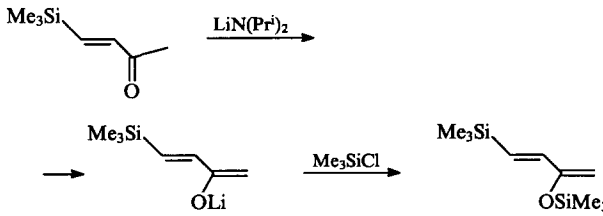
formally also belongs to the group of methods considered.

4. Isomerisation and ring opening

The keto–enol tautomerisation of silicon-containing aldehydes [138] and ketones [139,140] with subsequent fixation of the enol structure in the form of the corresponding ene-ethers has been widely used in the synthesis of acyloxy- and siloxy-buta-1,3-dienes. [112,138–141] Esters or anhydrides of the corresponding carboxylic acids may be used as the fixation reagents.

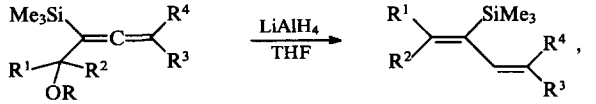


Siloxy-derivatives with a similar structure are obtained by treating an enolate (synthesised from a α,β-unsaturated ketone and lithium diisopropylamide [112] or dimethyllithium cuprate [142]) with chlorotrimethylsilane. [112]

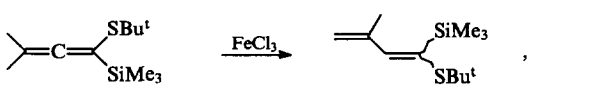


An instance of the photoinitiated isomerisation of non-conjugated unsaturated trialkylsilyl ketones to the conjugated ketones has also been described. [143]

The base-catalysed reactions of allene alcohols [144] and ethers, [145] i.e.

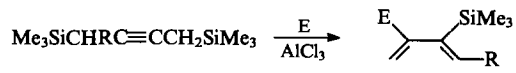


as well as the isomerisation of silicon-containing allenyl sulfides under the influence of $FeCl_3$, [146] i.e.

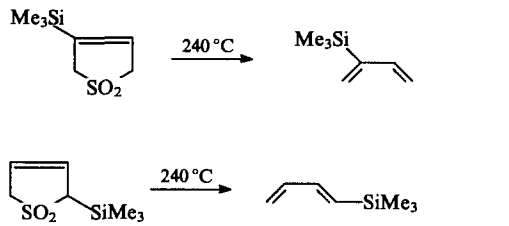


lead to the corresponding derivatives of silicon-containing 1,3-diene hydrocarbons. In certain cases, the base-catalysed isomerisation is combined with subsequent silylation. [144]

A novel method of synthesis of 2-trialkylsilylalka-1,3-dienes from the corresponding 1,4-bis(trialkylsilyl)alk-2-ynes is used in the treatment of an ethyne substrate by an electrophile (E = acetone, isobutyraldehyde, or trifluoroacetic acid) in the presence of anhydrous aluminium chloride. [147] The reaction involves a stage with a 1,2-shift of the trimethylsilyl group.

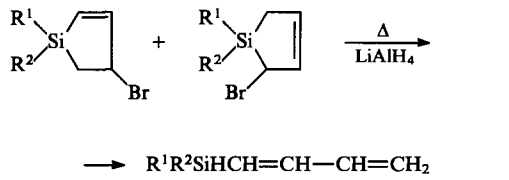


Pyrolysis of silicon-containing sulfolenes can also be included in the group of methods involving the isomerisation of the starting materials. This entails the cleavage of the heterocycle with formation of 1- or 2-trialkylsilylbuta-1,3-dienes, depending on the position of the trialkylsilyl group. [148–150]

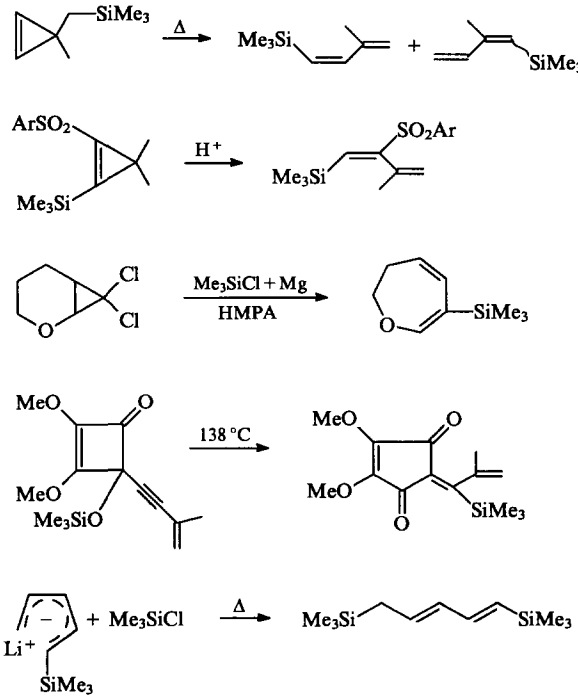


Mono- and di-alkyl-substituted silicon-containing sulfolenes afford mixtures of isomeric dienes under these conditions. [151]

Pyrolysis of silacyclopentenes and silacyclopentadienes ultimately also leads to silicon-containing alka-1,3-dienes. [152–156]

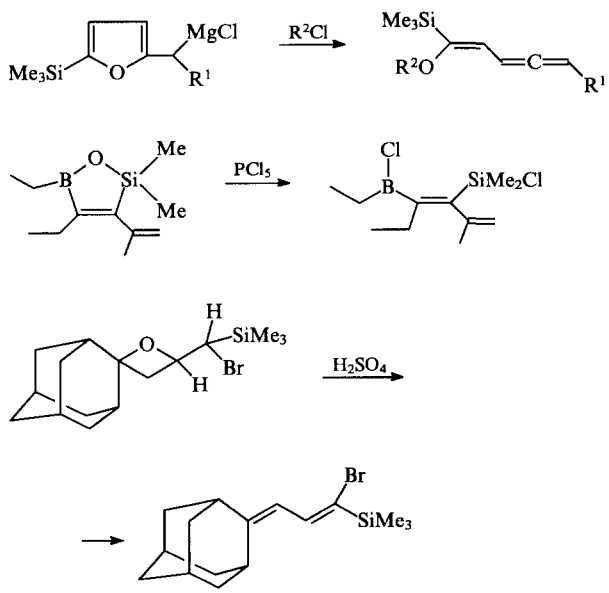


The opening of carbacycles is, under certain conditions, a very convenient preparative method of synthesis of conjugated silicon-containing 1,3-diene hydrocarbons and their derivatives. [99,157–161]



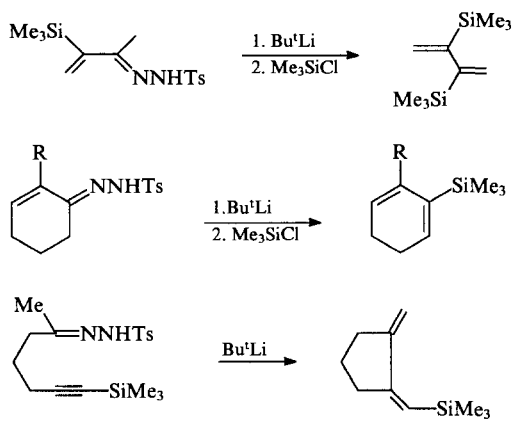
The methods of photochemical synthesis of silicon-containing 1,3-diene hydrocarbons and their derivatives are of interest.[162-165]

The opening of oxygen-containing heterocycles has been investigated only for isolated examples and has nowadays hardly any preparative interest.[166-169]

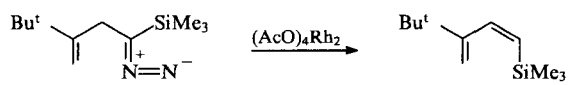


5. Synthesis of silicon-containing 1,3-diene hydrocarbons by the decomposition of tosylhydrazones or diazo-compounds

On treatment with lithium alkyls, tosylhydrazones decompose even at low temperatures with formation of the corresponding organolithium compounds, which give rise to the corresponding silicon-containing 1,3-diene hydrocarbon on interaction with trialkylchlorosilanes.[170-172]

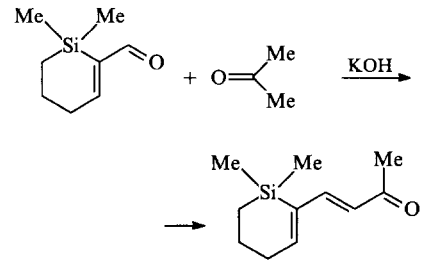


A stereoselective synthesis of (1*Z*)-isomers has been developed on the basis of the decomposition of the available aliphatic diazo-compounds by dirhodium-tetraacetate.[173]

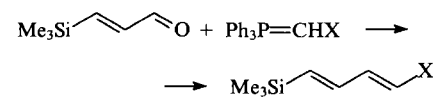


6. Methods for the construction of 1,3-diene fragments

In the synthesis of 1,3-diene fragments, the most important methods are those which presuppose their construction from simpler synthetic units. The corresponding reactions can occur as the condensation of two vinyl fragments, including silicon-containing fragments, or as the interaction of two fragments with the simultaneous formation of one or two double bonds. Owing to the low availability and the characteristic features of the spectra of α,β-unsaturated silicon-containing aldehydes and ketones, the latter are hardly used in the synthesis of silicon-containing 1,3-diene hydrocarbons and their derivatives. However, an example of the preparation of a ketone by the reaction of the corresponding aldehyde with acetone is known.[8] It was subsequently used in the synthesis of a sila-analogue of retinol.



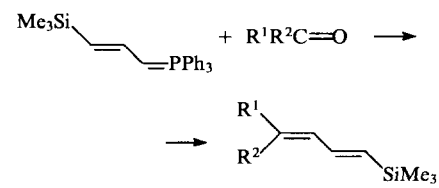
The Wittig reaction and its phosphonate (the Horner–Emmons reaction) and silyl (the Peterson reaction) modifications constitute nowadays a well developed method of synthesis of silicon-containing 1,3-dienes and their derivatives. The Wittig method was first applied in the synthesis of carbofunctional derivatives of silicon-containing 1,3-diene hydrocarbons in 1971 in the reaction of silicon-containing α,β-ethene aldehydes with phosphoranes.[174]

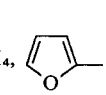


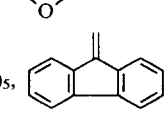
X = COMe, COOMe, CN.

It was later shown that the replacement of ether or THF, in which the Wittig reaction was usually carried out, by hexane simplifies significantly the purification and tends to increase the yield of the target products. (*Z*)- and (*E*)-aldehydes were introduced into the reaction.[175] The ethene fragment formed as a result of the condensation has predominantly or exclusively the (*E*)-configuration.[174-178] The introduction of a chlorine atom into the α-position relative to the silicon atom of the carbonyl component does not affect the yield and stereochemical result of the synthesis.[179]

An alternative version of the Wittig reaction, involving the interaction of a silicon-containing allylphosphorane with aldehydes and ketones, can also be used to obtain 1-trialkylsilylalka-1,3-dienes and their derivatives.[180,181]

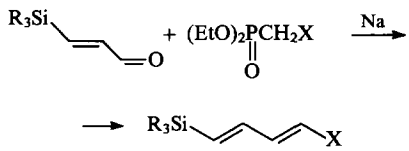


R^1 = H; R^2 = C_6H_{13}, PhCH=CH, 4-$NO_2C_6H_4$, 4-MeC_6H_4,  ;

R^1 = R^2 = Me, Ph; R^1 = R^2 = $(CH_2)_5$,  .

In such cases, the configuration of the 1,2-double bond does not change and the configuration of the newly formed ethene fragment depends in a complex manner on the structure of the carbonyl component and consists to the extent of 50% – 100% of the (*E*)-isomer.[181] The yields of the target products are 70% – 90%.

Judging from the available data, the phosphonate modification of the phosphorane synthesis (the Horner – Emmons reaction) also gives rise to satisfactory results in the synthesis of silicon-containing 1,3-diene compounds.[175,182-184]

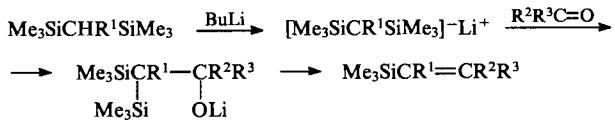


X = COOMe, COMe, CN.

The configuration of the double bond at the silicon atom does not change, as in the Wittig reaction, while the newly formed bond has predominantly the (*E*)-configuration. In the synthesis of ketones, the stereoselectivity of the reaction is higher when the Wittig method is used, while that of the reaction in the synthesis of nitriles is higher when the Horner – Emmons method is employed.[175]

The silyl modification of the Wittig reaction (the Peterson reaction) can be achieved in two ways: (1) by the reaction of the carbanions obtained from bis(trialkylsilyl)methanes with α,β-ethene aldehydes[11,136,185-188] and (2) by the reaction of the mesomeric carbanion of 1,3-bis(trialkylsilyl)prop-1-ene with carbonyl compounds (Scheme 2).[189-192]

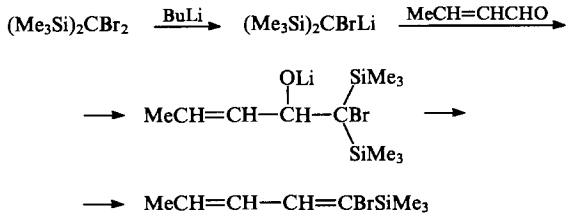
Scheme 2



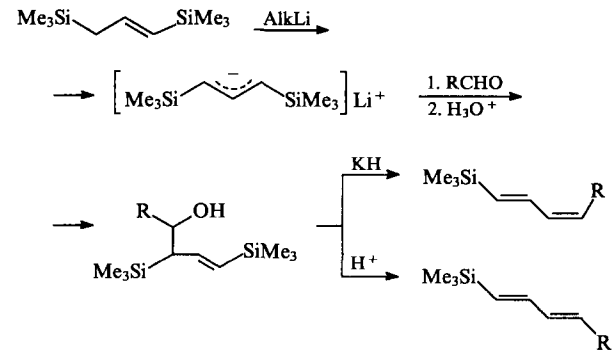
R^2 or R^3 = CH =CHX.

The carbanions needed in this reaction may be obtained also by the addition of lithium alkyls to 1,1-bis(trimethylsilyl)alk-1-enes.[185]

The interaction of dibromobis(trimethylsilyl)methane in succession with butyllithium and crotonaldehyde leads to a satisfactory yield of 1-bromo-1-trimethyl-silylpenta-1,3-diene [a mixture of the (1*E*)- and (1*Z*)-isomers in proportions of 2:1].[193]



A second version of the Peterson reaction in the synthesis of silicon-containing 1,3-diene hydrocarbons and their derivatives also includes a stage with formation of a carbanion and its condensation with the carbonyl compound.[118,189-192,194,195]



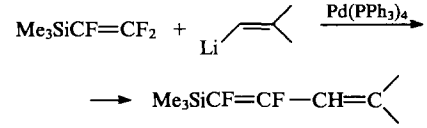
The stereochemical result of the reaction is determined by the nature of the silanol reagent split off.[189,192] In the presence of potassium hydride, the ethene fragment formed has predominantly the (*Z*)-configuration (60% – 90%) and in an acid medium the (*E*)-configuration (90%). The addition of magnesium bromide or trimethoxyboron to the reaction mixture reduces the stereoselectivity of the condensation and the isomer ratio *E,E*: *E,Z* is (60 – 70) : (40 – 30).[192] In the presence of silicates, (1*E*,3*E*)-trialkylsilylalka-1,3-dienes [R = H, Me, Bu^i, iso-C_5H_{11}, C_6H_{13}, Ph, $Ph(CH_2)_3$, $(CH_2)_nCH=CH_2$, n = 3,4] are formed exclusively;[190] in the presence of dicyclopentadienyltitanium chloride, the stereochemical result depends on the nature of the reagent promoting the elimination of trialkylsilanol. In an acid medium (sulfuric acid in THF), the (1*E*,3*E*)-isomers are formed exclusively, while on treatment with KF in THF the exclusive products are the (1*E*,3*Z*)-isomers.[191]

The data presented show that, in the synthesis of the (1*E*,3*E*)-isomers, preference should be given to the methods involving the Wittig or the Horner – Emmons reaction, while in the synthesis of the (1*E*,3*Z*)- or (1*Z*,3*Z*)-isomers the second version of the Peterson reaction is preferable.

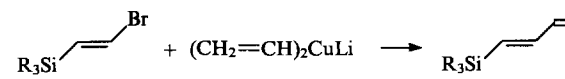
7. Organometallic synthesis

All the known methods including a stage in which a new carbon – carbon bond is formed with participation of classical organometallic compounds containing metal – carbon σ-bonds and the methods of synthesis of 1,3-diene structures as a result of the reacitons of unsaturated (including silicon-containing) compounds in the presence of metal complex catalysts are combined in this group. These reactions presuppose the formation of organometallic compounds of transition metals with classical or donor – acceptor carbon – metal bonds as an obligatory stage.

Organolithium α,β-ethene compounds do not alkenylate β-halovinylsilanes under the usual conditions. However, it is known that, in the presence of a palladium catalyst, trimethylperfluorovinylsilane reacts with vinyllithium to form the corresponding 1,3-dienes.[196-199]



Lithium vinylcuprates react similarly with β-bromovinylsilanes.[200]

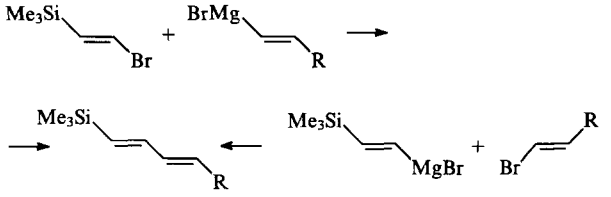


The interaction of vinylcuprates with halovinylsilanes afforded not only the corresponding silicon-containing 1,3-diene hydrocarbons but also their halo-[201] and amino-derivatives.[202]

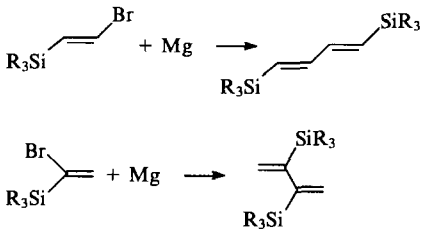
Mixed organomagnesium α,β-ethene compounds (the Norman reagent) interact with the corresponding vinyl halides also only in the presence of nickel and palladium complexes — $Ni(dppm)_2Cl_2$,[203,204] $Ni(dppe)_3Cl_2$, $Ni(dppp)_2Cl_2$,[205,206] $Ni(acac)_2AlMe_3$,[207] $NiCl_2(PPh_3)_2$,[136] and $PdCl_2(PPh_3)_2$,[203,204] where dppm = $Ph_2PCH_2PPh_2$, dppe = $Ph_2PCH_2CH_2PPh_2$, and dppp = $Ph_2PCH_2CH_2CH_2PPh_2$.

Both possible combinations have now been tested: organosilicon bromide–vinyl-magnesium halide and silicon-containing organomagnesium compounds–vinyl halide.

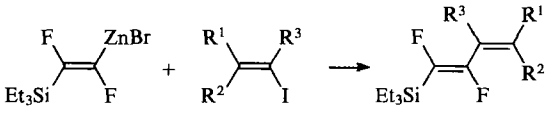
The stereoselectivity of the reaction in the synthesis of the (*E*, *E*)-isomers is about 90%[204] and in the synthesis of the (*E*, *Z*)-isomers it is somewhat lower (in the range 70%–80%).[203]



The 1,4- and 2,3-bis(trimethylsilyl)buta-1,3-dienes have been synthesised from the corresponding bromovinylsilanes and metallic magnesium without the preliminary preparation of the corresponding organomagnesium compounds.[208]



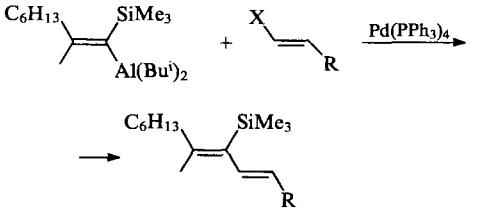
Mixed α,β-unsaturated organozinc compounds stereoselectively alkenylate vinyl halides in the presence of a palladium catalyst [$Pd(PPh_3)_4$[209,210] or $PdCl_2(PPh_3)_2$[211–213]].



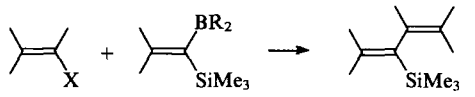
The target silicon-containing 1,3-diene hydrocarbons are obtained in satisfactory yields (80%–90%).

α,β-Unsaturated or organoaluminium compounds also react readily and stereospecifically with vinyl halides. The reaction is catalysed by the palladium complex $Pd(PPh_3)_4$.[199,214]

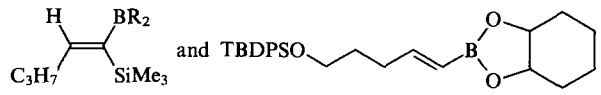
It has been shown in relation to 2-bromo-1-trimethylsilylethenes[214] that the (*E*)-isomer is more reactive than the (*Z*)-isomer.



In the presence of tetrakis(triphenylphosphine) palladium, α,β-unsaturated boranes interact with vinyl halides [CH_2=$CH(CH_2)_2$.$CH(OBz)CH$=$CBr(SiMe_3)$, Me_2C=$CHBr$, CH_2=$CHCH_2CH(OBz)CH$=$CI(SiMe_3)$] to form the corresponding silicon-containing conjugated dienes.[215–217]

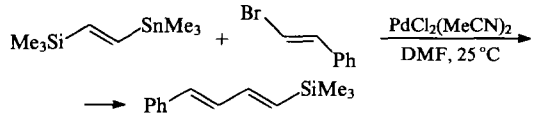


The boron-containing reagents investigated were

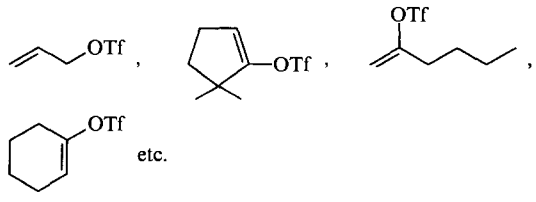


TBDPS = *tert*-butyl diphosphite-silane.

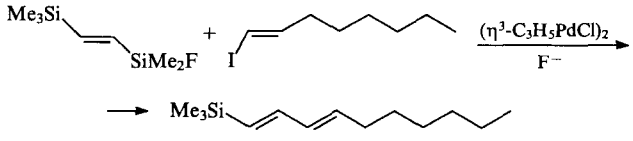
α,β-Unsaturated stannanes alkenylate vinyl halides under the conditions of the Stille reaction.[218]



The advantage of this method is manifested in the interaction of unsaturated stannanes with functional derivatives of vinyl halides containing as substituents groups which are reactive in relation to organolithium, organomagnesium, or organoaluminium compounds. Triflates can be used instead of halides.[219–223]



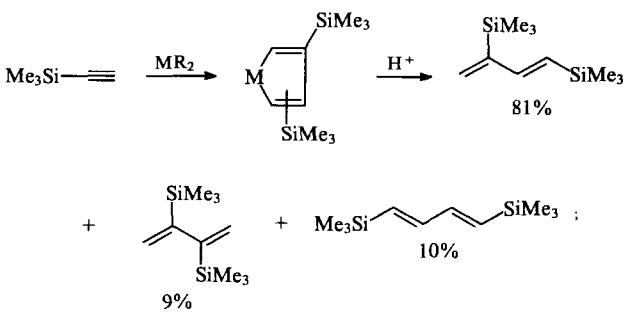
The ability of vinylsilanes to function as alkenylating agents in the synthesis of the corresponding silicon-containing 1,3-diene hydrocarbons has been recently discovered.[224]



The successful occurrence of this reaction requires fluoride anion donors [in the study quoted, the donor employed was tris(diethylamine)sulfenyl difluorotrimethylsilicate (TASF)]. Bis(trimethylsilyl)ethene does not react with vinyl iodides.

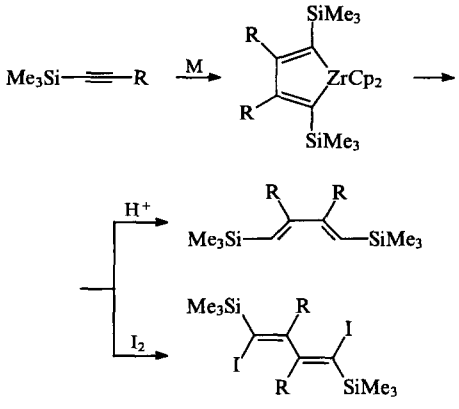
8. Dimerisation of ethynes and their codimerisation with ethenes catalysed by transition metal complexes

On interaction with zirconium complexes [Cp_2ZrPh_2, $Cp_2Zr.(CH_2$=$CH)_2$,[225] $Zr(C_5Me_5)_2MeB(4\text{-}FC_6H_4)_4$[226]], trialkylsilylethynes afford 1,3-diene complexes of zirconium, the proto-demetallation of which gives rise to the corresponding silicon-containing 1,3-diene hydrocarbons, for example:



M = Cp_2Zr.

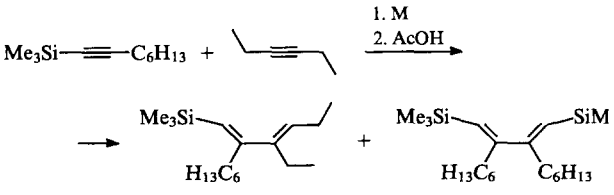
Disubstituted silylethynes behave similarly in this reaction.[227-229]



M = Cp_2ZrCl_2.

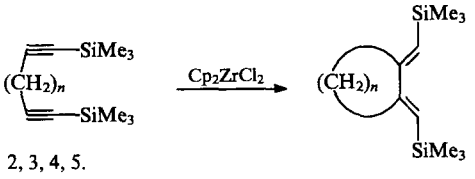
Zirconium compounds have been used as catalysts: Cp_2Zr(4-Me_2NPy).Z (Z = THF or CH_2=CHEt), Cp_2ZrCl_2,[229] and Cp_2ZrHCl,[227] while the demetallating agents were organic acids or iodine.

The codimerisation of disubstituted silylalkynes and dialkylethynes[227,228] leads to a cross-dimer and a dimer of the silicon-containing alkyne in proportions of 1:1.



It is striking that the 'head to head' principle operates in all cases in the dimers.

Nonconjugated silicon-containing alkenynes behave in this reaction as disubstituted ethynes,[230] while nonconjugated diethynes give rise to the corresponding cycloalkanes with conjugated endocyclic double bonds.[231-233]

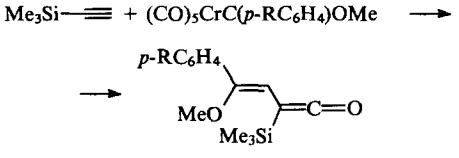


n = 2, 3, 4, 5.

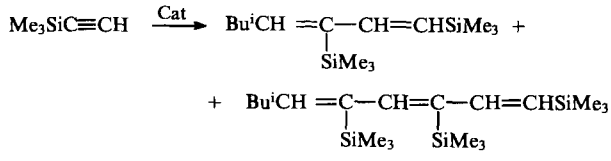
Nonconjugated diynes react similarly also in the presence of the palladium complexes $Pd_2(DBA)_3$ [234] and $PdCl_2Py_2$.[235]

The codimerisation of nonconjugated alkenynes with bis-(trimethylsilyl)ethyne in the presence of a cobalt catalyst leads to silicon-containing cyclohexadienes.[236]

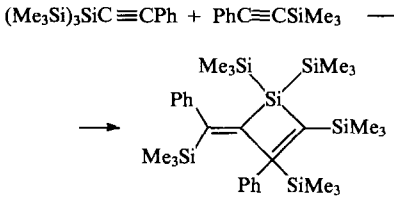
The interaction of trialkylsilylethynes with the pentacarbonyl[aryl(methoxy)carbene]chromium complexes $(CO)_5CrC.(p\text{-}RC_6H_4)OMe$ (R = H, Me, OMe, CF_3) proceeds in a more complex manner. The silylketenes formed indicate the involvement of the ligands forming part of the complex in the construction of the reaction product.[237,238]



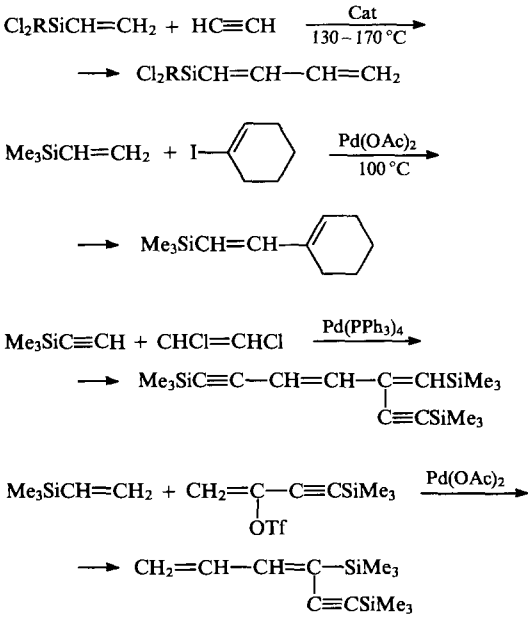
The use of trialkylaluminium complexes[72,239] or the complexes of these compounds with metal chlorides [$Bu^i_3Al.MX_n$, where MX_n = $TiCl_4$, $VOCl_3$, $VO(acac)_2$, VCl_3, $NbCl_5$, $CrCl_3$, $MoCl_3$[240]] as catalysts of the dimerisation of silylethynes leads to the formation of a mixture of the corresponding dimers and trimers, the proportions of which are determined by the nature of the catalyst.



The codimerisation of silylethynes in the presence of $Ni(PEt_3)_4$ gives rise to conjugated dienes, one of the double bonds of which is in the silacyclobutene ring.[241]



The codimerisation of vinylsilanes with ethyne (catalysts — Pd/Al_2O_3, $Pd/CaCO_3$, Pd/C, or Pt/Al_2O_3[242,243]), haloalkenes,[244,245] or triflates[244] [catalysts — $Pd(OAc)_2$ or $Pd(PPh_3)_4$] leads to 1- or 2-silylalka-1,3-dienes.



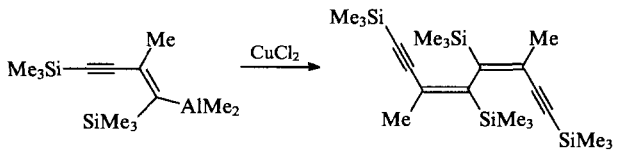
The reactions proceed as a rule under relatively severe conditions and the yields of the target products are low.

9. Other methods

A convenient preparative method of synthesis of disilylated alka-1,3-dienes involves the cleavage of the silylalkenyl derivatives of mercury,[246] silicon,[247] or aluminium[248] catalysed by transition metal compounds.

$$(Me_3SiCH{=}CH)_2Hg \xrightarrow{Pd(PPh_3)_4} Me_3SiCH{=}CH{-}CH{=}CHSiMe_3$$

$$K(Me_3SiCH{=}CHSiF_2) \xrightarrow{Ag\ or\ Cu} Me_3SiCH{=}CH{-}CH{=}CHSiMe_3$$



The catalytic reduction of ethynes with participation of hydrosilanes,[249-251] boranes,[252] or hydrogen[253] also leads to the formation of the corresponding alka-1,3-dienes, for example:

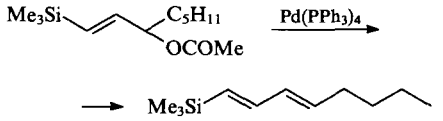
$$PrC{\equiv}CH + R_3SiH \xrightarrow{Cat} CH_2{=}CPr{-}CPr{=}CHSiR_3,$$

Cat = $Ni(acac)_2 \cdot AlEt_3$, $Ni(acac)_2 \cdot LiAlH_4$.

$$Me_3SiC{\equiv}CH + H_2 \xrightarrow{Cat} Me_3SiCH{=}CH{-}CH{=}CHSiMe_3,$$

Cat = $[(PPh_3)FeHX_2]BPy_4$.

Several examples of the synthesis of silicon-containing diene hydrocarbons and their aliphatic[254] and alicyclic[255,256] derivatives as a result of the [2+4]-cycloaddition reactions and subsequent isomerisation of the cyclic adducts as well as the β-elimination of carboxylic acids from the corresponding silicon-containing esters under the influence of a palladium catalyst[257,258] have been described.



Finally a comparatively interesting method of synthesis of 1-trialkylsilylalka-1,3-dienes has been developed by Japanese workers on the basis of the chromium(II) chloride-catalysed interaction of dibromomethyltrimethylsilane with cinnamaldehyde and its analogues.[259]

$$RCH{=}CH{-}CH{=}O + Me_3SiCHBr_2 \xrightarrow{CrCl_2} RCH{=}CH{-}CH{=}CHSiMe_3$$

The reaction takes place at room temperature and the yields of the dienes are ~80%.

III. Chemical properties of 1- and 2-triorganosilylalka-1,3-dienes and their derivatives

The chemical reactions of 1- and 2-triorganosilylalka-1,3-dienes and their carbofunctional derivatives known at the present time may be divided into three groups: (1) reactions with participation of multiple bonds — addition, polymerisation, and complex formation reactions; (2) reactions with participation of silicon–carbon bonds; (3) reactions with participation of functional groups.

The mode and selectivity of the addition of reagents of different nature are known to depend in a complex manner on the structure of the 1,3-dienes, their polarity, and their polarisability.[260] The study of the characteristic features of the variation of their reduction half-wave potentials,[56,208] the parameters of Raman and IR spectra,[175,261,262] as well as the bond lengths[263] and the enthalpies of formation of the bonds[264] on passing from 1,3-diene hydrocarbons and their derivatives to silicon-containing compounds with a similar structure permitted the conclusion that silicon-containing substituents at the double bond are weaker electron-donating agents than the analogous hydrocarbon groups. The measured molecular refractions indicate the high polarisability of the conjugated π-bonds in 1-trialkylsilylalka-1,3-dienes.[56,265]

Similar conclusions concerning the nature of the redistribution of electron density in silicon-containing dienes have been reached from the analysis of the ^1H and ^{13}C NMR spectra[125,175,266,267] and their dipole moments.[128,175,268]

In conformity with the existing tradition, the observed features of the electronic structure of the silicon-containing dienes have been explained by the delocalisation of the π-electron density of the multiple bonds to the unoccupied *d* orbitals of silicon ($d_\pi - p_\pi$ conjugation).

1. Addition of electrophiles

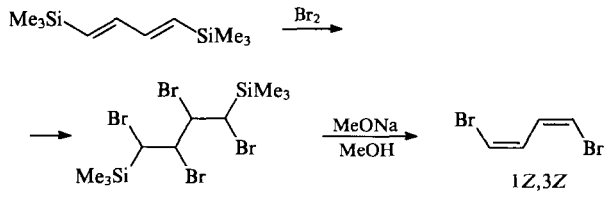
The interaction of silicon-containing 1,3-diene hydrocarbons and their derivatives with the halogens has been investigated only for reactions with bromine. Regardless of the structure of the substrates, it proceeds nonselectively in all cases. 1-Trialkylsilylalka-1,3-dienes combine with bromine at the double bond remote from the silicon atom and in the 1,4-positions,[50] the ratio of the dibromo-derivatives formed being ~1:1. On heating, the 1,4-dibromo-derivatives rearrange with migration of the double bond to the α,β-position relative to the silicon atom.

$$Me_3SiCHBrCH{=}CHCH_2Br \rightleftharpoons Me_3SiCH{=}CHCHBrCH_2Br$$

It is appropriate to recall that the allyl rearrangement of dibromo-derivatives obtained on bromination of 1,3-diene hydrocarbons is directed towards the formation of 1,4-dibromo-derivatives.[260] Silicon-containing dienes are brominated more slowly than hydrocarbons with a similar structure and the rate of reaction is described by a third-order kinetic equation.[269] The increase in the kinetic order of reaction to three is caused, according to the authors,[269] by the relative stability of the complexes $A_\pi \cdot Br_2$, where A_π is an alkene–bromine complex.

Ethyl 5-trimethylsilylpenta-2,4-dienoate also combines with bromine nonselectively at both double bonds. The 1,4-adducts were not detected.[175]

Exhaustive bromination of 1,4-bis(trimethylsilyl)buta-1,3-diene leads to the corresponding tetrabromo-derivative. On treatment with sodium methoxide in methanol, the latter affords 1,4-dibromobuta-1,3-diene in a satisfactory preparative yield.[270]



Judging from the available data,[271] the addition of the elements of hypohalites to silicon-containing 1,3-diene hydrocarbons proceeds chemo- and regio-specifically at the double bond remote from the silicon atom.

$$R^1_3SiCH{=}CH{-}CR^2{=}CHR^3 + \text{>N–X} \xrightarrow{R^4OH} R^1_3SiCH{=}CH{-}CR^2(OR^4)CHR^3X$$

X = Cl, Br.

The 1,3-diene was treated with the haloamide in an alcoholic medium.[271]

Alkyl hypohalites add to 3-*tert*-butyl-4-methyl-1-triethylsilylpenta-1,3-diene, containing a double bond subjected to a considerable steric hindrance, also only at the remote double bond.[272] This observation shows that the addition of alkyl hypochlorites and alkyl hypobromites to the double bond remote from the organosilicon substituents, which is unexpected from the standpoint of Ingold's classical ideas,[260] is due to nonsteric factors.

Organosulfenyl and organoselenyl halides also react at the double bond remote from the silicon atom with attachment of the electrophilic species to the terminal carbon atom of the 1,3-diene fragment.[120,273]

$$R^1_3SiCH{=}CH{-}CR^2{=}CHR^3 + R^4YX \longrightarrow$$
$$\longrightarrow R^1_3SiCH{=}CH{-}CR^2XCHR^3YR^4$$

X = Cl, Br; Y = S, Se.

The adducts containing mobile halogen atoms in the allylic position readily isomerise to 1,4-adducts, while on treatment with triethylamine they split off the hydrogen halide.[120,273]

On distillation, selenium-containing adducts are partly dehydrohalogenated, which hinders their isolation in a pure state.[273]

The addition of C-electrophiles has been investigated in relation to the interaction of 1-trialkylsilylbuta-1,3-dienes with chloromethyl ethers[118,274] or sulfides[142] catalysed by aprotic Lewis acids ($ZnCl_2$,[274] $ZnBr_2$,[142] $TiCl_4$[118]).

According to the data of Shikhmamedbekova and Khudieva, in the presence of zinc(II) chloride chloromethyl ether adds both in the 1,4-positions and to the double bond remote from the silicon atom in silicon-containing 1,3-diene hydrocarbons (the ratio of the adducts formed is 1:3:3).[274]

$$Me_3SiCH{=}CH{-}CH{=}CH_2 + ClCH_2OMe \xrightarrow{ZnCl_2}$$
$$\longrightarrow Me_3SiCHClCH{=}CHCH_2CH_2OMe$$
$$\longrightarrow Me_3SiCH{=}CH{-}CHClCH_2CH_2OMe$$

In the presence of titanium(IV) chloride, the interaction of dichloromethyl ether with 1-trialkylsilylalka-1,3-dienes leads to the corresponding silicon-free 1,3-diene aldehydes.[118]

$$R{-}\!\!\sim\!\!\sim\!\!SiMe_3 + Cl_2CHOMe \xrightarrow{TiCl_4}$$
$$\longrightarrow R{-}\!\!\sim\!\!\sim\!\!CHO$$

The possible paths in this interesting reaction are not discussed.

The reaction of 3-trimethylsiloxy-1-trimethylsilylbuta-1,3-diene with α-chlorosulfides results in the formation of the corresponding unsaturated carbonyl compounds, which presupposes the addition of the sulfide to the terminal double bond.[142]

$$Me_3Si{-}\!\!\sim\!\!\sim\!\!OSiMe_3 + ClCHRSPh \xrightarrow{ZnBr_2}$$
$$\longrightarrow Me_3Si{-}\!\!\sim\!\!\sim\!\!C(=O){-}\!\!\sim\!\!R$$

R = H, Pr.

2. Addition of nucleophiles

The interaction of 1-trialkylsilylalka-1,3-dienes with thiols in the presence of sodium thiolate had been described.[275] It has been shown that the reaction takes place only under severe conditions (100 °C, 70 h). The overall yield of the adducts does not exceed 20%. Chromatographic and spectroscopic analysis of the products showed that the thiol added to the 1,4-, 3,4-, and 4,1-positions (the yields of the corresponding products were 41%, 57%, and 2%).

The reactions of unsaturated organosilicon compounds with ammonia and amines are also nucleophilic addition processes, although their mechanism has not been investigated.

The attempts to add ammonia to 1-trialkylsilylbuta-1,3-dienes have not been successful: in the presence of metallic sodium, hydrogen undergoes 1,4-addition with formation of trialkylbut-2-enylsilane.[276]

Under the same conditions, secondary amines react with silicon-containing 1,3-dihydrocarbons, giving rise to mixtures of 1,4- and 3,4-adducts (~2:3) (Scheme 3).[277]

Scheme 3

$$R^1_3Si{-}\!\!\sim\!\!\sim\!\!C(R^2){=}CH{-}CHR^3 + R^4_2NH \xrightarrow{Na}$$
$$\xrightarrow{1,4} R^1_3Si{-}CH{=}CH{-}C(R^2)(NR^4_2){-}R^3$$
$$\xrightarrow{3,4} R^1_3Si{-}CH(R^2){-}CH{=}CH{-}NR^4_2\,(R^3)$$

The methyl group in the 3-position promotes addition in the 1,4-positions. The same group at the C(4) atom hinders the addition, but hardly affects the ratio of the isomeric products.[277]

The interaction with organometallic compounds was first achieved by Sadykh-Zade[278] in relation to the reaction of 1-trimethylsilylbuta-1,3-diene with butyllithium.

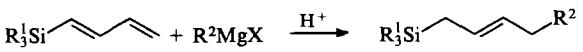
According to the author, the silicon-containing hydrocarbon obtained after demetallating the adduct with water had the structure of *trans*-1-trimethylsilyloct-2-ene. It was established somewhat later that silicon-containing alka-1,3-dienes are formed after the demetallation of a mixture of alk-1-enes and alk-2-enes.[279] The ratio of the isomers formed hardly depends on the structure of the 1,3-diene fragment. It is not possible to isolate the adducts in the reactions of 1-trialkylsilyl-3-methylbuta-1,3-diene with lithium alkyls: regardless of the structure of the organolithium compounds and the experimental conditions, the diene polymerises.[279]

It is also noteworthy that the decrease in temperature and the replacement of the ether employed as the solvent by THF in the reactions of 1-trialkylsilylbuta-1,3-diene and 1-trialkylsilylpenta-1,3-diene promotes the formation of 1,4-adducts. In hydrocarbon solvents, the dienes polymerise.

Judging from the available data, 1-dimethylboryl-1-trimethylsilylbuta-1,3-diene combines with butyllithium at the double bond remote from the silicon atom. The adducts formed are readily alkylated.[37]

$$Me_3Si{-}\!\!\sim\!\!\sim\!\!BMe_2 \xrightarrow{BuLi} Me_3Si{-}CH(Li){-}CH{=}CH{-}Bu \xrightarrow{MeI}$$
$$\longrightarrow Me_3Si{-}CH(Me){-}CH{=}CH{-}Bu\;(BMe_2)$$

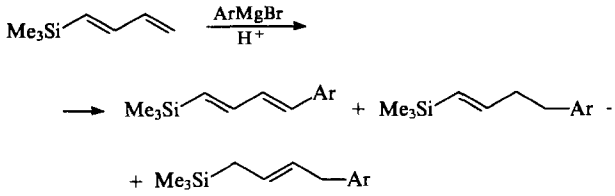
Mixed organomagnesium compounds add to 1-trialkylsilylbuta-1,3-dienes exclusively in the 1,4-positions.[280]



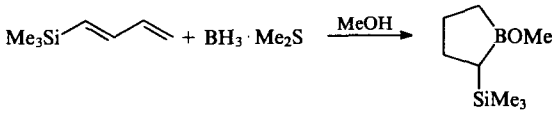
R^1 = Me, Et; R^2 = Et, Pr.

A change in temperature from −25 to 35 °C and of the solvent (Et_2O, glyme, THF) did not affect the mode of the reaction and the yield of its products.

On interaction with 1-trimethylsilylbuta-1,3-diene in the presence of transition metal complexes, arylmagnesium halides give rise to a mixture of products of substitutional arylation of the products of addition to the double bond and in the 1,4-positions.[281]



On interaction with 1-trimethylsilylbuta-1,3-diene, borane stabilised by trimethylsulfide gives rise to a cyclic adduct. The latter affords a satisfactory yield of (±)-1-methoxy-2-trimethylsilylborolane on treatment with methanol.[282]

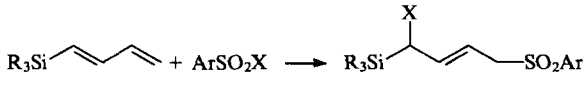


3. Free-radical addition

The free-radical addition of thiols has been investigated only in relation to the interaction of 1-triethylsilylbuta-1,3-diene with ethanethiol. *tert*-Butyl peroxide was used as the initiator.[275] As in nucleophilic addition reactions, a mixture of 1,4-, 4,1-, and 3,4-adducts is formed in this process in proportions of 65 : 10 : 25.[275]

The interaction of organic sulfonic acids with acid halides, initiated by copper(I) halides (the Asher – Vovsi reaction) or thermally, is also included among the free-radical addition reactions.

It has been shown in relation to the reactions of 1-methyldiethylsilylbuta-1,3-diene that benzenesulfonic acid chloride adds to the above 1,3-diene on heating in the presence of the Asher – Vovsi catalyst — copper(I), triethylamine, and acetonitrile — exclusively in the 1,4-positions;[126] the reaction with the acid bromide proceeds also without a catalyst. The addition of the latter does not alter the mode of reaction. The acid iodide adds spontaneously and exothermically even at room temperature and also only in the 1,4-positions.



R_3Si = Me_3Si, $MeEt_2Si$, Et_3Si;

Ar = Ph, *p*-MeC_6H_4, *p*-$NO_2C_6H_4$; X = Cl, Br, I.

Toluene-*p*-sulfonic and *p*-nitrobenzenesulfonic acids behave similarly in this reaction.[124] The chlorides of methane- and ethane-sulfonic acids react with 1-trialkylsilylbuta-1,3-diene under more severe conditions to form a mixture of 1,4- and 3,4-adducts.[124,125] It is of interest that 5,5-dimethylhexa-1,3-diene, a hydrocarbon with a similar structure, combines with the chlorides of alkane- and arene-sulfonic acids under milder conditions exclusively in the 1,4-positions.[124] Specially formulated experiments established that the 1,4-adducts do not isomerise to the 3,4-adducts on heating in the presence of the Asher – Vovsi catalyst.[124]

Within the limits of the accuracy of the method of competing reactions, the rate of addition is almost independent of the nature of the aromatic group (phenyl, *p*-tolyl, and *p*-nitrophenyl) attached to sulfur.[124] Variation of the alkyl groups at the silicon atom (R_3Si = Me_3Si, $MeEt_2Si$, Et_3Si) also does not affect the rate and mode of the reaction.[125]

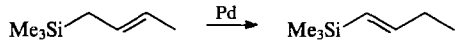
1-Methyldiethylsilyl-3-methylbuta-1,3-diene reacts with the chlorides of alkane- and arene-sulfonic acids with much more difficulty than dienes without substituents in the 1,3-diene fragment.[127] A mixture of the 1,4- and 3,4-adducts and of the product of substitutional sulfonylation — 4-alkanesulfenyl-1-methyl diethylsilyl-3-methylbuta-1,3-diene (~10%) — has been obtained in an overall yield not exceeding 25%. Attempts to carry out the reaction of this silicon-containing diene with the chlorides or bromides of arenesulfonic acids were unsuccessful: the initial reactants which failed to react are recovered at low temperatures while at high temperatures charring takes place.

1-Trialkylsilylpenta-1,3-diene behaves similarly in the reaction with arene-sulfonyl halides.[127]

The above data combined with those obtained in the study of the influence of the nature of the catalyst components (metal, ligands) and the solvent (benzene, toluene, acetone, dibutyl ether, carbon tetrachloride, acetonitrile, chloroform, pyridine, methanol, dimethyl sulfoxide, hexamethylphosphoramide)[283] enabled the author to conclude that the thermally initiated addition of the bromides and iodides of sulfonic acids proceeds as a classical free-radical chain process.[282] The addition of the acid chlorides and bromides with participation of copper salts is a redox-initiated intracomplex reaction of the ligands in which the 1,3-diene participates as a bidentate ligand. In those cases where the interaction requires relatively high temperatures, the reagent – metal – diene complex decomposes and the reaction proceeds as the usual redox-initiated free-radical addition with formation of a mixture of the 1,4- and 3,4-adducts.[283]

4. Reduction and oxidation of 1- and 2-triorganosilylalka-1,3-dienes

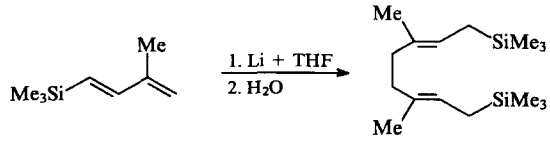
The catalytic hydrogenation of 1-trialkylsilylalka-1,3-dienes in the presence of platinum or palladium catalysts proceeds at room temperature and at atmospheric pressure with formation of a mixture of 1-triorganosilylalk-1-enes and 1-triorganosilylalk-2-enes.[41,42,284] The study of the composition of the hydrogenation products as a function of time has shown that 1-trialkylsilylalk-2-enes predominate in the mixture in the first stage, while 1-trialkylsilylalk-1-enes predominate in the concluding stage.[284] These results indicate that the alk-2-enes isomerise in the course of time with migration of the double bond towards the silicon-containing substituent.



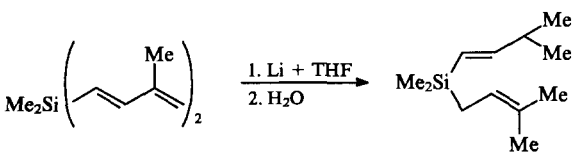
Under the same conditions in the presence of a palladium catalyst, 1,2-bis(trialkylsilyl)alka-1,3-dienes also combine with hydrogen in the 1,4-positions with formation of 1,2-bis-(trialkylsilyl)but-2-enes, which are not apparently hydrogenated further owing to steric factors.[52,53]

Exhaustive hydrogenation of 1-trialkylsilylalka-1,3-dienes and their functional derivatives in the presence of $Pd/CaCO_3$ or Pt/C afforded the corresponding saturated organosilicon compounds.[41,42,242,274]

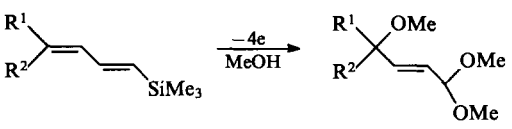
The interaction of 1-trimethylsilyl-3-methylbuta-1,3-diene with lithium in an aprotic medium results in the formation of hydrodimerisation products.[285]



Under the same conditions, dimethylbis(3-methylbuta-1,3-dienyl)silane is hydrogenated in the 1,4- and 3,4-positions.[285]



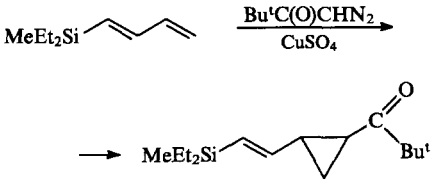
There is only one communication which describes results of the electrochemical oxidation of 1-trialkylsilylalka-1,3-dienes in methanol.[194]

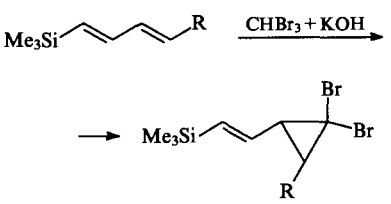


The reaction proceeds as the addition of methoxyl radicals accompanied by the substitution of the silyl group.

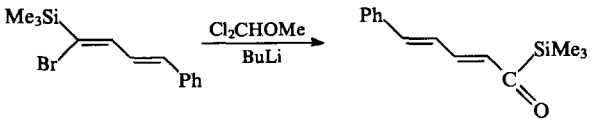
5. Cycloaddition reactions

The interaction with carbenes — [1+2]-cycloaddition — has been used as a method of synthesis of the corresponding alkenylcyclopropanes also in relation to silicon-containing dienes. Thus it is known that pivaloylcarbene[286] and dibromocarbene[22] add chemoselectively to the double bond of 1-trialkylsilylbuta-1,3-dienes remote from the silicon atom.





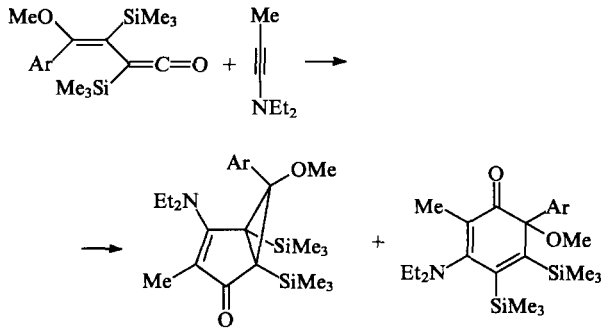
However, in the interaction of 1-bromo-4-phenyl-1-trimethylsilylbuta-1,3-diene with methoxymethylenecarbene a silicon-containing ketone was obtained instead of the expected cyclic adduct.[287]



The [2+2]-cycloaddition in the interaction of disilylated ketenes with 1-diethylaminoprop-1-yne takes place nonselectively (Scheme 4).[254]

Diene synthesis {[2+4]-cycloaddition} — the interaction of conjugated silicon-containing dienes with dienophiles — is one of the most thoroughly investigated reactions of 1- and 2-trialkylsilylalka-1,3-dienes and their derivatives. A considerable proportion of the studies in this field have been carried out in order to demonstrate the 1,3-diene structure of the silicon-containing

Scheme 4



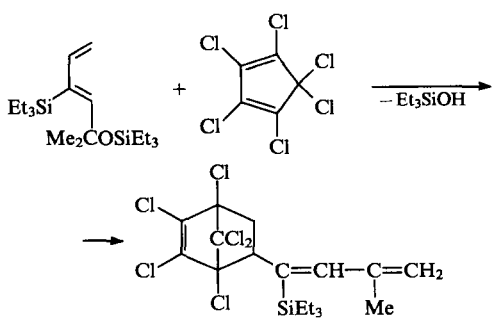
compounds (see, for examples, Refs 6, 27, 52, 109, 129, 175, 208, 249, 274, etc.). However, the studies of the influence of the structure of the diene and the dienophile on the relative rates and the regio- and stereo-selectivity of the ring formation are of greater interest.[18,170,177,288–290] Diene synthesis is also a key stage in the multistage synthesis of compounds such as (±)-daunomycin, (±)-isodaunomycin[139,140,289,291,292] the aglucone of chlorotricin,[216] the agilactones A and F,[293] and other complex polycyclic biologically active substances.[20,93,216,217,289,294,295]

The importance of this aspect increased sharply after the development of methods for the protodesilylation (the removal of the silyl protecting group) of the cyclic adducts by potassium fluoride[20,160,209,296,297] and especially for the replacement of the triorganosilyl group by hydroxy-groups on treatment of silicon-containing compounds with lead(IV) tetraacetate[170,291,298] or perfluorotetraacetate.[140]

Diene synthesis with participation of organosilicon 1,3-diene compounds was first carried out in 1954 by heating a mixture of the products of the hydrogenation of 1-trimethylsilylbut-3-en-1-yne with maleic anhydride.[1] Maleic anhydride,[1,6,27,42,52,53,104,105,109,111,112,130,138,170,175,177,201,208,274,299–303] methylmaleic anhydride,[138,304] maleimides,[130,170,201,300] acrolein,[177] methylacrolein,[104,304] acrylonitrile,[177] methyl acrylate,[138,288,304] ethyl acrylate,[18,104,112] dimethyl maleate,[104,177,205] diethyl maleate,[177] 1,4-benzoquinone,[104,170,201] 2-methylbenzoquinone,[304] 3-methylbenzoquinone,[304] 2,6-dimethylbenzoquinone,[112] 2,3-dimethoxybenzoquinone,[290] 1,4-naphthoquinone,[100,130,138,300] quinizarinquinone and its derivatives,[139–141,290,291] tetracyanoethene,[180,184,249,301] and other compounds containing a dienophile group[100,112,205,298,300] were used later as dienophiles.

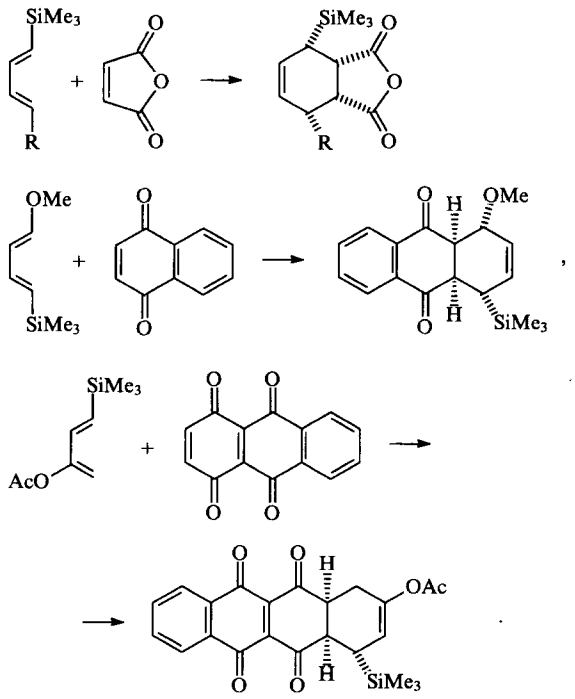
Examples of the cyclodimerisation of silicon-containing 1,3-dienes via the [2+4]-mechanism in which the diene itself plays the role of the dienophile are known.[305] The reaction is chemo- and regio-selective, but the preferred path involves condensation via the unsubstituted vinyl group of the 1,3-diene dienophile.

Hexachlorocyclopentadiene (diene) undergoes also an unusual condensation with the triethylsilyl ether of 2-methyl-4-triethylsilylhexa-3,5-dien-2-ol (dienophile):[116] the adduct formed splits off triethylsilanol under the conditions of the isolation process.

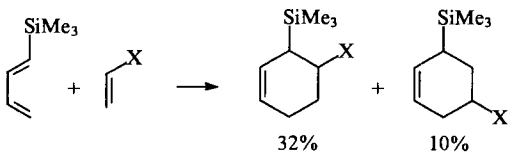


Compounds with activated triple bonds can also act as dienophiles: propiolic and methylpropiolic acids,[138,292,304] the nitrile[294] and ester[288,300,304] of propiolic acid, ethynedicarboxylic acid and its dimethyl ester,[100,104,170,300] and bis(trifluoro-methyl)ethyne.[35]

It has been noted that, in reactions with symmetrical dienophiles such as maleic anhydride, maleimide, etc., silicon-containing dienes condense with somewhat greater difficulty than silicon-free hydrocarbons.[112,305,306] Other conditions being equal, 2-silyldienes are more reactive than the isomeric compounds containing the organosilicon group at the first or fourth carbon atom of the conjugated fragment. The introduction of other substituents in the 1- and/or 4-position also hinders the cycloaddition. For example, 1,4-disubstituted dienes of the type $Me_3Si(CH{=}CH)_2X$ (X =COMe, COOMe) interact with the maleic anhydride only in the (*E*,*E*)-configuration on heating in a sealed tube.[112,175] As a rule, the reactions with symmetrical dienophiles are stereoselective: in relation to the plane of the ring, all the substituents are in the *cis*-positions, for example:



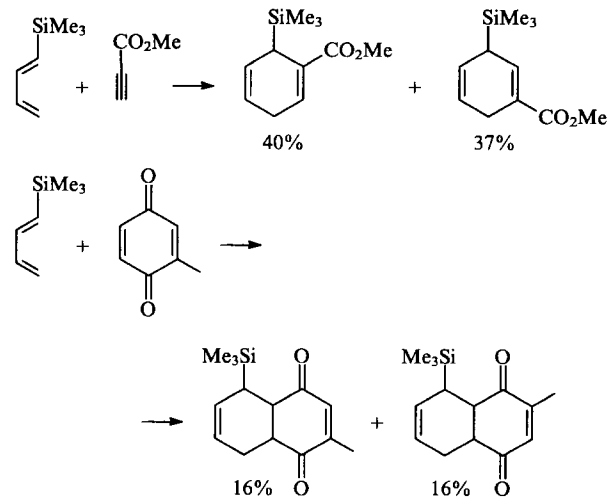
The acrylic dienophiles $CH_2{=}CHX$ (X = CHO, CN, COOR, etc.) can react with 1-trialkylsilylalka-1,3-dienes to form two regioisomers. The available data show that the reaction proceeds non-regioselectively, but 1,2-disubstituted cyclohexenes are formed in somewhat greater amounts (the *ortho*-effect).[112,304]



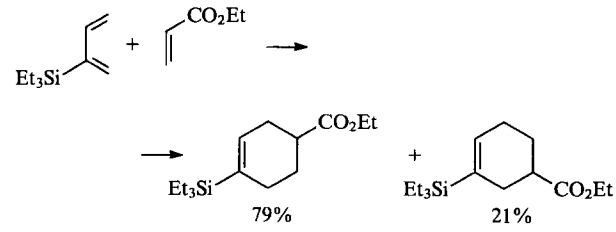
This difference virtually disappears in the reactions of silicon-containing dienes with methyl propiolate and methylbenzoquinone (Scheme 5).[304]

The isomeric 1,3- and 1,4-disubstituted cyclohexenes are formed in proportions of 1:3.3 in the interaction of ethyl acrylate with 2-triethylsilylbuta-1,3-diene. The use of catalysts (usually aprotic Lewis acids) promotes the formation of 1,4-isomers and increases the yield of cyclic adducts (Scheme 6).[18,104]

Scheme 5



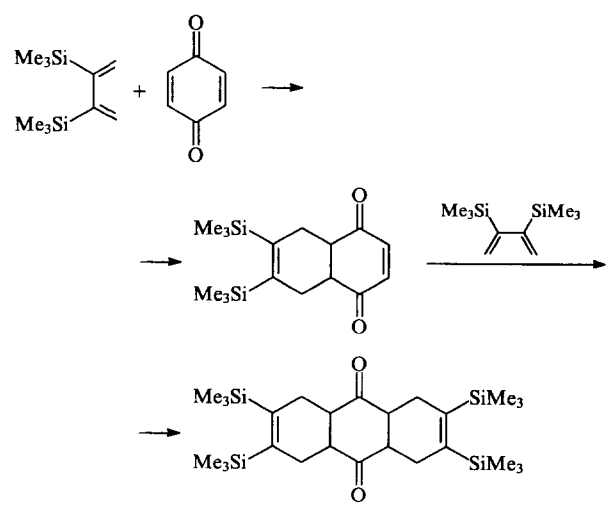
Scheme 6



In the presence of boron trifluoride etherate, the ratio changes to 1:7.3.[104]

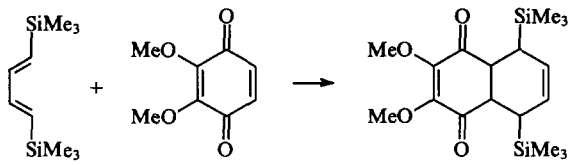
A comparative study of the regioselectivity of the cycloaddition of the diene $Me_3Si{-}CH{=}CH{-}CR^1{=}CHR^2$ (R^1 =H, R^2 = Me; R^1 =Me, R^2 =H, Me_3SiO) to various dienophiles by Fleming showed that it is controlled to a larger extent by the nature of the substituents R^1 and R^2 than by the trialkylsilyl fragment at C(1).[288]

The formation of adducts with both multiple bonds is also possible in the reactions of silicon-containing dienes with benzoquinones, naphthoquinones, and quinizarinquinones. In most of the instances investigated, only one of the monoadducts is formed:[201,290,304] The possibility of obtaining the second isomer has not been discussed, although there are indications that it is absent.[201] The formation of an adduct via both double bonds of benzoquinone has been specially emphasised only in the study of Garrat and Tsotins.[170]

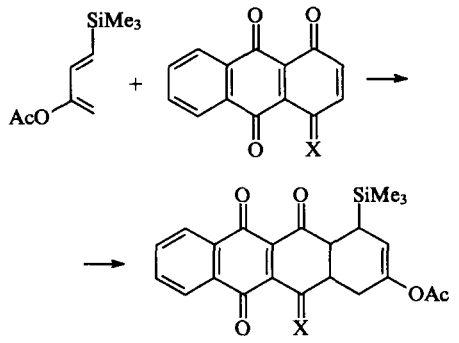


It is also appropriate to note that methyl-1,4-benzoquinone [304] and 2,3-dimethoxy-1,4-benzoquinone [290] combine with silicon-containing dienes only via the unsubstituted double bond (Schemes 5 and 7).

Scheme 7



Naphthoquinones, [130] quinizarinquinones, [139,140,289,291] and ketiminequinizarinquinones [289] form cyclic adducts exclusively via the 'external' double bond.



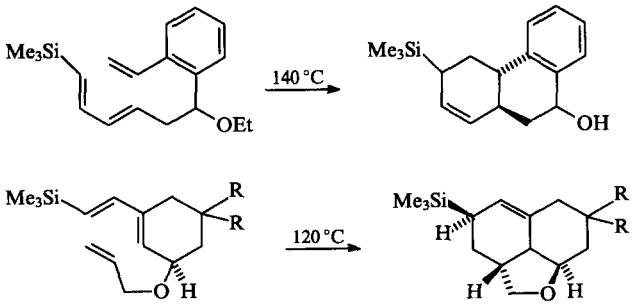
X = O, TsN.

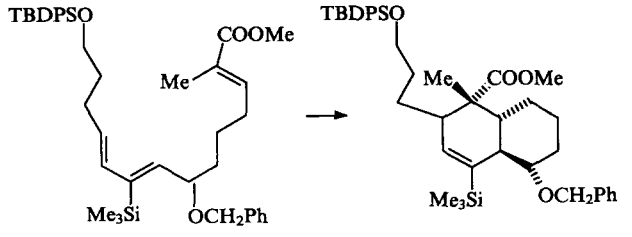
The high regio- and stereo-selectivity of the cycloaddition can be explained in terms of the perturbation of the frontier orbitals [306] of the electron-donating diene and the electron-accepting dienophile.

Examples of diene synthesis employing the dienes formed on pyrolysis of silicon-containing sulfolenes have been described. [148,151]

Intramolecular diene synthesis occupies a special place in the stereospecific synthesis of cyclic natural products.

1,3-Diene and dienophile fragments can be components of aliphatic [216,217] or alicyclic [20,105,131,293,295] compounds.





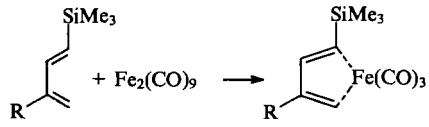
TBFDPS = *tert*-butyl diphosphite-silane.

This reaction is distinguished by a high stereoselectivity.

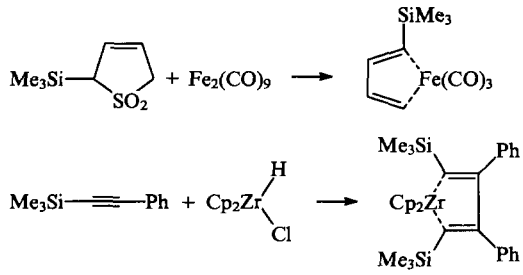
6. Synthesis of complexes with silicon-containing 1,3-diene ligands

Numerous iron, [96,106,167,190,307–310] cobalt, [311,312] zirconium, [313–315] and other transition metal [190,316] complexes of acyclic silicon-containing 1,3-dienes have now been obtained. In all cases, the 1,3-dienes behave as bidentate ligands.

The synthesis of the complex may include both the interactions of silicon-containing 1,3-diene structures already formed with metal complexes (ligand exchange), i.e.



and the interaction of metal complexes with organic precursors of 1,3-dienes. [307,310,315] The method presupposes the synthesis of silicon-containing 1,3-diene compounds in the course of the formation of the complex.



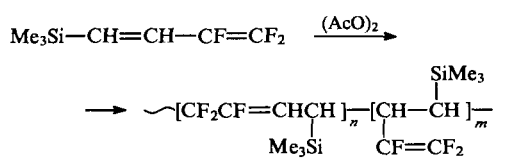
In the vast majority of cases, the structure of the silicon-containing complexes has been demonstrated by X-ray diffraction.

The reactions of silicon-containing complexes with carboxylic acids, [226–229] their halides, [106,308,309] and ketones, [314] as well as photochemical isomerisation reactions [316] have been described.

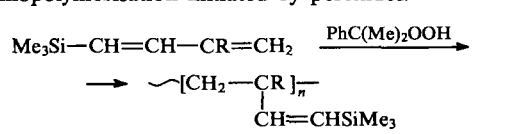
7. Polymerisation and copolymerisation of silicon-containing alka-1,3-dienes

The polymerisation of silicon-containing 1,3-dienes was first reported in 1956. According to the data of Shchukovskaya et al., [5] 3-methyl-2-triethylsilylbuta-1,3-diene gives rise to a viscous oil with a molecular mass of 9 000 on heating with *tert*-butyl peroxide. The structure and physicochemical properties of the polymer obtained were not investigated.

Somewhat later, Haszeldine and coworkers [107] showed that 3,4,4-trifluoro-1-trimethylsilylbuta-1,3-diene polymerises nonregioselectively under the influence of acetyl peroxide.



In contrast to fluorinated monomers, 1-trialkylsilylbuta-1,3-dienes and 3-methyl-1-trialkylsilylbuta-1,3-dienes give rise to high-molecular-mass compounds containing only 3,4-units on homopolymerisation initiated by peroxides. [317–319]

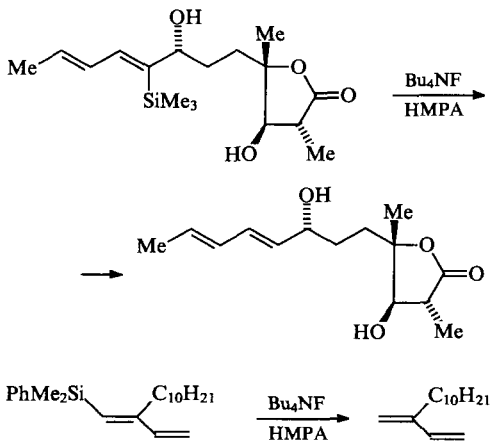


The copolymerisation of silicon-containing 1,3-diene hydrocarbons with vinyl monomers has also been investigated. [320,321] and the copolymerisation constants and activity factors have

been determined for 1-triethylsilylbuta-1,3-diene and styrene.[320,322,323] Similar high-molecular-mass compounds have been obtained by the copolymerisation of 1-triethylsilylbuta-1,3-diene with styrene on a cathode.[324] Copolymers having effective mechanical characteristics have been synthesised from arylvinyl monomers and 2-trimethoxysilylbuta-1,3-diene.[321]

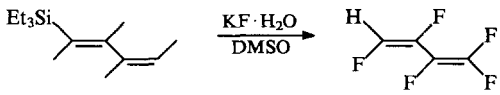
8. Reactions with participation of silicon–carbon bonds

The protodesilylation of 1- and 2-triorganosilylalka-1,3-dienes takes place with much greater difficulty than that of structurally similar 1-trialkylsilylalk-3-en-1-ynes.[26] This method has come to be fairly widely used only when the possibility of removing the silyl group from silicon-containing dienes by means of the fluoride anions had been demonstrated. Tetrabutylammonium fluoride[20,160,296,297] or potassium fluoride[168,169] are usually employed as fluoride anion donors. Both silicon-containing 1,3-diene hydrocarbons[296] and their derivatives[169,209,297] have been desilylated.



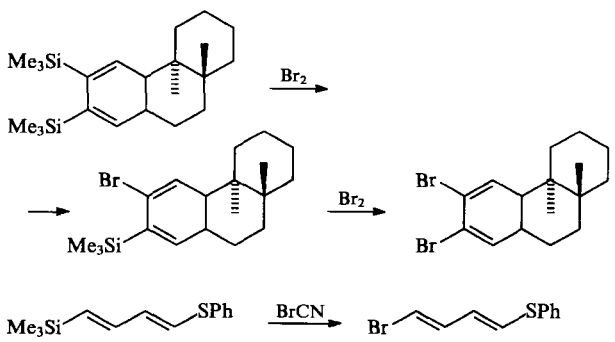
HMPA = hexamethylphosphoramide.

The protodesilylation by tetrabutylammonium fluoride is as a rule carried out in hexamethylphosphoramide or tetrahydrofuran[296,297] and that by potassium fluoride is performed in dimethyl sulfoxide.[209]



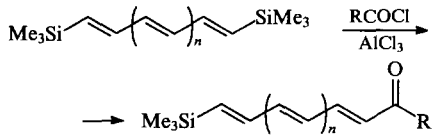
The use of alkalis or alkoxides as the nucleophile is relatively effective in the removal of the silyl protecting group, although it is known that dehydrohalogenation and desilylation take place on treatment of 1,2,3,4-tetrabromo-1,4-bis(trimethylsilyl)butane with sodium methoxide. (1*E*,4*E*)-dibromobuta-1,3-diene was first obtained by this method.[270]

Examples of the replacement of triorganosilyl groups by halogen on interaction of the corresponding 1,3-dienes with bromine[256] or bromocyanogen[204] are known.



The attempt to introduce iodine instead of the trimethylsilyl group by treating 1-trimethylsilylnona-1,3-diene with iodine was unsuccessful.[31]

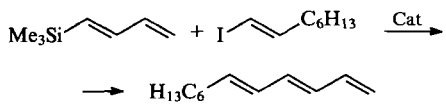
The reaction involving the replacement of the trialkylsilyl group by an acyl group in the presence of anhydrous aluminium chloride may be recommended as a convenient preparative method of synthesis of 1,3-diene ketones.[32,325,326]



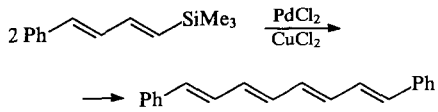
The use of dibasic acid dichloride in this reaction leads to the corresponding polyenepolyones.[325]

A similar acylation reaction is also known for complexes of 1-trialkylsilylalka-1,3-dienes with iron carbonyl.[106]

The alkenylation[327] and arylation[328] of silicon-containing 1,3-dienes by the corresponding halides occurs only in the presence of palladium catalysts — $Pd(OAc)_2.P(OEt)_3$, $PdCl(\eta^3\text{-}C_3H_7)$, etc.

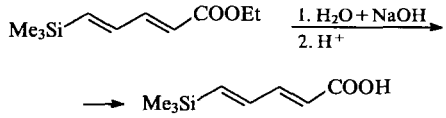


Naso[204] described a very interesting 'dimerisation' reaction of 1-trialkyl silylalka-1,3-dienes on treatment with copper and palladium chlorides accompanied by desilylation.

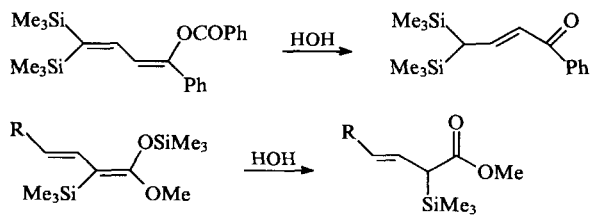


9. Reactions with participation of functional groups

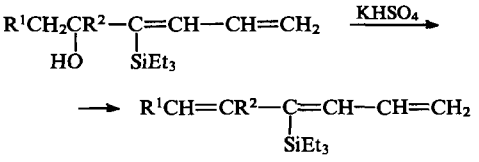
Reactions of this type of derivatives of silicon-containing 1,3-diene hydrocarbons have been least investigated. It has been reported that ethyl (5*E*,*E*)-trimethylsilylpenta-2,4-dienoate is hydrolysed by an aqueous alcoholic solution of sodium hydroxide without the cleavage of the silicon–carbon bond and a change in configuration.[175]



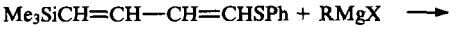
Hydrolysis of alkoxy-1,3-dienes,[14,131] acyloxy-1,3-dienes,[136] and mixed acetals[101] in an acid medium leads to unsaturated ketones or esters respectively.



Primary silicon-containing 1,3-diene alcohols give rise to the corresponding aldehydes in satisfactory yields on oxidation with pyridinium chlorochromate.[329] Tertiary silicon-containing alcohols are dehydrated on heating with acid potassium sulfate, but there is no elimination of the corresponding trialkylsilanols.[61,62]

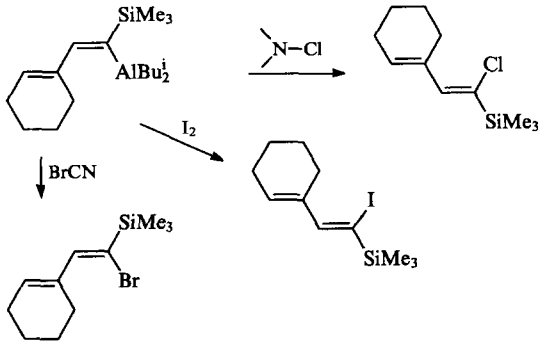


Silicon-containing 1,3-dienyl sulfides are alkylated by organomagnesium compounds in the presence of palladium or nickel complexes.[204]



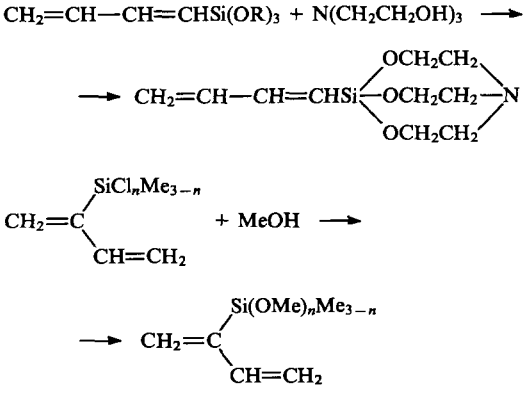
Derivatives of silicon-containing 1,3-diene hydrocarbons containing the BX_2 (X = Cl, Br, OAlk) group at the double bond lose boron on treatment with carboxylic acids[35] and are alkylated by mixed organozinc compounds or α-haloalkenes in the presence of palladium complexes.[210,211,213] On oxidation, these hydrocarbons give rise to silicon-containing ketones,[34] whilst their interaction with carbon monoxide in an alcoholic medium affords the esters of silicon-containing 1,3-dienoic acids.[212]

Organoaluminium derivatives of silicon-containing alka-1,3-dienes give rise to the corresponding halides on treatment with donors of the electrophilic halogens.[33]



Alka-1,3-dienes containing halogens or alkoxy-groups at the silicon atom enter into alcoholysis[105] or transalkylation (Scheme 8)[301] reactions.

Scheme 8



Analysis of the data examined in this review permits the following generalisations.

(1) The methods based on the Wittig, Horner–Emmons, Peterson, and dehydration reactions of silicon-containing alcohols make it possible to obtain any silicon-containing 1,3-diene hydrocarbons and their carbofunctional derivatives with a specified structure in a satisfactory preparative yield. In the synthesis of (1*E*,3*E*)-isomers, preference should be given to the methods based on the Wittig, Horner–Emmons, or dehydration reactions, whereas in the synthesis of (1*E*,3*Z*)- or (1*Z*,3*Z*)-isomers the second version of the Peterson reaction is preferred.

(2) Regardless of the structure of the substrate and the nature of the reagent, in the reactions of conjugated silicon-containing dienes the attacking species is almost always attached to the C(4) atom of the 1,3-diene fragment remote from the silicon atom. The occurrence of this reaction path in the addition reactions cannot be accounted for by the steric influence of the triorganosilyl group and is probably due to the stabilisation of the allyl intermediates containing the organosilyl group (formal analogy with 1-phenylbuta-1,3-diene).

(3) In terms of the overall electron-donating effect, the trialkylsilyl group occupy an intermediate position: $R_3C > R_3Si > H$.

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Reduction methods in the synthesis of low-valence platinum and palladium complexes

N Yu Kozitsyna, I I Moiseev

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Abstract. The use of the reduction reactions of platinum(II) and palladium(II) complexes for the synthesis of compounds of these metals in the lowest oxidation states ($0 \leqslant n < 2$) with stabilising π-acceptor type ligands, such as phosphines, phosphides, phenanthroline, and bipyridyl, is discussed. The mechanisms of these reactions as well as the behaviour of tertiary phosphine ligands under the conditions of the reactions between the complexes and reductants are examined. The available structural data on the mononuclear and polynuclear compounds of platinum and palladium in the lowest oxidation states are surveyed. The bibliography includes 138 references.

I. Introduction

Among the known preparative methods of synthesis of complexes of metals in the nickel triad in the lowest oxidation states,[1,2] the following are most frequently employed: direct synthesis from the metals; substitution of the ligands in complexes with the metal in low oxidation states or addition of neutral ligands; reductive elimination; reduction reactions. The reduction reactions are simplest and possess extensive synthetic possibilities. Alkali metals, their alkoxides, hydrazine, sodium tetrahydroborate, carbon monoxide, and hydrogen are usually employed as reductants for the synthesis of complexes containing the metal atoms in the formal '0' oxidation state.

Among the compounds of platinoid metals, those with tertiary phosphines occupy a special place. Platinum(0) and palladium(0) compounds with aromatic tertiary phosphines and related ligands were obtained for the first time in 1957–1958 on reduction of phosphine complexes of platinum(II) and palladium(II) by hydrazine or an alcoholic solution of KOH.[3,4] In the 1970s–1980s, there was an appreciable growth of interest in the chemistry of transition metal complexes with ligands of the type PR_3 because many of them manifested a catalytic activity in processes such as hydrogenation, hydroformylation, and polymerisation. It was believed that these complexes are thermally fairly stable and do not undergo significant changes under the conditions of the catalysed reactions. An extensive set of ligands of the type PR_3 has been used to stabilise complexes in which the metal atom is bound to the H and C atoms as well as the atoms of other nontransition elements.

N Yu Kozitsyna, I I Moiseev Metal-Complex Catalysis Laboratory, Kurnakov Institute of General and Inorganic Chemistry, Russian Academy of Sciences, Leninskii prosp. 31, 117907 Moscow, Russian Federation.
Fax (7-095) 954 12 79. Tel. (7-095) 952 12 03 (I I Moiseev)

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II. Synthesis of phosphine complexes of the type ML_n [M = Pt(0), Pd(0); L = PR_3; $n = 2-4$]

1. Reduction by metals

The reduction of halophosphinepalladium and halophosphineplatinum complexes by metallic sodium in liquid ammonia leads to the formation of the complexes $M(PF_3)_4$ (M = Pd, Pt).[5] This reduction method is not extensively used because of a series of disadvantages. These are principally experimental difficulties associated with the employment of metallic sodium in liquid ammonia and a low yield of the target product because of the insolubility of the reactants in the reaction medium. The same compounds have been obtained by the reaction of MCl_2 (M = Pt, Pd) with PF_3 and metallic copper at 100 °C and 100–300 atm. However, in this case one cannot rule out the possibility that not only the copper but also PF_3 behaves as the reducing agent.[6]

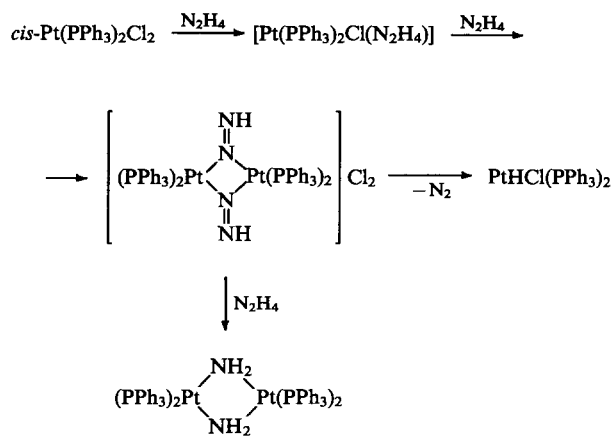
2. Reduction by hydrazine

This method is used successfully to reduce platinum(II) and palladium(II) compounds with tertiary phosphines, phosphites, and arsines.[3,4,7] The first studies on the reduction of platinum complexes by hydrazine led at first sight to contradictory results. Data were obtained indicating that, depending on: the reaction conditions, the nature of the ligands and the halogen atom bound to the metal, and the reaction time, it is possible to obtain both platinum(0) compounds and platinum(II) hydrides.[8] Furthermore, the unusual stability of the compounds described by Malatesta[4] as zero-valent complexes suggested that they are in fact platinum(II) hydrides.[9] However, later independent and careful studies definitely confirmed that platinum(0) compounds are formed in these syntheses.[7,10,11]

The interaction of metal complexes with hydrazine is as a rule a complex multistage process.[12] After the reduction of *cis*-$Pt(PPh_3)_2Cl_2$ at room temperature, certain stable intermediates were isolated. These are cationic dehydrodiimido- and amino-complexes soluble in the reaction medium (ethanol)[13] (Scheme 1).

The hydride complex *trans*-$Pt(PPh_3)_2HCl$ formed in the first stage of the reduction process is isolated from the reaction solution after several hours at room temperature or on heating the solution. This platinum(II) hydride is subsequently converted

Scheme 1



into a platinum(0) complex on treatment with an excess of hydrazine.[4,12]

$$cis\text{-}Pt(PPh_3)_2HCl \xrightarrow[PPh_3]{N_2H_4} Pt(PPh_3)_n$$

$n = 3, 4.$

Thus, by varying the amount of hydrazine, the time, and the reaction temperature, it is possible to obtain either a platinum(0) complex or a platinum(II) hydride. The reduction of *cis*-$Pt(PPh_3)_2Cl_2$ to $Pt(PPh_3)_2$ by an excess of hydrazine at 70–80 °C apparently proceeds via the same mechanism.[8]

The presence of an excess of the phosphine in the reaction solution makes it possible to obtain platinum(0) complexes with a maximum yield. The need for an excess of the phosphine arises from the ability of the zerovalent complexes to dissociate in solution, affording coordinatively-unsaturated compounds.[14]

$$M(PR_3)_4 \rightleftharpoons M(PR_3)_3 \rightleftharpoons M(PR_3)_2 \rightleftharpoons [M(PR_3)]_n$$

M = Ni, Pd, Pt.

The platinum complex of triphenylphosphine $Pt(PPh_3)_4$ is almost fully dissociated and the tricoordinate complex $Pt(PPh_3)_3$ exists in benzene. Further dissociation with formation of $Pt(PPh_3)_2$ takes place to a very slight extent—the equilibrium constant $[Pt(PPh_3)_2][PPh_3]/[Pt(PPh_3)_3]$ is $(1.6 \pm 1.1) \times 10^{-4}$ mol litre^{-1} in benzene at 25 °C.[14]

Such behaviour of the complexes $[M(PR_3)_4]$ in solution suggested that the PR_3 ligands in these compounds are non-equivalent. A later X-ray diffraction study of the tetrakis(triphenylphosphine)palladium complex $Pd[PPh_3]_4.0.5C_6H_6$ showed, however, that the coordination of the palladium atoms hardly differs from the ideal tetrahedral coordination;[15] admittedly, the average Pd–P bond length in this compound (2.443 Å) greatly exceeds the Pd–P distances in all other structurally characterised phosphine complexes.[16–18] This lengthening of the bond and also the extremely loose packing of the molecules in the crystal are apparently a consequence of the steric repulsion between the ligands in the complex. All these factors are responsible for the lability of the complex both in the solid state and in solutions.

The influence of steric factors on the stability of complexes of zerovalent metals has been confirmed by X-ray diffraction data for the entirely stable complex $Pd[P(C{\equiv}CPh)_3]_4$,[19] where the bulk of the phenyl substituent are separated from the phosphorus atom by the C≡C groups, which creates more favourable conditions for unstrained spatial packing. Similar data have been obtained also for the complex $Pd[P(CH_2OH)_3]_4$.[20] The environment of the palladium atom is tetrahedral in both cases and the Pd–P distances are 2.28 and 2.32 Å respectively.

A series of relatively stable tricoordinate platinum(0) and palladium(0) compounds have been isolated in the solid state and have been reliably characterised by X-ray diffraction.[3,4] According to the X-ray diffraction data for the complex $Pt(PPh_3)_3$, the PtP_3 fragment has the form of a greatly flattened trigonal pyramid.[21] The Pt atom is located 0.1 Å above the plane in which the three phosphorus atoms are present. The $Pt(PPh_3)_3$ molecule is much less strained than the $Pt(PPh_3)_4$ molecule and the Pt–P distances in it are in the usual range 2.25–2.28 Å. In the analogous palladium complex $Pd(PPh_3)_3$, the palladium atom is raised by 0.16 Å above the P_3 plane.[22] The PtP_3 fragment in the complex $Pt(PCy_3)_3$ (Cy = cyclohexyl) is almost planar,[23] the platinum atom being displaced from the plane by only 0.04 Å. All the cyclohexane rings have the chair conformation.

The dicoordinate platinum and palladium complexes are extremely unstable. Only a few complexes with bulky phosphine ligands such as PCy_3, PBu^t_3, and PBu^t_2Ph have been isolated and characterised (see below).[24–27]

Complexes of the type PdL_4 and PtL_4 (L = $Ph_2PC{\equiv}CMe$) can also be obtained from solutions of K_2PtCl_4 or K_2PdCl_4 by reduction with hydrazine in the presence of an excess of the phosphine ligand.[28] Compounds containing methoxy- and n-butoxy-diphenylphosphine ligands $Ph_2P(OR)$ (where R = Me, Bu) have been synthesised similarly.[29] The complex $Pd(PPh_3)_4$ has been obtained by reducing $PdCl_2$ and PPh_3 at 140 °C in dimethyl sulfoxide (DMSO).[30] DMSO is also used as a convenient solvent in the synthesis of ML_4 with ligands such as *m*- and *p*-tolylphosphines from the corresponding platinum and palladium chlorides.[31]

3. Reduction by sodium tetrahydroborate

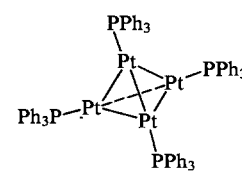
Apart from hydrazine, the reduction by sodium tetrahydroborate is used to synthesise platinum(0) and palladium(0) containing phosphines and tertiary diphosphines and diarsines.[11,32,33] The nature of the compounds obtained on reduction with sodium tetrahydroborate remained controversial for some time, but it has been shown that these are indeed compounds with the metal in the zero oxidation state and not hydrido-complexes.[11] $M(PPh_3)_4$ and $M[C_2H_4(PPh_2)_2]_2$ (M = Pd, Pt),[34] $Pd[C_3H_6(PPh_2)_2]_2$,[35] PtL_4 [L = $PMePh_2$, $PPhMe_2$, $PPh(OMe)_2$, $P(OPh)_3$, $AsPh_3$],[36,37] and $Pt(PMe_2C_6F_5)_4$[37] have been obtained by reduction with sodium tetrahydroborate.

$$Pt[C_2H_4(PPh_2)_2]_2Cl_2 \xrightarrow{NaBH_4/C_2H_5OH} Pt[C_2H_4(PPh_2)_2]_2$$

The synthesis of the tetramer of the monocoordinate compound $Pt(PPh_3)$ by reducing $Pt(PPh_3)_2O_2$ with sodium tetrahydroborate has been reported.[38]

$$Pt(PPh_3)_2O_2 \xrightarrow{NaBH_4/C_2H_5OH} \underset{\mathbf{1}}{[Pt(PPh_3)]_4} \qquad (1)$$

The data obtained in the determination of the molecular mass of this compound indicate the formation of the complex $[Pt(PPh_3)]_4$. The authors[38] proposed a tetrahedral structure of the complex.



The interaction of $[Pt(PPh_3)]_4$ with KCN leads to the displacement of free PPh_3 from the platinum complex, which agrees with the proposed interpretation of the experimental data.

Diphenylphosphine was not detected in the products of this reaction, but the conditions of reaction (1), in the course of which compound **1** was obtained (heating for 6 h at 90 °C),[38] and the fact that the formation of benzene or biphenyl were not monitored during the synthesis casts doubt on the view that complex **1** contains no phosphide or phosphene groups as ligands.[38]

The palladium(0) complexes formed on reduction are known to be incapable of catalysing the reduction of unsaturated hydrocarbons under mild conditions.[39] However, it has been shown in a series of studies that, after contact with air, solutions of $(PPh_3)_2PdCl_2$ treated with sodium tetrahydroborate acquire the capacity to absorb molecular hydrogen and to catalyse hydrogenation reactions in DMF, like solutions of authentic $Pd(PPh_3)_4$.[40,41] This effect can be accounted for by the formation of complexes with oxygen. Indeed a solution of $Pd(PPh_3)_2O_2$, obtained after the reduction of $(PPh_3)_2PdCl_2$ with sodium tetrahydroborate in air, proved to be catalytically active.[41] The increase in the reactivity of palladium compounds in relation to molecular hydrogen when oxygen-containing ligands are introduced into the coordination sphere agrees well with the reaction mechanism according to which the hydrogen molecule is cleaved heterolytically with simultaneous heterolysis of the Pd–X bond. Quantum-chemical analysis[42] of the interaction of the complexes *trans*-$XYPd(PH_3)_2$, where X = OH or OAc and Y = Cl, with molecular hydrogen showed that the presence of the oxygen-containing ligands facilitates the heterolysis of the hydrogen molecule.

The influence of oxygen and oxygen-containing ligands on the reactivity of palladium compounds in the reaction with hydrogen and on the formation of the centres responsible for the catalysis of the hydrogenation reaction has been observed not only for palladium complexes with organophosphorus ligands but also for systems containing N- or S-ligands. Thus it has been shown that the reduction of palladium complexes of pyridine, aliphatic amines, and sulfides or sulfoxides of petroleum origin by sodium tetrahydroborate or diisobutylaluminium hydride when the system is promoted by water or molecular hydrogen leads to highly active selective catalysts for the hydrogenation of conjugated dienes to alkenes.[43,44]

Systems obtained in the reduction of palladium salts by sodium tetrahydroborate in the presence of *o*-phenanthroline, α,α-bipyridyl, and polyethyleneimines in aqueous media may also be active in hydrogenation reactions,[45,46] but the composition of the complexes formed has not been investigated.

4. Reduction with an alcoholic solution of KOH

The reduction of platinum and palladium complexes with an alcoholic solution of KOH leads to the formation of compounds similar to those obtained with the aid of hydrazine and sodium tetrahydroborate. It was first used to synthesise the complex $Pt(PPh_3)_4$ by reducing $(Ph_3P)_2PtCl_2$.[4,47] Potassium tetrachloroplatinate in the presence of a phosphine ligand can also be used as the initial platinum compound. The complexes $Pt[P(OEt)_3]_4$,[48,49] $Pt(PMe_2Ph)_4$,[37] and $Pt(PMePh_2)_4$[50] have been obtained in this way. The combined reduction of K_2PtCl_4 by hydrazine and KOH in the presence of a tertiary phosphine has been used to synthesise $Pt[P(CH_2Ph)Ph_2]_4$.[50]

Depending on the reaction conditions, the reaction can proceed in accordance with the equations

$$K_2PtCl_4 + 5\,PPh_3 + 2\,KOH \longrightarrow$$
$$\longrightarrow Pt(PPh_3)_4 + OPPh_3 + 4\,KCl + H_2O;$$

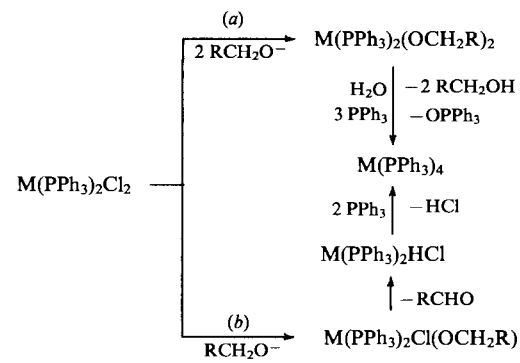
or

$$K_2PtCl_4 + 4\,PPh_3 + 2\,KOH + EtOH \longrightarrow$$
$$\longrightarrow Pt(PPh_3)_4 + 4\,KCl + MeCHO + 2\,H_2O.$$

In the former case, the reducing agent is the phosphine, while in the latter ethanol participates directly in the reaction, being oxidised to acetaldehyde.

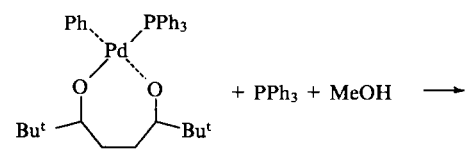
Sodium propoxide may also be used as the reductant for the preparation of $Pt(PPh_3)_4$ from $Pt(PPh_3)_2Cl_2$. Secondary and tertiary alcohols and also phenols may be used instead of propanol.

The reduction of $Pd(PPh_3)_2Cl_2$ by sodium propoxide in propanol is carried out at room temperature in the presence of an excess of the phosphine.[51] The intermediates in this reaction were later investigated,[52] which made it possible to obtain a clearer picture of the process. The reaction apparently proceeds via two parallel routes:



In the case of route (*a*), the reducing agent is the phosphine, which gives up one or two electrons to the metal atom and is apparently subjected to inner-sphere nucleophilic attack by the hydroxide ion. For tertiary alcohols, this is the only possible pathway. Route (*b*) explains the formation of the products of the oxidation of primary and secondary alcohols. It has been shown that the contributions of both routes are approximately the same.[52] When the reaction was carried out in benzene, the intermediate $M(PPh_3)_2(OPh)_2$ was isolated and was then reduced in the presence of water to $M(PPh_3)_4$ with triphenylphosphine. In the first stage of this reaction, the hydroxo-complex $M(PPh_3)_2(OH)_2$ is probably formed [this complex has not been detected in the reaction of $M(PPh_3)_2(OC_6H_5)_2$ with water]. It has been shown that $Pt(PPh_3)_2(OH)_2$ is formed from $Pt(PPh_3)_2Cl_2$ and sodium propoxide in benzene in the presence of water and that its subsequent reaction with PPh_3 leads to the formation of $Pt(PPh_3)_4$ and triphenylphosphine oxide.

Treatment of phenylpalladium complexes with methanol in the presence of PPh_3 leads to the reductive dissociation of the Pd–C bond accompanied by the formation of $Pd(PPh_3)_4$ and benzene. In this case, methanol readily reduces the palladium, being oxidised to formaldehyde.[53]



$$\longrightarrow Pd[PPh_3]_4 + CH_2O + C_6H_6 + Bu^t{-}\overset{O}{\overset{\|}{C}}{-}(CH_2)_2{-}\overset{O}{\overset{\|}{C}}{-}Bu^t$$

Hydrides such as $[PtH(PPh_3)_3]HSO_4$ may be reduced to $Pt(PPh)_3$ by a solution of KOH in ethanol.[54] In essence, the platinum(II) compound is reduced in this reaction as a result of the deprotonation of a complex hydride on reaction with a base,

$$L_3PtH^+ + OH^- \longrightarrow L_3Pt + H_2O,$$

where the coordinated hydride ligand behaves as the 'reductant'.

The absence of an excess of the ligand from the solution makes it possible to obtain formally more coordinatively unsaturated compounds containing only two phosphine ligands at the central atom instead of four.

Attempts have also been made to synthesise coordinatively unsaturated complexes of the type ML_2 by creating conditions for the simultaneous reduction of the metal and the oxidation of the excess ligand. O_2 and H_2O_2 may be used as oxidants for the oxidation of PPh_3 to Ph_3PO. Thus Ugo et al.[24] reported the preparation of the yellow compound $Pt(PPh_3)_2$ in different ways. The first involved the addition of an alcoholic solution of KOH to an alcoholic solution of $[PtH(PPh_3)_3]HSO_4$ and subsequent treatment of the solution with oxygen.

$$2\,[PtH(PPh_3)_3]HSO_4 + 2\,KOH + O_2 \longrightarrow$$

$$\longrightarrow 2\,[Pt(PPh_3)_2] + 2\,Ph_3PO + 2\,KHSO_4$$

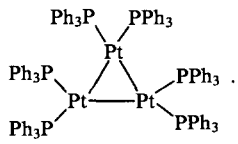
In the second procedure, stoichiometric amounts of H_2O_2 and KOH in alcohol were added slowly to an alcoholic solution of $[PtH(PPh_3)_3]HSO_4$.

$$[PtH(PPh_3)_3]HSO_4 + KOH + H_2O_2 \longrightarrow$$

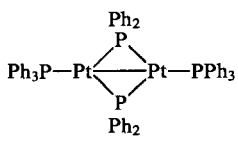
$$\longrightarrow [Pt(PPh_3)_2] + 2\,Ph_3PO + 2\,KHSO_4 + H_2O$$

The coordinatively unsaturated compound obtained as a result of these reactions was identified by elemental analysis. The molecular mass proved to be lower than the value calculated for the monomer $[Pt(PPh_3)_2]$.[24]

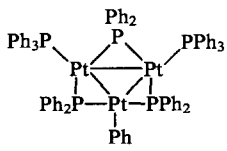
It has been reported that the isolation of pure $[Pt(PPh_3)_2]$ is extremely difficult as a consequence of its instability. A more stable red compound is formed on refluxing $[Pt(PPh_3)_2]$ in benzene under an argon atmosphere.[55] The results of the determination of the molecular mass indicate the existence of the complex $[Pt(PPh_3)_2]$ in the form of a trimer, for which the following structure has been proposed:



In 1966, when the study of Ugo and coworkers[55] was carried out, the ability of triphenylphosphine to undergo degradative reactions in the coordination spheres of platinum metals was not yet known. At the beginning of the 1970s, studies were published[56–66] in which doubt was cast on the postulate that the phosphine ligand is stable both under the conditions of the synthesis and under the conditions of the subsequent reactions of the phosphine complexes of platinum and palladium. In view of this, the above structure was re-examined.[63] It was observed[63] that, on heating $Pt(PPh_3)_4$ in benzene under an argon atmosphere, a dark-red solution is formed from which the two cluster complexes $[Pt_2(PPh_3)_2(PPh_2)_2].C_6H_6$ **2** and $[Pt_3(PPh_3)_2(PPh_2)_3(Ph)].C_6H_6$ **3** were isolated and characterised by X-ray diffraction.



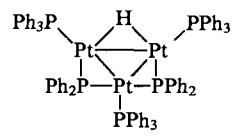
2



3

According to X-ray diffraction data, compound **2** is a dinuclear complex with a very short metal–metal distance (Pt–Pt = 2.604 Å), two bridging ligands PPh_2, and two terminal ligands PPh_3. The Pt_2P_2 skeleton is planar. Compound **3** is constructed as a trinuclear cluster with three Pt–Pt bonds and three bridging PPh_2 groups. The Pt–Pt distances (2.785 Å) are greater than in compound **2**, but are comparable to the bond lengths in the carbonylphosphineplatinum clusters. One of the platinum atoms is coordinated to two PPh_2 groups and to a σ-linked Ph group. This is one of the first compounds where a phenyl residue, formed as a result of the dissociation of the P–C bond, remains bound to the metal.[63]

The platinum complex $[Pt_3(PPh_3)_3(\mu\text{-}PPh_2)_2[\mu\text{-}H)]^+BF_4^-$ **4**, having a similar structure



4

has been obtained on UV irradiation of $Pt(PPh_3)_2C_2O_4$ under a hydrogen atmosphere and subsequent precipitation with $NaBF_4$.[64] The Pt_3P_2 skeleton is significantly nonplanar. The Pt–Pt distance between the atoms linked by the bridging hydrogen atom (2.638 Å) is appreciably shorter than the other two (2.795 Å). The presence of the bridging hydrogen atom was established from ^{31}P NMR spectroscopic data.

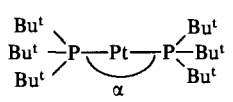
Nevertheless, the mononuclear complexes $[ML_2]$ can be obtained in solution in the case of phosphine ligands containing 'bulky', frequently branched, aliphatic or aryl-substituted aliphatic substituents at the phosphorus atom (L = PCy_3,[25,67] PBu^t_3,[26] PPr^i_3, PBu^t_2Ph,[27] and PBu^t_2Me[68]) by substituting the ligands in platinum(0) and palladium(0) complexes.

$$Pd(\eta^5\text{-}C_5H_5)(\eta^3\text{-}C_3H_5) + 2\,L \longrightarrow PdL_2 + \text{hydrocarbons}$$

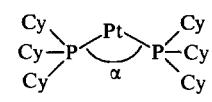
$$Pt(\eta^4\text{-}COD)_2 + 2\,L \longrightarrow PtL_2 + 2\,COD$$

L = PR_3, COD = cycloocta-1,5-diene.

Several such complexes have been characterised by X-ray diffraction (Table 1). It was found that the P–M–P angle in these compounds varies in the range from values close to 180° in the case of $Pt[PBu^t_3]_2$ **5**[26] to 160.5° for $Pt[PCy_3]_2$ **6**.[25]



5



6

The bent structure of the P–M–P fragment in the complex $Pt[PCy_3]_2$ cannot be a result of the packing effect in the crystal structure, since not one H...H packing distance shorter than 2.32 Å has been observed.[25] Nor can one account for the decrease in the angle α by electronic factors because the quasilinear geometry of the complex $Pt[PBu^t_3]_2$ does not fit within the framework of this scheme. Although the conical angle for the PBu^t_3 ligand is greater than for PCy_3 (Table 1),[69] the steric repulsion of the *tert*-butyl groups cannot exert a significant influence on the geometry of the complex because all the distances between the hydrogen atoms of the neighbouring groups are greater than 5.0 Å.[25]

For the less stable dicoordinate complexes with the triphenylphosphine ligand, the stable adducts $[Pt(PPh_3)_2].BCl_3$ with trichloroborane[70] or $[Pt(PPh_3)_2].SiF_4$ with tetrafluorosilane[71] are known.

Table 1. X-Ray diffraction data for the complexes $M[PR_3]_2$ and the conical angles of the PR_3 ligands.

Compound	M–P/Å	P–M–P angle/deg	Conical PR_3 angle[a]/deg	Ref.
$Pt[P(Bu^t)_3]_2$	2.249	180	182(2)	26
$Pt[P(Bu^t)_2Ph]_2$	2.25	177.0	170(2)	18
$Pt[PCy_3]_2$	2.23	160.5	179(10)	67
$Pd[PCy_3]_2$	2.26	158.4	179(10)	25
$Pd[P(Bu^t)_2Ph]_2$	2.28	175.7	170(2)	25

[a]The conical angles were taken from Tolman.[69]

5. Reduction by metal alkyls

The reduction of palladium(II) acetylacetonate by $AlEt_3$ in the presence of PCy_3 leads to the formation of a product described as $Pd(PCy_3)_2$.[72] The complexes $PdL_2(C_2H_4)$ [L = PPh_3, PCy_3, $P(OC_6H_4Me\text{-}o)_3$] have been obtained similarly in the presence of ethene and various phosphines.[73] HX can be removed from hydrido-complexes such as *trans*-$Pt(PPh_3)_2HX$ (X = halogen) by treating them with n-butyllithium. The complex $Pt(PPh_3)_2$, first synthesised by treating $[PtH(PPh_3)_3]HSO_4$ with alcoholic alkali,[24] has been obtained by this method.[54]

6. Reduction by phosphine ligands

Phosphine ligands may reduce the central metal atom in the absence of halide ions or other strongly coordinated ligands lowering the oxidation-reduction potential of the platinoid atom. The reaction is usually carried out in ethanol. This method has been applied successfully in the synthesis of PdL_4 [L = PPh_3, $P(OPh)_3$] by treating $Pd(NO_3)_2$ or freshly precipitated palladium oxide with an excess of the ligand.[3] When metal halides are used as the initial compounds, amines are added to the reaction mixture in order to displace the halide ions. $Pd[P(OEt)_3]_4$ has been obtained in this way.[74]

Phosphite ligands are capable of reducing palladium halides in the absence of an amine. The complexes $Pd[PhP(OR)_2]_4$ (R = Me, Et) have been synthesised in this way from $PdCl_2$ and the corresponding phosphite.[75]

$$PdCl_2 + 4\,PhP(OMe)_2 \longrightarrow Pd[PhP(OMe)_2]_4$$

The complex $Pd(PF_3)_4$ has been obtained by reducing $Pd(CO)_2Cl_2$[76] or $Pd(C_6H_5CN)_2Cl_2$[77] using PF_3 as the reductant at room temperature. The ability of PF_3 to reduce platinum group metals appears unexpected at first sight. However, one should bear in mind that the tendency of trivalent phosphorus to form bonds with oxygen, which are some of the strongest in inorganic chemistry, is very great. It would seem that powerful electronegative substituents (fluorine atoms) should diminish the electron-donating capacity of the phosphorus atom and its ability to give up a lone electron pair in order to form a bond with a 'singlet' oxygen atom. However, the effect of these substituents leads apparently to a very considerable lowering of the unoccupied *d* levels of the phosphorus atom, which is reflected by an increased electron-accepting capacity of the phosphorus atom in PF_3. As a consequence of this, the P–O π-bond in the corresponding (possibly hypothetical) oxide F_3PO should be very strong. In other words, the contribution of the covalent canonical structures

$$\overset{-}{O}\!-\!\overset{+}{P}F_3 \longleftrightarrow O{=}PF_3\,,$$

in the description of F_3PO should be extremely large.

As a consequence of the increased tendency towards the acceptance of electrons manifested by PF_3, the latter is believed to be the most powerful π-acceptor in coordination compounds and is superior to the cyanide ion, alkyl isocyanides, carbon monoxide, etc. Numerous complexes of PF_3 with metals in low oxidation states are known.[78] Thus both factors — the tendency towards the formation of stable complexes with the metal in a low oxidation state and the energy of the bond formed in F_3PO — play the role of the driving force by virtue of which PF_3 is able to function as a reductant in relation to platinum group metal complexes.

The platinum complexes PtL_4 [L = PF_3, CF_3PF_2, $(CF_3)_2PF$] have been synthesised by the reaction of platinum(II) chloride[79] or K_2PtCl_4[80] with phosphorus trifluoride.

In virtually all the reactions described above, mononuclear compounds were employed as the starting materials. The reaction was carried out in the presence of an excess of the phosphine ligand, coordinatively saturated mononuclear compounds of the type ML_4 with the metal in the zero oxidation state being obtained. Similar complexes have been frequently used as the initial form of the catalyst in a wide variety of catalytic reactions (oxidation, hydrogenation, isomerisation, etc.) of organic substrates.[81] The chemistry of these compounds suggests that they are unstable under the conditions of the catalytic reactions and undergo partial oxidation, elimination, and/or dehalogenation of the phosphine ligands usually with formation of aggregated species of cluster type. The latter are in fact apparently responsible for catalysis in most cases. We shall therefore consider in the next section the conditions for the reduction of platinum(II) and palladium(II) leading to the formation of platinum and palladium clusters in nonzero oxidation states.

III. Synthesis of cluster compounds of platinum metals in the oxidation states $0 < n < 2$

Polynuclear and cluster compounds of platinum metals in low oxidation states are formed when reductants such as carbon monoxide, formic acid, or hydrogen are used, while the initial compounds are platinum(II) or palladium(II) dinuclear or polynuclear carboxylate complexes. As a rule, the reaction is carried out for low concentration ratios L : M, where L is the stabilising ligand. When halide compounds, which are reduced by the above reductants under severe conditions, are the starting materials, sodium amalgam is employed.

1. Reduction by carbon monoxide

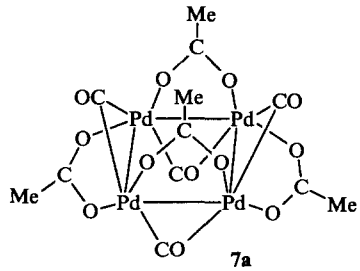
Treatment of solutions of palladium(II) salts with CO usually leads to the reduction of palladium to the metal. Thus the reduction of $Pd(OAc)_2$ by carbon monoxide in glacial acetic acid containing alkali metal acetates leads to the formation of metallic palladium, acetic anhydride, and CO_2.[82,83]

$$Pd(OAc)_2 + CO \xrightarrow{NaOAc} Pd^0 + Ac_2O + CO_2$$

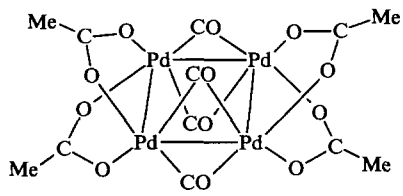
However, in the absence of alkali metal acetates, palladium carbonyl acetate (PCA) having the composition $Pd_4(CO)_4.(OAc)_4.2AcOH$ was obtained from $Pd(OAc)_2$ and CO.[84,88]

$$4\,Pd(OAc)_2 + 8\,CO \longrightarrow Pd_4(CO)_4(OAc)_4 + 2\,Ac_2O + 4\,CO_2$$

According to X-ray diffraction data,[85] crystals of this substance consist of tetranuclear clusters $Pd_4(CO)_4(OAc)_4$ **7** with a rectangular metal core (the Pd–Pd distances are 2.66 and 2.91 Å). However, according to EXAFS data complex **7** exists in the form of two isomers with a square metal core **7a** (the Pd–Pd distance is 2.72 Å) and a rectangular core **7b**.[86] The authors attribute their existence to the presence or absence of molecules of acetic acid of crystallisation in complex **7**.



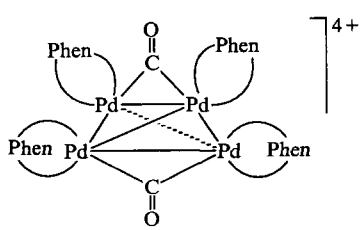
7a



7b

Similar clusters having the composition $Pd_4(CO)_4(RCOO)_4$ have been obtained by reducing palladium(II) propionate and benzoate (R = Ph, Et) with carbon monoxide and also by the exchange of the carboxylate ligands by treating the PCA with the corresponding carboxylic acids (R = CF_3, CH_2Cl, Bu^t).[87-90] IR spectroscopic data for these compounds permit the conclusion that they all have similar structures. Nevertheless, their investigation by the EXAFS method revealed appreciable differences between the geometries of the metal cores for not very significant differences in the acido-ligand.[86] Thus the palladium carbonyl monochloroacetate complex (R = CH_2Cl) has a square metal core (the Pd–Pd distance is 2.70 Å), similar to one of the isomers of PCA. The metal core in the palladium carbonyl trifluoroacetate complex (R = CF_3) has the form of a rhombus with a side of 2.70 Å and diagonals of 3.75 and 4.08 Å. The observed Pd–Pd distances for palladium carbonyl benzoate (R = Ph) and carbonyl pivalate (R = Bu^t) correspond to a mixture of isomers with metal cores in the form of a square and a rectangle.[86] The causes of such sensitivity of the geometry of the metal core to the ligand environment require the analysis of not only steric but also electronic factors.

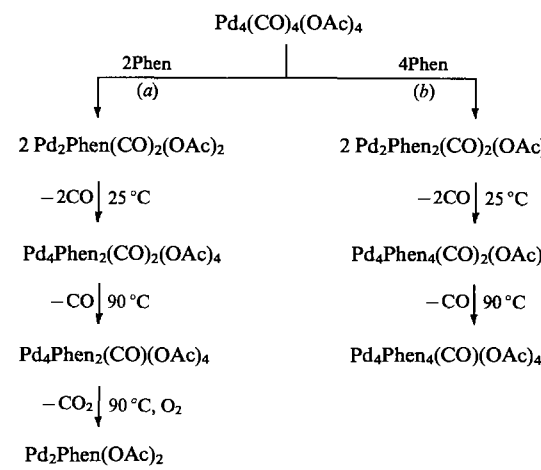
In contrast to the substitution of acido-ligands, the exchange of carbonyl groups for other neutral ligands and, what is more important the displacment of the acido-ligands from the inner coordination sphere of palladium lead to appreciable changes in the cluster metal core. Thus the interaction of the PCA with phenanthroline in the proportions [Pd]:[Phen] = 1:1 in acetic acids results in the formation of the complex $Pd_4Phen_4(CO)_2$.$(OAc)_4$ with a nearly tetrahedral metal core.[88]



This complex is also formed on the reduction of $Pd(OAc)_2$ by carbon monoxide in the presence of phenanthroline. According to X-ray diffraction data, the crystals of the complex contain the almost tetrahedral cluster cation $[Pd_4Phen_4(CO)_2]^{4+}$ as the main structural unit. On formation of this complex from the PCA, all the metal–metal distances change significantly: the Pd–Pd bonds in the Pd(μ-CO)Pd fragments are lengthened to 2.890 Å (in the PCA this distance is 2.663 Å) and become longer than the Pd–Pd bonds in the absence of ligands (2.718 Å). This ratio of bond lengths could be accounted for by the fact that, in terms of its disposition in space, each Pd(μ-CO)Pd bond is in fact bridging in relation to the opposite ligand-free Pd–Pd bond. The acetate groups are not coordinated to the Pd atoms, as in the PCA, but are located in the outer sphere in the form of AcO^- anions.[88]

The replacement of the CO groups by neutral ligands such as phenanthroline (Phen) or bipyridyl (Bipy) also takes place readily on interaction of the PCA with the free ligands at extremely low concentrations—$[L]_\Sigma:[Pd]_\Sigma \leqslant 1:1$. The extremely labile complexes formed under these conditions (Scheme 2) have been characterised on the basis of indirect data for the stoichiometry of the reaction, but have not been isolated in a pure form.[91,92]

Scheme 2



It has been shown[91-93] that the complete removal of the coordinated CO molecules requires heating under an oxygen atmosphere above 90 °C, the polynuclear palladium complexes formed exhibiting a catalytic activity in the oxidation of CO and in the oxidative acetoxylation of alkenes and alkylarenes (Scheme 2).

The combination of the effect of CO as a stabilising ligand and reductants such as alkali metals or their hydroxides, $Fe(CO)_5$, or cobaltocene on platinum compounds such as Na_2PtCl_6, $H_2PtCl_6.xH_2O$, Na_2PtCl_4, and $Pt(CO)_2Cl_2$ made it possible to obtain a series of dianions having the general formula $[Pt_3(CO)_6]_n^{2-}$ (n = 1–6, 10).[94]

$$3n[PtCl_6]^{2-} + (12n+1)\,CO + (12n+2)\,OH^- \longrightarrow$$

$$\longrightarrow [Pt_3(CO)_6]_n^{2-} + 18n\,Cl^- + (6n+1)\,CO_2 + (6n+1)\,H_2O$$

The structure of a series of platinum carbonyls $[Pt_3(CO)_6]_n^{2-}$ (n = 2, 3, 5) in the form of tetraphenylphosphonium salts has been determined by X-ray diffraction.[95] The Pt_3 triangles are linked by three bridging carbonyl ligands and are arranged one on top of the other, forming a layered structure. The Pt–Pt distances in the triangular Pt_3 fragment are 2.66 Å and those between the layers reach 3.01–3.04 Å. The layers have rotated relative to one another by angles ranging from 8.1° to 28.6°, which disturbs the regular prismatic packing of the platinum atoms.[95] This geometrical disorder is apparently a result of an increase in the distances between the CO ligands.

In the search for catalytically active complexes and, what is more important, complexes selective in hydrogenation reactions, studies have been made of phosphine and phenanthroline complexes of palladium, which are formed when $Pd(OAc)_2$ interacts with various reductants in the presence of the above ligands.[96-98]

2. Reduction of the complexes $[Ph_3PMX_2]_2$ (M = Pd, Pt) by sodium amalgam

Sodium amalgam is used as a reductant for palladium and platinum halide complexes because the latter are reduced by hydrogen only under very severe conditions.[99]

The interaction of the dinuclear complex $[Ph_3PPdCl_2]_2$ with sodium amalgam in CH_2Cl_2 at 20 °C leads to the formation of solutions from which a compound described as a dinuclear palladium(0) complex $(Ph_3P)_2Pd_2$ was isolated.[100]

$$[Ph_3PPdCl_2]_2 \xrightarrow{Na/Hg,\ CH_2Cl_2} (Ph_3P)_2Pd_2$$

A similar compound is obtained also when the carboxylate complex $[Ph_3PPd(OAc)_2]_2$ is used as the starting material.[100]

$$[Ph_3PPd(OAc)_2]_2 \xrightarrow{Na/Hg,\ CH_2Cl_2} (Ph_3P)_2Pd_2$$

The experiments on the synthesis of this compound are poorly reproducible, which may be associated with the characteristic features of the purification of the solvent.

The reduction of $[Ph_3PPtCl_2]_2$ by sodium amalgam in benzene at 20 °C leads to the dissociation of the P–Ph bond of the coordinated PPh_3 ligand and the formation of a phosphide complex, which is $[Ph_2PPtCl]_n$ according to elemental analysis and IR spectroscopy.[101]

$$[Ph_3PPtCl_2]_2 \xrightarrow{Na/Hg,\ C_6H_6} [Ph_2PPtCl]_n$$

The molecular mass of this compound corresponds to a polymer with $n = 16$ and it may be that the Pt atoms are linked to phosphide and chloride bridges.

In tetrahydrofuran (THF), the reaction of the platinum(II) chloride complex with sodium amalgam proceeds further and terminates with the formation of the complex $[Ph_2PPt]_n$, where $n = 6$. According to elemental analysis, the compound contains no chlorine and its IR and ^1H NMR spectra contain only the signals due to phosphide groups.[101]

$$[Ph_3PPtCl_2]_2 \xrightarrow[-C_6H_6]{Na/Hg,\ THF} [Ph_2PPt]_n$$

Gas–liquid chromatography of the reaction mixture revealed the presence of 1 mol of C_6H_6 per gram-atom of the platinum of the complex introduced into the reaction. Measurements of the electrical conductivities of the solutions in dimethylformamide showed that the compounds $[Ph_2PPtCl]_n$ and $[Ph_2PPt]_n$ are electrically neutral.

The complex $[Ph_2PPtCl]_n$ does not react with hydrogen under mild conditions, but, after the replacement of Cl^- by AcO^- (on treatment with AgOAc), it is reduced by hydrogen. Benzene was detected in the reaction product.

The platinum acetate complex $[Ph_3PPt(OAc)_2]_2$ is also reduced by sodium amalgam with formation of a platinum phosphide complex and benzene.[101]

$$[Ph_3PPt(OAc)_2]_2 \xrightarrow[-C_6H_6]{Na/Hg,\ THF} [Ph_2PPt]_n$$

3. Reduction of platinum(II) and palladium(II) carboxylate complexes with phosphine ligands by hydrogen

In connection with the study of the homogeneous hydrogenation of alkenes in systems containing a palladium carboxylate and PR_3, the reduction of palladium by molecular hydrogen has been studied in greatest detail. Analysis of literature data shows that both the mode of the reaction and the nature of the compounds formed depend greatly both on the nature of the acido-ligand coordinated to the metal atom and on the reaction conditions.[100,102]

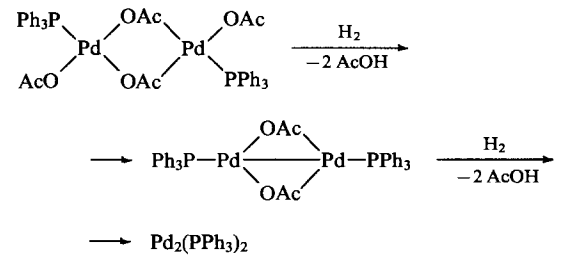
Treatment of the palladium acetate trimer $[Pd(OAc)_2]_3$ with a phosphine ligand leads primarily to the rupture of the acetate bridges. Depending on the metal : ligand ratio, the following reactions can take place:[103]

$$2\,[Pd(OAc)_2]_3 + 6\,PPh_3 = 3\,[Ph_3PPd(OAc)_2]_2,$$

$$[Ph_3PPd(OAc)_2]_2 + 2\,PPh_3 = 2\,(Ph_3P)_2Pd(OAc)_2.$$

For the ratio $[PPh_3] : [Pd(II)] = 1$, predominantly dinuclear palladium(II) complexes exist in solutions in DMF and CH_2Cl_2.[104] These actually react with hydrogen in this system.

The interaction of molecular hydrogen with $[Ph_3PPd(OAc)_2]_2$ leads to the formation of palladium(I) and palladium(0) complexes.[41,100]



The presence of the bridging ligands coordinated as bidentate species in the initial compounds apparently creates favourable conditions for the formation of the metal–metal bond on reduction.

The final product of this reaction — tentatively bis(triphenylphosphine)dipalladium — combines reversibly with molecular hydrogen, but is incapable of catalysing the hydrogenation reaction. Solutions of this complex acquire catalytic activity only after contact with a gas containing at least traces of oxygen in addition to H_2. In the joint presence of oxygen and hydrogen, hydrogen peroxide is formed and oxidises part of this complex, affording phosphine oxide and palladium(II) acetate. The latter reacts with H_2 and with the $Pd_2(PPh_3)_2$ which failed to enter into the oxidation reaction, being converted into the cluster **8**.

$$n\,(Ph_3P)_2Pd_2 + n\,[Pd(OAc)_2]_3 + 5n\,H_2O \longrightarrow$$

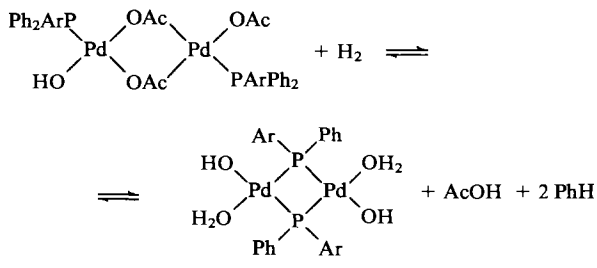
$$\longrightarrow [(PhP)_2Pd_5]_n + 6n\,AcOH + 4n\,C_6H_6$$

8

The kinetics and mechanisms of the hydrogenation of various organic substrates in the presence of the complexes described above have been investigated in detail.[96,105–112]

The use of the triarylphosphine ligand (L), containing the lyophilic SO_3Na group in the benzene ring, made it possible to synthesise by the above procedure phosphine complexes of the type (LPd_2X_2) (X = oxygen-containing acido-ligand). These compounds are soluble in water and may be used to hydrogenate unsaturated compounds in aqueous solution at 1 atm and 20 °C.[97,113–115]

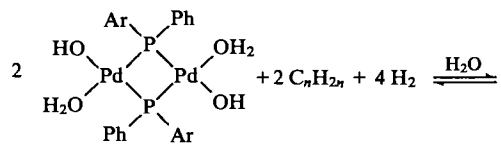
In aqueous solutions, the palladium(II) complex of phosphine, containing the lyophilic SO_3Na group, reacts with hydrogen, affording complex **9** with a phosphide ligand.



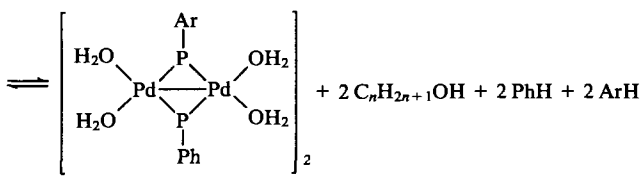
9

where Ar = *m*-$NaO_3SC_6H_4$.

Complex **9** in water is inert to molecular hydrogen, probably as a consequence of the influence of the strong electron-donating ligands — phosphide groups, which reduce the effective positive charge on the palladium atom. However, after the addition of an unsaturated hydrocarbon (propargyl or allyl alcohol, etc.) the absorption of hydrogen due to the reduction of the complex begins. Stoichiometric (in relation to the absorbed hydrogen) formation of an alcohol is observed simultaneously.[113,116]



9



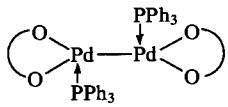
10

Under an argon atmosphere at 293 K, the cluster **10** catalyses the hydration of allyl alcohol to 1,2-propylene glycol and of propene to propan-2-ol.[115]

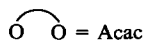
The clusters **8–10** have also been obtained as X-ray-amorphous powders and conclusions about their structures are based on the results of elemental analysis, IR and ^1H NMR spectroscopic data, and also the stoichiometry of the reactions involving them.

The formation of the complex $Pd(Acac)_2PPh_3$ is observed in the $Pd(Acac)_2$ + PPh_3 system. Therefore, in the study of the interaction of $Pd(Acac)_2$ with H_2 in the presence of PPh_3, the reduction of the complex already formed by hydrogen was in fact investigated.[98,117,118] In contrast to the palladium(II) acetate complex, the reduction of $Ph_3PPd(Acac)_2$ by hydrogen leads to the formation of the cluster $[(Pd_3P)_8.PPh_3]_n$.[122] In both cases, the palladium phosphide complexes are regarded as intermediates and the principal reaction products are obtained as a result of the far-reaching dephenylation of the triphenylphosphine ligands.

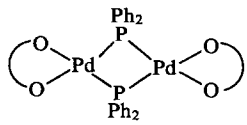
In the first stage of the reaction of $Pd(Acac)_2$ with H_2, the formation of an unstable intermediate was detected by IR and NMR spectroscopic methods. The formula **11** was proposed for it.[117]



11

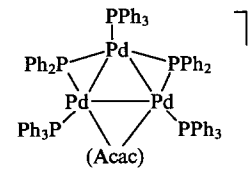


The subsequent treatment with hydrogen leads to the appearance of benzene and the formation of the stable intermediate complex $[Ph_2PPdAcac]_2$, isolated in the solid state, in which the palladium atoms are assumed to be linked by two bridging diphenyl phosphide groups.

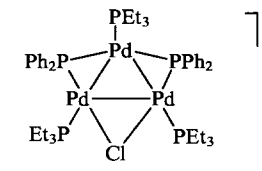


12

After the complete cessation of the absorption of hydrogen, complex **12** as well as the dinuclear cluster $[Pd_3(PPh_3)_3(PPh_2)_2.Acac]^+Acac^-$ [13] were detected in solution. The structures of complexes **12** and **13** were proposed on the basis of ^{31}P NMR spectroscopic data. In reaching conclusions about the structure of complex **13**, the authors were guided by the available data on the structure of the trinuclear palladium complex with diphenylphosphide ligands $[Pd_3(PPh_3)_3(PPh_2)_2Cl]^+Cl^-$ **14**,[119] containing chloride ions instead of acetylacetonato-groups. Complex **14** was first isolated together with *trans*-$Pd(Ph)Cl(PPh_3)_2$ when attempts were made to obtain $Pd(PPh_3)_2$ from $Pd(PPh_3)_4$ with $PdCl_2$ as the PPh_3 acceptor.[58] A series of analogues of this compound $[Pd_3(PPh_2)_2.(PR_3)_3X]^+BF_4^-$ (R = Ph, Et; X = Cl, Br, SCF_3) were later synthesised and the structure of the cluster $[Pd_3(PPh_2)_2.(PEt_3)_3Cl]^+BF_4^-$ **15** was determined by X-ray diffraction.[119]



13



15

The structure of this complex is based on a triangle made up of palladium atoms. The Pd_3P_2 skeleton is almost planar. The Pd–Pd bond lengths (2.89, 2.93, and 2.93 Å) are very similar and indicate a significant metal—metal interaction. The triangular Pd_3 fragment is almost equilateral in contrast to that observed in the cluster $[Pt_3(PPh_2)_3(PPh_3)_3Ph].C_6H_6$, where the metal atoms have the same formal oxidation state (4/3) as in the cluster **15**, but one Pt–Pt distance is longer than the other two.[63]

In the reaction of $Pd(Acac)_2$ with H_2 in the presence of PPh_3, a small amount of a product containing as the ligands P atoms or PPh groups, arising as a result of the removal of the phenyl group from the phosphorus atom of triphenylphosphine, is formed in addition to benzene and complexes **12** and **13**. This compound proved to be an active catalyst of hydrogenation, carbonylation, and arylation reactions.[98]

In order to increase the yield of the catalytically active substance, a study was made of the reduction of $Pd(Acac)_2$ in the presence of PPh_3 with the ratio Pd : P = 0.7–5.0. The substance obtained with the ratio Pd : P = 4 and having the composition $Pd_8P_3C_6H_{15}$ **16** proved to be most active in catalysing the hydrogenation of phenylethyne.[118]

According to ^{31}P NMR data, complex **16** contains phosphorus atoms, as an interstitial element, and triphenylphosphine ligands. According to small angle scattering data, the size of the particles is ~30 Å. EXAFS data for complex **16** were interpreted within the framework of a cluster model constructed from a set of trihedral Pd_6 prisms with a 2.54 Å edge and a height of 3.14 Å. The phosphorus atoms are located in their centres. In addition, about 11% of the initial PPh_3 is not dephenylated and is coordinated to the palladium phosphide Pd_3P formed. On the basis of the data obtained, the formula $[(Pd_3P)_8.PPh_3]_n$ was attributed to complex **16**.[102,118]

In contrast to platinum(II) chloride complexes, which are reduced by hydrogen only under very severe conditions,[99] platinum(II) acetate complexes are readily reduced by hydrogen, like the palladium(II) complexes. Treatment of the complex $[Ph_3PPt.(OAc)_2]_2$ with hydrogen (20 °C, 1 atm H_2) in acetic acid leads to the formation of the compounds $[Ph_2PPt]_n$ **17** (yield 85% with respect to platinum), $[Ph_2PPt(OAc)]_n$ **18** (yield 5% with respect to platinum), and a mixture of products of the far reaching dephenylation of triphenylphosphine having the general formula $[PhPPt]_m$ (yield 5% with respect to platinum).[101]

$$[Ph_3PPt(OAc)_2]_2 \xrightarrow[-C_6H_6]{H_2,\ AcOH} [Ph_2PPt]_n + [Ph_2PPt(OAc)]_n + [PhPPt]_m$$

17 **18**

The reaction is accompanied by the formation of benzene, which indicates the cleavage of the P–C bond of the coordinated triphenylphosphine under the conditions of the reaction with H_2. Furthermore, the main bulk of the compounds isolated contain PPh_2 groups and even the product of the incomplete reduction of the acetate groups $[Ph_2PPt(OAc)]_n$ contains diphenylphosphide groups and not triphenylphosphine. Thus, in contrast to palladium, where the complex $[Ph_3PPd]_2$ is formed under analogous conditions,[104] in the reduction of the complex $[Ph_3PPt(OAc)_2]_2$ by hydrogen the dephenylation of triphenylphosphine apparently proceeds in parallel with the hydrogenolysis of the Pt–OAc bonds linking the acetate groups and the complex $[Ph_3PPt]_n$ cannot be synthesised under these conditions.

It was expected[101] that the formation of heteronuclear platinum and palladium phosphide complexes is possible in the reduction of $(\eta^3\text{-}C_3H_5)Pd(OAc)_3Pt(PPh_3)$ **19** by hydrogen in acetic acid. However, metallic palladium is formed almost simultaneously with the heteronuclear complex on contact of complex **19** with H_2 and then platinum(II) is reduced slowly with formation of benzene and a platinum complex. According to IR spectroscopic data and elemental analysis, the latter complex is analogous to the $[Ph_2PPt]_n$ obtained on reduction of $[Ph_3PPt(OAc)_2]_2$ by hydrogen.[101]

$$(\eta^3\text{-}C_3H_5)Pd(OAc)_3Pt(PPh_3) \xrightarrow[-C_6H_6]{H_2,\ AcOH} \underset{\mathbf{19}}{} \longrightarrow Pd^0 + \underset{\mathbf{17}}{[Ph_2PPt]_n}$$

The reduction of $[Ph_3PPt(OAc)_3Ag]_2$ **20** by hydrogen in acetic acid also leads to the partial dephenylation of the triphenylphosphine ligands. On reduction, 1–2 molecules of benzene are formed from two molecules of compound **20**. The silver is reduced quantitatively to the metal. According to elemental analysis and the determination of the molecular mass, the main reaction product is the complex $[Pt_2(PPh_3)(PPh_2)(OAc)]_3$ **21**. According to data obtained by transmission electron microscopy (TEM), the particle size is ~5 Å, which can be correlated with the size of the particle containing the Pt_6 group.[101]

$$\underset{\mathbf{20}}{[Ph_3PPt(OAc)_3Ag]_2} \xrightarrow[-C_6H_6]{H_2,\ AcOH} \underset{\mathbf{21}}{[Pt_2(PPh_3)(PPh_2)(OAc)]_3}$$

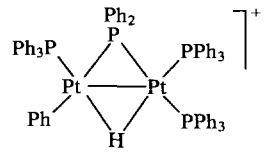
The acetate groups of complex **21** are manifested in the IR spectrum at 1580 and 1440 cm^{-1} and in the ^1H NMR spectrum at 2.09 p.p.m. (the hydride signals are not observed). A superposition of complex multiplet signals in the range 17–58 p.p.m. is observed in the ^{31}P NMR spectrum, which can be attributed to both Ph_2P and Ph_3P groups.

Complex **21** absorbs hydrogen reversibly in solutions in acetic acid (1 mol of H_2 per gram-atom of Pt). The cycles involving evaporation, admission of argon, and subsequent absorption of hydrogen may be repeated several times.

$$[Pt_2(PPh_3)(PPh_2)(OAc)]_3 \underset{-H_2}{\overset{H_2}{\rightleftharpoons}} \underset{\mathbf{22}}{[Pt_2(PPh_3)(PPh_2)(OAc)(H_2)_2]_3}$$

The reversible absorption of hydrogen is not characteristic of this complex alone. Thus, when $[Ph_3PPt(OAc)_2]_2$ and $(\eta^3\text{-}C_3H_5)$. $Pd(OAc)_3Pt(PPh_3)$ are reduced, more hydrogen is absorbed (2 mol and 1.5 mol per gram-atom of the metal respectively) than is required for the stoichiometric reduction reaction. The superstoichiometric amount of hydrogen is also absorbed reversibly in such cases. Similar results were obtained previously in the case of the palladium complex $Pd_2(PPh_3)_2$.[100] The signal due to the coordinated hydrogen in the ^1H NMR spectra was not recorded in all cases, which can probably be explained by the low stability of the complexes and the very large signal width, characteristic of complexes with molecular hydrogen.[120]

When a mixture of $Pt(1,5\text{-}C_8H_{12})_2$, [*trans*-PtPh(MeCOMe). $(PPh_3)_2]^+$, and PPh_3 was treated with hydrogen, the formation of the platinum phosphide complex **23** was also observed.[66]



23

The question of the origin of the phenyl group linked to the platinum atom was solved by replacing the initial cation by $[trans\text{-}Pt(p\text{-}MeC_6H_4)(MeCOMe)(PPh_3)_2]^+$. Since the cation **23** is in this case detected among the reaction products, it is evident that the phenyl group was formed as a result of the dissociation of the P–C bond involving the PPh_3 ligand.

4. Reduction of $Pd(OAc)_2$ by hydrogen in the presence of phenanthroline and bipyridyl

The products of the reduction of $Pd(OAc)_2$ by hydrogen in acetic acid containing phenanthroline or bipyridyl have been investigated.[121–123] The noncrystalline substances obtained are capable of catalysing the oxidation of alkenes, alcohols, and other organic substrates.

The product of the reduction of palladium(II) acetate by hydrogen in solution in acetic acid containing 0.5 mol of phenanthroline per gram-atom of palladium has the composition $Pd_4Phen(OAc)_2H_4$ **24.**

$$4\ Pd_3(OAc)_6 + 3\ Phen + 15\ H_2 = 3\ \underset{\mathbf{24}}{[Pd_4Phen(OAc)_2H_4]_n} + 6\ AcOH$$

The hydride nature of complex **24** was confirmed by ^1H NMR spectroscopic data. A broad band with a maximum in the range $\delta = -30$ to -50 ppm (width 5 kHz) was found in the broad-band spectrum (frequency range 250 kHz).[130] The appreciable broadening of the hydride signals was explained by the fact that the palladium atoms in these complexes form a polynuclear structure with a system of metal–metal bonds similar to the lattice of metallic palladium or its hydride phases.

The study of this substance by high-resolution transmission electron microscopy showed that its particles contain a nearly spherical metal core 20 ± 5 Å in diameter.[124] A radial distribution curve for the atoms (RDA), on which there is a single maximum corresponding to the Pd–N interatomic distance (2.1 ± 0.1 Å) and a single peak corresponding to the short Pd–Pd distance (2.62 ± 0.05 Å) was obtained from EXAFS data.

The sizes of the metal core of the hydrido-complex molecules found from TEM data enabled the authors to estimate the number n in the formula $[Pd_4Phen(OAc)_2H_4]_n$, which proved to be approximately 100 on the assumption that the packing density of the palladium atoms in the core of this cluster is the same as in the metallic palladium lattice.

The chemical properties of the hydrido-complex indicate its high reactivity.[125,126] Treatment of the polynuclear hydrido-complex with various electrophiles leads as a rule to unstable products, which decompose into monomeric or oligomeric palladium complexes. In contrast to this, the reaction with O_2 leads to the formation of clusters in which a massive metal skeleton is retained. These clusters proved to be effective catalysts for many oxidation reactions.[127,128]

5. Giant palladium clusters

On reaction with oxygen, the polynuclear hydrido-complex **24** loses its hydride atoms, which are bound to form H_2O. A small proportion of the palladium atoms are then oxidised to Pd(2+) complexes and the main bulk are converted into a cluster compound the simplest formula of which is $Pd_9Phen(OAc)_3$ **25**. Complex **25** is stable in air and is soluble, like the hydrido-complex **24**, in water and polar organic solvents.[127]

The molecular mass of complex **25**, which is $(1.0 \pm 0.05) \times 10^5$, was estimated from the measured rates of sedimentation in an aqueous solution under ultracentrifugation conditions. Such a large molecular size required the use of a set of analytical methods for the identification of these compounds. More definite information about the molecular size of compound **25** was obtained with the aid of small angle X-ray scattering methods, high-resolution transmission electron microscopy, and electron diffraction.[128-130]

The metal cores of the molecules of compound **25** are observed on the electron photomicrographs in the form of almost regular spherical particles 26.0 ± 3.5 Å in diameter with a unimodal size distribution. The packing of the palladium atoms in the cluster **25** was determined with the aid of EXAFS spectra.[128,129] The set of atomic Pd–Pd distances found (2.60 ± 0.04, 3.1 ± 0.1, 3.7 ± 0.1, 4.1 ± 0.1) agrees best with the icosahedral model of the packing of palladium atoms in the metal core of the cluster **25**. Taking into account the chemical composition, the idealised formula $Pd_{561}Phen_{60}(OAc)_{180}$ was proposed for the cluster **25**. This formula apparently corresponds to an average size and composition of the cluster and not to definite fixed dimensions and chemical composition, i.e. there is a distribution of the particles of the cluster **25** about an average value $d \approx 25$ Å and the idealised composition $Pd_{561}Phen_{60}(OAc)_{180}$.

In this structure, 60 Phen ligands are coordinated as bidentate species by the palladium atoms at the vertices and on the edges of the icosahedron. The overall formal charge on the metal core together with the electrically neutral Phen ligand is 180+ and is balanced by 180 anionic ligands OAc^-, which are distributed in the outer sphere of the cluster cation **25** (Fig. 1). A similar outer-sphere arrangement of acetate anions has been observed with the aid of X-ray diffraction in the tetranuclear cluster $[Pd_4Phen_4(CO)_2](OAc)_4$.[131]

The cluster **25** can be precipitated from aqueous solution by adding salts such as NaX or KX (X = Cl, Br, ClO_4, HSO_4, PF_6, AsF_6), which is accompanied by the substitution of the OAc^- anions by X^-. When compound **25** was treated with the salt KPF_6, a giant cluster having a similar composition and structure and represented by the idealised formula $Pd_{561}Phen_{60}O_{60}(PF_6)_{60}$ **26** was obtained.[130]

$$Pd_{561}Phen_{60}(OAc)_{180} + 60\,PF_6^- + 60\,H_2O$$

$$= Pd_{561}Phen_{60}(PF_6)_{60}O_{60} + 120\,AcOH + 60\,AcO^-$$

EXAFS data led to the conclusion that the packing of the metal atoms in the metal core of the cluster **26** is cubooctahedral and not icosahedral.

The giant clusters obtained serve as a bridge between the usual molecular clusters and colloidal metals and their homogeneous solutions are a model of the colloidal solutions of metals. The size of the metal core in giant clusters greatly exceeds the size of the larger molecular clusters, such as $Pd_{38}(CO)_{28}(PEt_3)_{12}$[132] and $Au_{55}(PPh_3)_{12}Cl_6$,[133] approaching the lower limit of the size of the colloidal particles of metals. In contrast to the latter, giant clusters have a distinct ligand environment with a definite stoichiometry characteristic of molecular clusters. However, in those cases where the number of metal atoms approaches several hundreds, a set of more or less imperfect metallopolyhedra is formed with a certain distribution with respect to size and chemical composition.

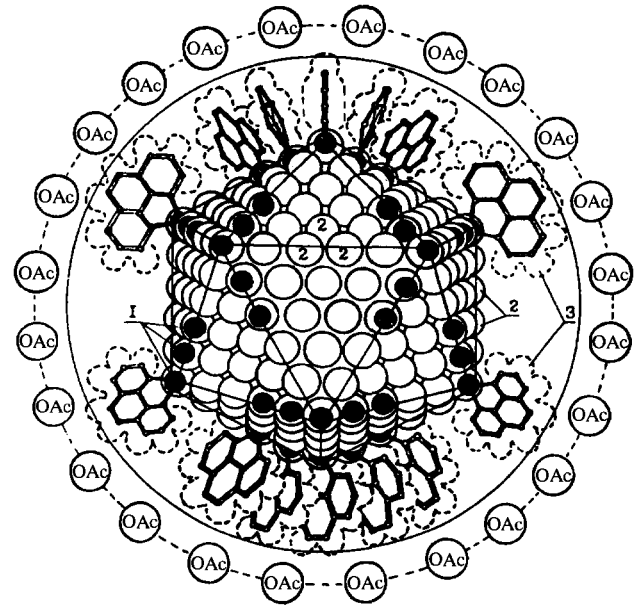


Figure 1. An idealised model of the cluster **25**: (*1*) palladium atoms coordinated to the Phen ligands; (*2*) palladium atoms accessible for the coordination of the AcO^- anion and substrate or solvent molecules; (*3*) the van der Waals volume of the coordinated phenanthroline molecules.

The clusters **25** and **26** behaved as catalysts in a series of reactions. Oxidative acetoxylation of ethene to vinyl acetate, of propene to allyl acetate, and of toluene to benzyl acetate takes place in the presence of acetic acid in solutions of these clusters.[130] They effectively catalyse the oxidation by molecular oxygen of primary alcohols to esters and of secondary alcohols to ketones.[134]

6. Reduction of platinum(II) and palladium(II) carboxylate complexes by formic acid

As shown above, the reduction of $[Ph_3PPd(OAc)_2]_2$ or $Ph_3PPd.(Acac)_2$ by molecular hydrogen leads to the final products $[Pd_5(PPh)_2]_m$ and $[(Pd_3P)_8.PPh_3]_n$ respectively.[100] These are formed as a result of the far reaching dephenylation of the triphenylphosphine ligands. In both cases, palladium phosphide complexes are regarded as intermediates. Presumably it will be possible to obtain palladium phosphide complexes by the reduction of palladium carboxylates with formic acid.

Indeed, the study of the interaction of $Pd(Acac)_2PPh_3$ with formic acid under an atmosphere of an inert gas or hydrogen showed that the initial complex is reduced much faster by formic acid than by hydrogen. The latter does not affect the course of the reaction and the composition of the products under these conditions.[98,117,135] In the first stage, all the acetylacetonate ligands are substituted by formate ligands.

$$Pd(Acac)_2PPh_3 + 2\,HCOOH \longrightarrow Pd(HCOO)_2PPh_3 + 2\,HAcac$$

Analysis of the gas phase revealed the presence of CO_2 and H_2, which is characteristic of the catalytic decomposition of HCOOH.[136] According to a number of investigators,[98,117,137,138] the dimeric complex $[PdPPh_3]_2$ should also be formed in the reduction of $Pd(HCOO)_2PPh_3$, similarly to what happens in the reduction of $[(Ph_3P)_2Pd(OAc)_2]_2$ by hydrogen.[41,100]

$$[Pd(HCOO)_2PPh_3]_2 \longrightarrow [PdPPh_3]_2 + 4\,CO_2 + 2\,H_2$$

However, the complex $[PdPPh_3]_2$ could not be detected. It is apparently unstable under the reaction conditions and interacts in accordance with the following scheme with the hydrogen formed:

$$[PdPPh_3]_2 + H_2 \longrightarrow [PdPPh_2]_2 + 2\,C_6H_6.$$

The final product of the reduction reaction is a complex to which the formula $[Pd_4(PPh_3)_2(PPh_2)_2]_n$ was attributed on the basis of the results of elemental analysis and UV and IR spectroscopic data.[117] In this product, half of the PPh_3 ligands have been dephenylated. the complex obtained exhibits a high activity in the arylation of styrene by iodobenzene, but is inactive in the hydrogenation and oligomerisation of phenylethyne.[117]

The interaction of $[Ph_3PPt(OAc)_2]_2$ with HCOOH also begins with the replacement of all the acetate ligands by formate ligands (according to GLC data). After an induction period, the platinum(II) complex is subsequently reduced with formation of benzene and CO_2. According to the results of elemental analysis and IR spectra, the main reaction product corresponds to the composition $[Ph_2PPt]_n$ **27**. In addition, a small amount (~5%) of the product of more far reaching dephenylation $[PhPPt]_m$ **28** is formed (Scheme 3).[101,102]

Scheme 3

$$[Ph_3PPt(OAc)_2]_2 \xrightarrow[-AcOH]{HCOOH} [Ph_3PPt(OCOH)_2]_2 \xrightarrow{-CO_2}$$

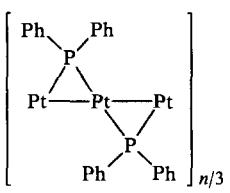
$$\longrightarrow [Ph_3PPtH_2]_n \xrightarrow{-C_6H_6} [Ph_2PPt]_n \xrightarrow{-C_6H_6} [PhPPt]_m$$

27 **28**

The molecular mass of complex **27** in benzene corresponds to 10 $[Ph_2PPt]$ fragments, i.e. $n = 10$. According to the results of the study of complexes **27** and **28** by high-resolution transmission electron microscopy, their particle size does not exceed 6 Å, which corresponds to small clusters and does not conflict with the determination of the molecular mass.[101]

A very broad signal (50 mHz), apparently associated with the occurrence of rapid exchange in the system, is observed in the ^{31}P NMR spectra. A decrease in temperature to −90 °C in toluene or to the glass point (−60 °C) in DMF does not induce slow exchange conditions in this case. ^{31}P NMR spectra of a similar type have been observed for all platinum phosphide complexes.

According to EXAFS spectroscopic data, there is only one shortest Pt–Pt distance in complex **27**, amounting to 2.53 Å, while the next nonbonding distance is 3.01 Å; only one maximum also corresponds to the Pt–P distance (2.22 Å). Bearing in mind that the Pt:P ratio is 1:1 on the basis of the composition of complex **27** and that according to EXAFS spectroscopic data the intensity of the Pt–P peak exceeds significantly that of the Pt–Pt peak, the authors suggested that complex **27** is a linear chain polymer in which the platinum atoms are linked by the metal–metal interaction and by bridging phosphido-groups. In addition, the authors do not rule out the possibility of the existence of pentacoordinate phosphorus atoms in this structure.



The fixed long Pt–Pt distance can apparently be explained by the fact that the chain structure is bent and not linear. The bent form of the chain can be accounted for by the molecular packing effects in the solid phase (EXAFS spectra were recorded for the specimens). However, the EXAFS spectroscopic data for a solution of complex **27** are virtually identical with the spectra of solid specimens.

The size distribution and form of the particles of complex **27** have been investigated by the small angle X-ray scattering method (SAXS). According to SAXS data, the particles of complex **27** are nearly spherical with a diameter of 15.2 ± 0.5 Å.

In contrast to platinum, treatment of the palladium acetate complex $[Ph_3PPd(OAc)_2]_2$ with formic acid leads to the formation of the polyhydride complex $[Pd_2(PPh_2)H_x]_n$ **29** as the main reaction product (60% and 70% relative to palladium). Furthermore, the complex $[Pd(\mu\text{-}O_2PPh_2)(Ph)(PPh_3)]_2$ **30** was obtained in 8%–10% yield relative to palladium. According to GLC data, the reaction also results in the formation of acetic acid (2 mol per mol of palladium) and benzene (0.9 mol per mol of PPh_3).[137]

$$[Ph_3PPd(OAc)_2]_2 \xrightarrow[-C_6H_6]{HCOOH}$$

$$\longrightarrow [Pd_2(PPh_2)H_x]_n + [Pd(\mu\text{-}O_2PPh_2)(Ph)(PPh_3)]_2$$

29 **30**

The dynamics of the variation of the volume of the gas phase of the system corresponds to the autocatalytic nature of the reaction, the volume of the gas exceeding the calculated value by a factor greater than 2.5. According to GLC data, the evolved gas is a ~1:1 mixture of CO_2 and H_2. Carbon monoxide was not detected even in trace amounts. The presence of hydrogen in the gas mixture and the volume of the evolved gas indicate that the reduction of the palladium(II) complex is accompanied by the decomposition of formic acid by the complex.

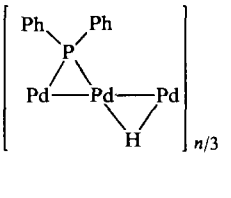
$$Pd(II) \xrightarrow{HCOOH} Pd(0) + CO_2 + 2\,H^+$$

$$HCOOH \xrightarrow{Pd^{0-1}} CO_2 + H_2$$

Nor can one rule out [the possibility] that the hydrogen formed on decomposition of formic acid is consumed on the reduction of the initial palladium(II).

The IR spectrum of complex **29** (the main reaction product) contains only the absorption bands of the phosphorus-containing ligands. Those of the OAc^- groups are absent (the Pd–H vibrations are inactive in the IR spectrum). In the ^1H NMR spectrum, the signal due to the aromatic protons is broadened and in addition a broad signal is observed (signal widths ~0.9 ppm) with the centre at −9.5 ppm and may correspond only to complexes with hydrogen. According to SAXS data (small angle scattering), the particles of complex **29** are spherical and their size is 15.6 ± 0.5 Å. The $[Pd_2(PPh_2)H_x]_n$ particle size is virtually the same as for the analogous platinum complex $[Ph_2PPt]_{10}$ (15.2 ± 0.5 Å). Thus the number of metal atoms in the palladium phosphide complex is apparently also close to ten.

The RDA curve for complex **29** was obtained from EXAFS data. It has a peak corresponding to a single shortest distance between the palladium atoms (2.55 Å), the next nonbonding distance being 3.66 Å. Only a single maximum corresponding to a Pd–P distance of 2.15 Å is also observed in the EXAFS spectrum. In conformity with these data, the authors[137] suggest that, like the platinum phosphide complex, complex **29** is a linear chain polymer in which the palladium atoms are linked by the metal–metal interaction, bridging phosphido-ligands, and, apparently, bridging hydrido-ligands.



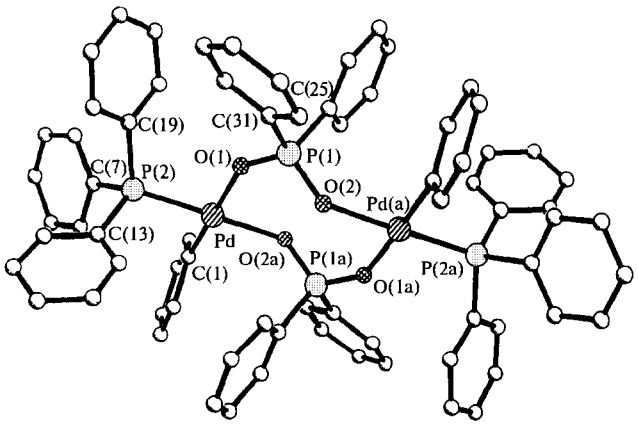


Figure 2. Molecular structure of $[Pd(\mu\text{-}O_2PPh_2)(Ph)(PPh_3)]_2$ **30**.

The structure of the second product of the interaction of $[Ph_3PPd(OAc)_2]_2$ with HCOOH — the dimeric complex $[Pd(\mu\text{-}O_2PPh_2)(Ph)(PPh_3)]_2$ **30** was established by X-ray diffraction.[138] The Pd^{2+} species of the centrosymmetrical dimeric complex **30** are linked by two bridging diphenylphosphinate groups. The Pd...Pd distance is 5.35 Å, which rules out the possibility of a metal–metal interaction (Fig. 2). The coordination of the palladium atoms is close to the ideal square-planar. The central eight-membered ring has the chair conformation and, as a consequence of its centrosymmetrical structure, the atoms of the central part of the ring P(1), O(2), P(1a), and O(2a) are strictly coplanar, while the plane comprising the atoms of the 'angular' fragment P(1), O(1), Pd, and O(2a) forms a dihedral angle of 47.3° with the plane of the central part.

The Pd–O(1) and Pd–O(2a) bonds in the *trans*-positions relative to the Ph and Ph_3P substituents at the metal atom are virtually the same [2.115(6) and 2.100(9) Å]. On the other hand, the P(1)–O(1) [1.482(6) Å] and P(1)–O(2) [1.516(9) Å] bond lengths differ by 0.034(9) Å, which justifies the assumption that the P(1)–O(1) bond is multiple, while Pd–O(1) is a coordinate bond. Nevertheless, the Pd–O bond lengths are equalised, which is apparently induced by the electronic influence of the Ph_3P and Ph groups in the *trans*-positions relative to these bonds.

It is noteworthy that the formation of complex **30** in the reaction of $[Ph_3PPd(OAc)_2]_2$ with HCOOH is the outcome of an unusual oxidation-reduction process because it indicates the oxidation of P^{III} to P^{V} in the presence of a powerful reductant (HCOOH) and in the absence of any kind of traditional oxidant. The only source of oxygen atoms, which become attached to the phosphorus atom of the phosphine ligand during the formation of complex **30** under the reaction conditions (Ar atmosphere, reagents carefully freed from O_2), is the carboxylate ligands.

The fact that the P–C bond dissociation reaction in the formation of complex **30** includes an intermediate decrease in the oxidation state of the metal is confirmed both by the very fact of the formation of complex **30** with a Pd–C(Ph) bond and by data on the reduction of palladium(II) by formic acid in the presence of hydroquinone and *p*-benzoquinone. The presence of hydroquinone, which is incapable of oxidising palladium(0), under these conditions merely shortens somewhat the induction period and hardly affects the form of the curve. On the other hand, the addition of *p*-benzoquinone increases sharply the induction period, at the end of which gas is evolved at a significantly higher rate. On the basis of these data, one may conclude that the low-valence palladium complex formed in the system is immediately oxidised by *p*-benzoquinone to palladium(II) and, as long as any amount of the quinone remains in the system, there is virtually no gas evolution.

IV. Conclusion

The extensive and independent field of the chemistry of cluster compounds such as the carbonylphosphineplatinum(0) and carbonylphosphinepalladium(0) compounds remains outside the scope of the present review.

Complexes with phosphine ligands have played an enormous role in the establishment and development of the modern chemistry of transition metals. The electronic properties of these ligands (their *n*-donor capacity and their fairly low-lying unoccupied *d* orbitals) as well as the steric factors which vary within wide limits have been used widely to stabilise labile complexes containing M–H, M–C, M–Si and other bonds and also to obtain numerous catalysts from them.

In the first stage of the study of complexes of this type, it appeared that the phosphine ligand can migrate, as a stable fragment, from one compound to another or can leave the coordination sphere without changing and without entering into any kind of reactions involving the P–C bonds.

The data examined above show that in reality tertiary phosphines lose their organic groups fairly readily under the conditions of reactions leading to a decrease in the oxidation state of the central atom. The dissociation of the P–C bond is observed when virtually any reductants are employed. It now appears surprising that these reactions remained unnoticed in the first stages of the development of the chemistry of complexes with tertiary phosphines when numerous mononuclear complexes of metals in the zero oxidation state were synthesised. Studies in later years showed that, when the M : L ratio is varied, it is possible to obtain in the same systems clusters in which the role of the bridging groups is assumed by phosphide or phosphene ligands, arising when the organic groups are removed from the molecule of the initial tertiary phosphine. The nature of these reactions is still insufficiently clear. There is no doubt about the role which the coordinative unsaturation of the metal atom in the corresponding intermediate plays in the dearylation and dealkylation of the tertiary phosphine. However, the comparative stability of the complexes containing only two phosphine ligands at the metal atom in the zero oxidation state suggests that, apart from the formal coordinative unsaturation, some other factors are also responsible for the course of these unusual processes.

The cluster formation reactions are a phenomenon characteristic not only of complexes with phosphine ligands. As can be seen from the concluding sections of the present review, palladium clusters are formed readily when palladium acetate is treated with reductants in the presence of stabilising ligands such as carbon monoxide and aromatic nitrogen-containing bases coordinated as bidentate species. The formation reactions of these clusters constitute the basis of the synthesis of catalytically active compounds exhibiting an unusual selectivity and activity under mild conditions. The interest of the authors in the topic to which this review is devoted is partly due to these factors.

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Intermediates and mechanisms of heterogeneous catalytic reactions. Reactions involving hydrogen and the monoxides of carbon and nitrogen

O V Krylov, V A Matyshak

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Abstract. The structure of intermediate surface compounds in heterogeneous catalytic reactions involving H_2, CO, and NO is discussed. The relative reliability of the role of various structures in catalysis is discussed. Schemes for the reaction mechanism which have been developed from information on the surface complexes are described. The bibliography includes 248 references.

I. Introduction

We have previously discussed the intermediates which have been detected by spectroscopic measurements in situ in the simplest heterogeneous catalytic reactions of hydrocarbons.[1] This review is concerned with somewhat more complex reactions involving H_2, CO, or NO. In most cases two substances are the initial reactants, and the catalysts are metals or transition metal oxides. The hydrogenation of olefins and the dehydrogenation of paraffins are reaction of the general type

$$A + B \leftrightarrows AB .$$

In the forward direction we may observe the activation of both the olefin (A) and the hydrogen (B), and therefore possible intermediates formed from both the hydrocarbons and the hydrogen must be considered.

As in our previous review[1] we shall define three levels of reliability of the existence of intermediate substances: a low level (L), obtained from spectroscopic data recorded before and after the catalysis, a medium level (M), obtained from spectroscopic data in situ but without kinetic measurements, and a high level (H), from spectroscopic data in situ aimed at comparing the kinetics of the heterogeneous catalytic reactions with those of the change in concentration of the surface compounds.

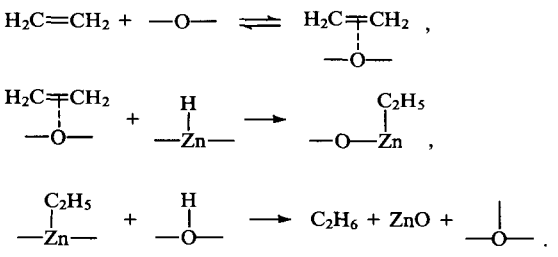
O V Krylov, V A Matyshak N N Semenov Institute of Chemical Physics, Russian Academy of Sciences, ul. Kosygina 4, 117 977 Moscow, Fax (7-095) 938 21 56

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In the reactions with H_2, CO, and NO the observed spectra are usually stronger than those seen in the reactions of the hydrocarbons. This effect is attributed to the high extinction coefficients of the C–O, O–H, and N–H bonds. Accordingly, the reliability of the results is also generally higher.

II. Hydrogenation of hydrocarbons

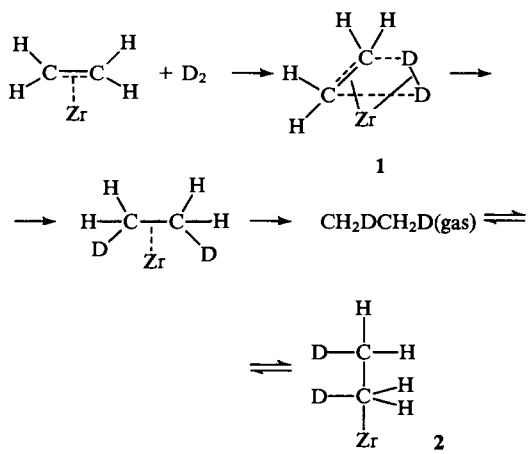
In our previous review,[1] devoted to the simplest reactions of the hydrocarbons, alcohols, and acids, we discussed the intermediate complexes formed by the isomerisation of the olefins on ZnO.[2,3] The same workers[4–6] used kinetic methods and IR spectroscopy to study the mechanism of the hydrogenation of C_2H_4 on ZnO. According to their results there are two types of adsorption of H_2 on ZnO: (1) a fast, reversible adsorption, with formation of Zn–H bonds (1710 cm^{-1}) and of O–H bonds (3510 cm^{-1}), and (2) a slow, irreversible adsorption, with diffusion of the hydrogen into the bulk of the catalyst. Adsorption of the first type occurs when C_2H_4 is hydrogenated at 300 °C. After the adsorption of C_2H_4 the Zn–H band persists in the IR spectra but the O–H band disappears. This led to the conclusion that hydrogen is adsorbed as a π complex on the oxygen atoms, with absorption bands (a. b.) at 1438, 1451, and 1600 cm^{-1}; the heat of adsorption is about 58 kJ mol^{-1}. A new band assigned to a π complex, appears when the C_2H_4 is hydrogenated in a flow reactor. When C_2H_4 is replaced by C_2D_4 the initial rate of disappearance of the C_2H_5 absorption bands is close to the stationary rate of hydrogenation: the step corresponding to this process may be rate-limiting. The proposed mechanism can be represented as



The adsorbed hydrogen can migrate over the oxygen centres of the surface towards the adsorbed C_2H_4.

The mechanism proposed[4-6] for the hydrogenation of C_2H_4 was subsequently confirmed.[7,8] However, the only deuteration products of C_3H_6, C_4H_8, and C_4H_6 were the deuterated hydrocarbons $C_3H_6D_2$, $C_4H_8D_2$, and $C_4H_6D_2$. This shows that the hydrogen takes part in the reaction in a molecular form rather than in the atomic form seen in the hydrogenation of ethylene: this difference can be attributed to the weaker chemisorption of C_2H_4 on ZnO as compared with C_3H_6, C_4H_6, and C_4H_8. Therefore C_3H_6 and C_4H_8 are adsorbed as π-allyl complexes.

The IR spectra of hydrogen adsorbed on ZrO_2 at 0-100 °C also indicate a heterolytic dissociation of H_2 with formation of Zr-H and O-H groups.[9] However, when bound in this way hydrogen does not react with ethylene from the gas phase, but is simply replaced by it: the intensity of the Zr-H band decreases, and the absorption bands of π-C_2H_4 (1446 cm^{-1}) and of the tightly bound C_2H_4 complex (1338 cm^{-1}) are formed. However, the hydrogenation of C_2H_4 is detectable even at −100 °C, when the heterolytic dissociation of H_2 is inconceivable. Under these conditions the adsorbed ethylene interacts with D_2 from the gas phase by the following mechanism:

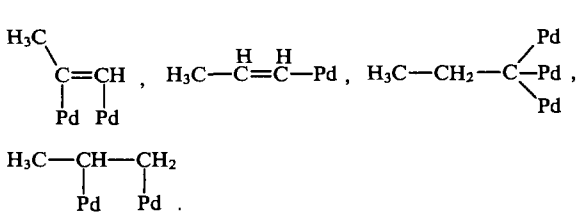


In this reaction the complex **1** is the intermediate and the complex **2** is a side product.

On clean Pd(111) and Pd-Cu(111) metallic surfaces π-C_2H_4 and ethylidene (=CH-CH_3) are observed[10] in the electron energy loss spectroscopy (EELS) spectra, whereas in the adsorption of C_2H_2 the corresponding species are π-C_2H_2 and ethylidyne (≡C-CH_3). At high temperatures (200 °C) even more highly dehydrogenated intermediates of composition Pd-C_xH_y are formed (where $x > y$). It was concluded that the hydrogenation reaction takes place through the formation of these complexes.

An IR spectroscopic study[11] of the interaction of C_2H_4 with Rh/SiO_2 and with VO_x-Rh/SiO_2 also suggested the formation of the ethylidene groups =CH-CH_3. In the presence of hydrogen these are hydrogenated to give alkyl groups, and beyond to CH_4 and C_2H_6.

An analysis[12] of the IR spectra obtained after the hydrogenation of propylene on Pd/ZrO_2 detected the formation of the surface compounds

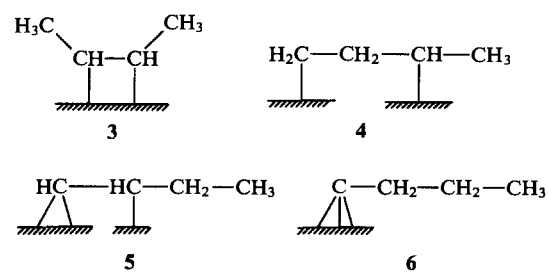


The hydrogenation of butadiene on Pt(100), studied[13] by low-energy electron diffraction (LEED) and by Auger spectroscopy, was found to proceed through the formation of the intermediate C_4H_7:

$$C_4H_6 \rightleftharpoons C_4H_6\,(ads) \underset{-H^+}{\overset{H^+}{\rightleftharpoons}} C_4H_7\,(ads) \xrightarrow{H^+} C_4H_8\,(ads) \longrightarrow C_4H_8\,(gas).$$

The conversion of butadiene into butene is the rate-limiting step, characterised by an activation energy of 39 kJ mol^{-1}. The fact that the rate of H/D exchange is an order of magnitude greater than the rate of hydrogenation of C_4H_6 points to the same conclusion.

The IR spectra of butenes adsorbed on Ni/SiO_2 [14] and on Co/SiO_2 [15] revealed absorption bands denoting the formation of metal-butane



and of π-allyl complexes. The allyl complexes are probably the precursors of the metal butanes **3**-**5**. The complex **3** is loosely bound to the surface, and is easily hydrogenated to butane. The complexes **4** and **5** are tightly bound, and are probably hydrogenated through the intermediate formation of the complex **6**. The formation of butane is observed in the range 20-100 °C, but above 90 °C the hydrogenation is accompanied by some dissociation of the C-C bond.

Data on the intermediate compounds taking part in the hydrogenation of the hydrocarbons are summarised in Table 1.

The hydrogenation of olefins on ZnO was studied by a combination of in situ spectroscopic and kinetic measurements, which unambiguously demonstrated the participation of the π-allyl complexes of C_3H_6 and of the π complexes of C_2H_4, and also the interaction of the H atoms with C_2H_4 and of the H_2 molecules with C_3H_6 and with C_4H_8. However, the kinetic parameters obtained by spectroscopic methods could not be compared with those obtained by analysing the gaseous products.[4-8]

Adequately reliable data on the intermediate compounds taking part in the dehydrogenation of the paraffins do not appear to be available.

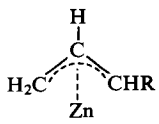
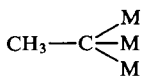
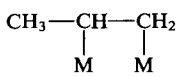
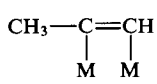
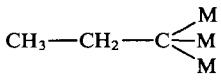
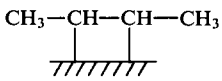
Addigo et al.[16] studied the IR spectra of the complexes of ethylbenzene and styrene adsorbed on iron oxide catalysts after the dehydration of the ethylbenzene to styrene. Under ordinary (non-reactive) conditions on non-promoted Fe_2O_3 the binding of the adsorbed styrene to the surface takes place through the aromatic ring, and the vinyl group suffers only a negligibly small perturbation. However, under the conditions favourable to the dehydrogenation reaction the interaction with the surface takes place through the vinyl group.[16]

III. Decomposition of ammonia

The synthesis of ammonia is carried out under high pressures. Spectroscopic measurements are difficult under these conditions, and therefore the reverse reaction (decomposition of NH_3) is often used in studies of the mechanism of the ammonia synthesis.

The decomposition of NH_3 on polycrystalline tungsten has been studied by Auger spectroscopy,[17] and on W(100),[18] Ru(001), and Ru(111)[19] it was studied by X-ray photoelectron spectroscopy (XPS). At 800 °C the tungsten surface (according to in situ Auger spectroscopy data) is covered with nitrogen atoms, and no NH_x species are found on the surface. The number of adsorbed

Table 1. Intermediate compounds in the hydrogenation of olefins.

Reaction, catalyst	Intermediate complex	Reliability	Ref.
Hydrogenation of ethylene on ZnO	Zn–H	H	4–6
	$H_2C{=}CH_2$ (O)	H	4–6
Hydrogenation of ethylene on ZrO_2	$H_2C{=}CH_2$ (Zr)	M	9
Hydrogenation of C_3H_6, C_4H_6, C_4H_8 on ZnO		M	7,8
		M	7,8
Hydrogenation of ethylene on metals		L	10,11
Hydrogenation of propene on Pd/ZrO_2		L	12
		L	12
	$CH_3{-}CH{=}CH{-}M$	L	12
		L	12
Hydrogenation of C_4H_6 on Pt(110)	C_4H_7(ads)	L	13
Hydrogenation of butenes on Co/SiO_2 and Ni/SiO_2		L	14,15

N atoms is much greater than the number corresponding to equilibrium adsorption

$$N_2 \rightleftharpoons 2N(ads),$$

in the absence of NH_3 and H_2 but under otherwise similar conditions. A combined study (by Auger spectroscopy) of the kinetics of the decomposition of NH_3 and of the desorption of N_2 showed that an increase in the coverage of the surface by nitrogen (θ_N) lowers the rate of decomposition of NH_3 and increases the rate of desorption of N_2, which become identical under steady-state conditions. Hydrogen from the gas phase has no effect on the adsorption of N_2 or on the rate of the reaction.

These results show that the reaction takes place by the mechanism of 'dynamic equilibrium' between two successive rate-limiting steps: (1) the formation on the catalyst surface of a layer of N atoms as a result of the decomposition of the NH_3 molecules, and (2) the desorption of the N atoms with formation of the N_2 molecule. The nitrogen is not in equilibrium with the NH_3 and H_2, as it is in the well known Temkin–Pyzhev mechanism of NH_3 synthesis on iron,[20] and for this reason the hydrogen does not affect the rate of absorption of nitrogen or the overall reaction rate. At high pressures the iron penetrates into the bulk of the catalyst and forms a nitride.

The decomposition of ammonia on Fe, W, and Re catalysts has also been studied by the electron projector method under thermal desorption conditions.[21] Nitrogen and hydrogen atoms adsorbed under the reaction conditions were detected. The activated adsorption of N_2 was observed on iron, and on rhenium and tungsten non-activated adsorption of nitrogen took place in two different forms, one of which contributes to the decomposition reaction whereas the other does not.

Thus it has been reliably shown by spectroscopic methods that adsorbed nitrogen atoms are the intermediate species in the decomposition of NH_3. Obviously, nitrogen atoms must act as intermediate complexes also in the synthesis of ammonia.

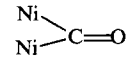
IV. Water gas conversion

Reactions involving CO are most conveniently studied by spectroscopic methods because the C≡O vibrations have high extinction coefficients. The interaction of CO with water vapour

$$CO + H_2O \rightleftharpoons CO_2 + H_2,$$

(the 'water gas conversion'), like its reverse reaction (the reverse water gas conversion'), is one of the simplest reactions involving CO. Both associative and dissociative mechanisms have been proposed for this reaction.

A purely dissociative mechanism was put forward on the basis of an IR spectroscopic study of this reaction on $Ni/(La_2O_3-MgO-Al_2O_3)$.[22] The vibration band of the bridging CO group



is shifted from 1960 to 1930 cm^{-1} after the adsorption of water, and under these conditions the linear form Ni–C≡O disappears. It was concluded that the adsorption of H_2O weakens the C=O bond in the bridging CO group (probably by shifting the electron density from H_2O towards the Ni) and thus favours its dissociation and disproportionation with formation of CO_2. The CO_3^{2-} and CH_3 groups, which do not take part in the conversion of CO, were also detected on the Ni surface. The following reaction mechanism was proposed:

$$H_2O(ads) \longrightarrow OH(ads) + H(ads),$$

$$CO(br) \longrightarrow C(ads) + O(ads),$$

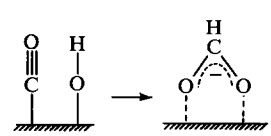
$$CO(br) + O(ads) \longrightarrow CO_2(ads),$$

$$2\,H(ads) \longrightarrow H_2,$$

$$C(ads) + OH(ads) \longrightarrow CO(br) + H(ads).$$

A dissociative mechanism for the reaction of CO with H_2O on Cu was proposed on the basis of IR spectroscopic data,[23] and for the same reaction on Co–Mo oxides by interpreting the results obtained by the response method.[24]

Most of the workers engaged in IR spectroscopic studies of the conversion of CO by water vapour observed the formation on the catalyst surface of formate groups (in addition to CO groups of various types). Therefore the formates are treated as intermediates in the mechanisms proposed for the reaction. The following formal mechanism was proposed after a study[25,26] of the conversion of CO on Cu–ZnO and $Cu-ZnO-Al_2O_3$ catalysts:



$$\rightleftharpoons H_2 + CO_2.$$

A similar mechanism was discussed for the reaction of H_2 with CO on Ru/NaY at 200–300 °C, but the observed first-order kinetics with respect to P_{H_2O} exclude the participation of tightly bound OH groups in the reaction.[27] An in situ study of the UV spectra allowed the valence state of the Ru to be determined: the results led to the reaction mechanism

$$Ru^+(H)(CO) + H_2O \longrightarrow Ru^{2+}(HCOO^-) + H_2,$$

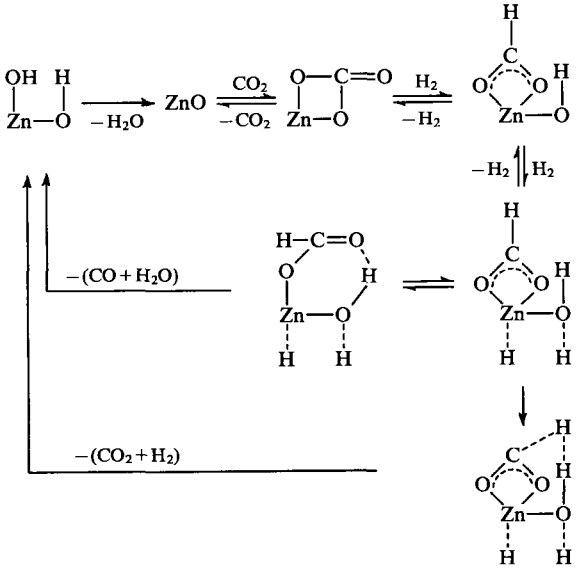
$$Ru^{2+}(HCOO^-) \rightleftharpoons Ru^+(H) + CO_2,$$

$$Ru^+(H) + CO \rightleftharpoons Ru^+(H)(CO),$$

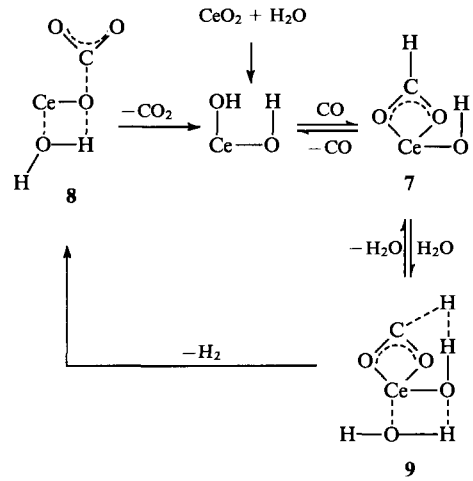
in which the formation of formate is the rate-limiting step.

On ZnO at 230 °C the rate of dissociation of the surface formate is equal to the rate of evolution of H_2O and CO into the gas phase after the hydrogenation of the CO_2.[28,29] On the other hand, if CO + H_2O is used as the initial mixture the production of formate is not observed. The opposite state of affairs is found on MgO:[28] formate is produced more easily from a mixture of CO + H_2O than from H_2 + CO_2. Under the conditions of the catalysis the MgO surface is covered mainly (90%) by carbonate, but the latter does not take part in the reaction.

The difference in structure between the surface complexes formed in the forward (CO + H_2O) and in the reverse reaction (CO_2 + H_2) on ZnO was reported also by Shido and Iwasawa.[30] By combining IR spectroscopy and labelled atom methods these workers showed that two types of formate complex exist on the surface. The first, formed from H_2 and CO_2, is 70% decomposed into H_2 and CO_2 at 250–300 °C, and 30% into H_2O (or surface OH groups) and CO. A different formate complex is obtained from OH and CO: this species is 70% decomposed with formation of OH and CO and 30% with formation of H_2 and CO_2. The activation energy for the decomposition of the formate complexes of the second type is 15–18 kJ mol^{-1} lower than for the first type. The rate of decomposition of the formate is much lower (by a factor of 10–30) in the presence of CO_2 than in a vacuum. Conversely, in the presence of H_2 the decomposition is faster. Under stationary conditions a balance is established between the promotion of the reaction by hydrogen and its suppression by CO_2. As reported,[30] the rate-limiting step is the dissociation of H_2 on a pair of Zn(HCOO)(OH). The overall reaction scheme can be written as follows.



The study of the interaction of CO and H_2O was extended to CeO_2 promoted by rhodium.[31] The activation energy for the decomposition of the formate complex produced from CO and OH was 56 kJ mol^{-1} (for the decomposition into H_2 + CO_2) and 122 kJ mol^{-1} (for the decomposition into OH + CO). In the presence of water vapour the rate of decomposition of $HCOO^-$ by the first path is increased 100-fold, and the activation energy falls to 33 kJ mol^{-1}. The rate-limiting step is assumed[31] to be the decomposition of the bidentate formate **7** into H_2 and the monodentate carbonate **8**. The evolution of CO_2 from the monodentate carbonate is promoted by H_2O through the intermediate complex **9**.



8 **7** **9**

The proposed mechanism differs from the mechanism of the same reaction on ZnO by the presence of the carbonate complex **8**. Rhodium itself is not active, but when added to CeO_2 it induces a rearrangement of the charges in the Ce–O pair which results in the activation of the C–H bond in the intermediate formate, in a closer approach of the formate to the neighbouring OH bridging group in the transition state **9**, and in a lowering of the activation energy.

Of the intermediates suggested above as participants in the water gas conversion the possible existence of the bridging carbonyl and carbonate complexes **8** can be assigned a reliability level L, and the existence of the formate complexes **7** a level M. However, the associative mechanism seems to be the most probable for the reaction: in this case the intermediate complex is not simply the formate but its associative complex with H_2O or H_2. The observation of various formate complexes, dissociating with different activation energies, suggests the possible migration of $HCOO^-$ from some centres to centres of other types.

V. Synthesis and decomposition of methanol

Methanol is synthesised at high pressures from a mixture of CO + H_2. According to Rozovskii[32] the species hydrogenated is CO_2, and not CO. The carbon dioxide is formed in the first step of the water gas conversion discussed in the previous section. The mechanism of the synthesis of methanol from CO + H_2 and from CO_2 + H_2 has been studied extensively.[33–47] The reverse reaction (decomposition of CH_3OH) has also been studied, because it takes place at low pressures and is therefore experimentally easier.

The Cu–ZnO–Al_2O_3 system is the most generally used methanol synthesis catalyst: most of the reported spectroscopic studies have relied on the use of this catalyst and of its components. IR spectroscopy measurements on the catalyst surface have revealed the presence of formates,[29,33–46] carbonates,[33,37–39,41,43] methoxy groups,[29,34,35,44,47] and formyl groups HCO,[34,36,40,43,46] as well as adsorbed forms of CO and CO_2. Adsorbed CH_2O has also been reported.[47] Many of these workers have formally proposed the following series of transformations for these compounds:

$$H_2 + CO\,(ads) \rightleftharpoons HCO \rightleftharpoons HCOO^- \overset{H_2}{\rightleftharpoons}$$

$$\rightleftharpoons CH_3O^- \overset{H_2}{\rightleftharpoons} CH_3OH.$$

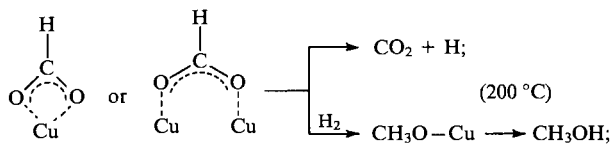
The same sequence of reactions was assumed[48] for the synthesis of methanol from CO_2 and H_2 on $Cu-ZnO-SiO_2$, in which the IR spectra of the surface compounds were examined after the reaction.

A detailed study[49] of the kinetics and of the mechanism of synthesis of CH_3OH on $Cu-ZnO-Al_2O_3$ led to the following scheme:

$$H_2 \rightleftharpoons 2\,H(ads),$$
$$CO_2 \rightleftharpoons CO_2(ads),$$
$$CO_2(ads) + H(ads) \rightleftharpoons HCOO(ads),$$
$$HCOO(ads) + 3\,H(ads) \rightleftharpoons CH_3OH + O(ads),$$
$$CO + O(ads) \longrightarrow CO_2,$$
$$H_2 + O(ads) \longrightarrow H_2O.$$

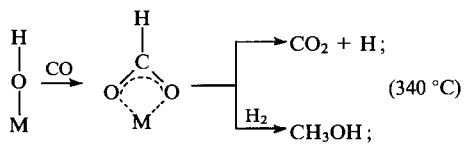
The location of these complexes is a problem of the greatest importance. Three types of adsorbed formate were detected by combining IR spectroscopic methods with temperature-programmed desorption (TPD) and with the method of chemical traps:

(1) formates adsorbed on Cu



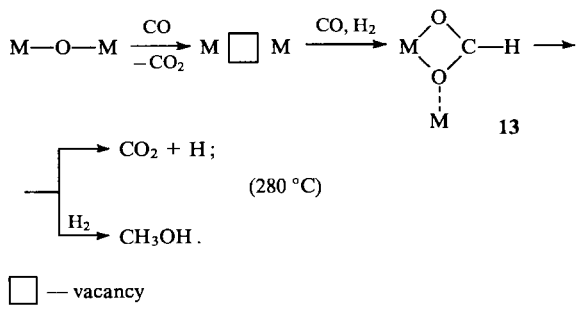
10 **11**

(2) formates adsorbed on Zn and Al atoms (with the participation of OH groups)



12

(3) formates produced after the partial reduction of the surface by carbon monoxide (evidently, near the boundary between Cu and ZnO)

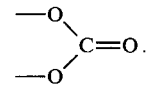


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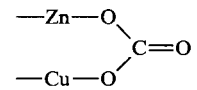
Many workers have detected a proportionality between the rate of the reaction of CO with H_2 (or of CO_2 with H_2), or of the amount of formate produced, and the copper content of the catalyst (or the surface area of the copper phase).[35,39,40,42] They concluded that the reaction takes place on the copper. There are also suggestions that $HCOO^-$ is formed near the Cu–ZnO boundary.[41,47] The hydrogenation of $HCOO^-$ to CH_3O (and even to CH_3OH) is treated as rate-limiting in the synthesis of CH_3OH from CO and H_2 (see Neophytides et al.[39]) or from CO_2 and H_2 (see Amenomiya and Tagawa[40]).

However, according to other workers[38,46,47] the formate is not an intermediate but a side-product of the methanol synthesis and decomposition processes. In a study of the synthesis of CH_3OH from CO and H_2 or from CO_2 and H_2 the IR spectra were obtained under high-pressure conditions.[38,48] At 200–220 °C both carbonate and formate complexes were detected on both Cu and ZnO. It was found that the formate complexes **10–13** are stable under the reaction conditions, and that upon further heating they decompose with evolution of CO (and not CO_2, as had been previously thought). Thus adsorbed CO is not a source of CH_3OH. On the other hand carbonate complexes are formed immediately after the adsorption of CO_2 and are converted into methanol during the subsequent hydrogenation. Thus it was concluded, in keeping with Rozovskii's views,[32] that the CH_3OH is formed from CO_2 and not from CO.

The role of carbonates in the synthesis of methanol was studied on the basis of IR spectroscopic measurements.[37,41,44] On ZnO the weakly bound bicarbonate HCO_3^- and the strongly bound carbonate CO_3^{2-} are formed, but on Cu we find the bidentate carbonate



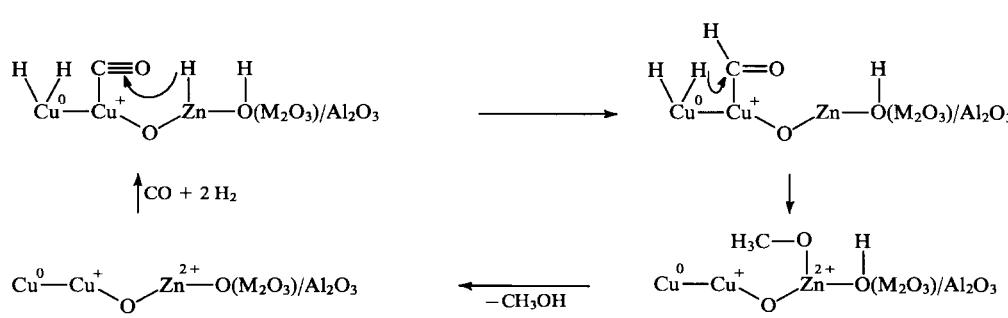
On mixed Cu–ZnO catalysts an absorption band at 1615 cm^{-1} was also found, and assigned to the carbonate



located at the phase separation boundary (known to be an active complex in the synthesis of methanol).[41] The hydrogenation of this carbonate produces formate. The formation of CO_3^{2-} during the adsorption of CO_2 is associated with the $Cu^0 \rightleftarrows Cu^+$ transition. It was also found that the formation of carbonates is approximately eight times greater in the adsorption of a mixture of $CO_2 + 2H_2$ than in the adsorption of CO_2 only,[37] i.e. that the hydrogen not only assists the adsorption of CO_2 (associative mechanism) but it also regenerates the centre needed for the subsequent adsorption of CO_2.

The adsorption of H_2 on ZnO at low temperatures results in the formation of Zn–H and O–H bonds, but at higher temperatures these bonds are not formed.[46] On this mixed catalyst we observe the migration (spill-over) of the hydrogen from the Cu to the ZnO and backwards, and this hydrogen contributes to the hydrogenation of the carbonate groups.[42]

Scheme 1



The nature of the synergism observed in the synthesis of methanol on a $Cu-ZnO-M_2O_3$ catalyst (M = Sc, Cr, V) has been studied by in situ Raman spectroscopy.[45] The Cu–H, Cu–O–H, Cu–CO, and Cu–CHO groups were detected on the catalyst surface. The mechanism of this reaction is shown in Scheme 1.

According to the Raman spectra additions of N_2O promote the adsorption of CO.

The simultaneous use of in situ IR spectroscopy and kinetic response methods showed that the formation of methanol from $CO + H_2$ and $CO_2 + H_2$ mixtures takes place by different mechanisms.[36] In the first of these mixtures surface formyl is produced from M–CO and M–H, and this step is rate-limiting, as shown by the appearance in the IR spectrum of an absorption band due to HCO immediately after the passage of a pulse through the $H_2 + CO$ mixture. In the $CO_2 + H_2$ mixture carbonates and formates are formed:

$$CO_2 + M \rightleftharpoons M{-}CO_2,$$

$$H_2 + M \longrightarrow M{-}H,$$

$$M{-}CO_2 + M{-}H \longrightarrow M{-}O{-}\overset{\overset{O}{\|}}{C}{-}H + M,$$

$$M{-}O{-}\overset{\overset{O}{\|}}{C}{-}H + 2\,M{-}H \longrightarrow M{-}O{-}CH_2{-}OH + 2\,M,$$

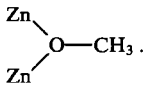
$$M{-}O{-}CH_2{-}OH + M{-}H \longrightarrow CH_3OH + M{-}OH + M,$$

$$M{-}OH + M{-}CO \longrightarrow M{-}O{-}\overset{\overset{O}{\|}}{C}{-}H + M.$$

In this case the rate-limiting step is (apparently) the dissociative adsorption of H_2 on ZnO and Cu and the migration of the hydrogen from the ZnO to the Cu. However, this dissociation is faster than the synthesis of CH_3OH from CO and H_2. Furthermore the CO_2 inhibits the disproportionation of CO into CO_2 and C, thus preventing the poisoning of the catalyst.

It has been shown[29] that the decomposition of the surface formates, which is very slow in the absence of a gas phase, is greatly accelerated by the presence of CH_3OH in the gas phase, i. e. the decomposition takes place by an associative mechanism.

The mechanism of the decomposition of CH_3OH on a $Cu-ZnO/Al_2O_3$ catalyst has been studied also by in situ ^{13}C and ^1H NMR methods.[50] The methanol is adsorbed on Al_2O_3 as $Al-OCH_3$, and on ZnO as



When heated on copper the OCH_3 group is oxidised to the symmetrical formate and beyond (to HCO_3^- and CO_3^{2-}), and CO_2 is evolved when the system is further heated to 250 °C. Under the conditions of the synthesis of CH_3OH many intermediate substances are adsorbed on ZnO and Al_2O_3, but in order to contribute to the synthesis these must migrate towards the copper. Experiments on the adsorption of CH_2O also show that this species can participate in the reaction, for example by disproportionation into CH_3O^- and $HCOO^-$, though in the synthesis process CH_2O is not adsorbed on the surface. Carbon dioxide is easily adsorbed on $Cu-ZnO/Al_2O_3$, giving a carbonate, whereas CO is adsorbed to a much smaller extent. The carbon monoxide also is converted into a carbonate during the oxidation. This indicates the participation of CO_2 (rather than CO) in the synthesis of methanol.

An NMR study[51] of the decomposition of CH_3OH on $Cu-ZnO/Al_2O_3$ detected methoxy among the adsorbed compounds.

Fu and Somorjai[52] studied the interaction of CH_3OH with Cu–ZnO by a combination of XPES, LEED, and temperature-programmed reaction (TPR) methods. The methanol reduces the ZnO and removes the adsorbed oxygen from the copper centres. The formate produced on clean copper decomposes into CH_2O and H_2. On Cu–ZnO also we observe the decomposition of $HCOO^-$ into $CO_2 + CO + H_2O$ at 380 °C and the decomposition of CH_3O^- into CH_2O and H_2 at 280 °C. The decomposition of $HCOO^-$ on ZnO produces a mixture of $CO + CO_2 + H_2O + CH_4$.

The formation of compounds on the individual components of the catalyst was studied in parallel with the mechanism of the synthesis of CH_3OH on $Cu-ZnO/Al_2O_3$. It was found that copper can catalyse all the stages. Nevertheless under the conditions of the synthesis of CH_3OH many compounds formed as intermediates are found on the support phases (ZnO and Al_2O_3): we should therefore stress the important role of synergism and spill-over effects in this process.

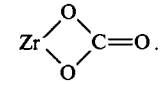
Spectroscopic methods have been used also in the study of other catalysts. For example, in situ IR spectroscopy was used to study the synthesis of CH_3OH on a K–Cr–Zn–O catalyst.[53] After the reaction CH_3O^- and $HCOO^-$ fragments were detected on the surface. In the presence of potassium we note a large increase in the $HCOO^-:CH_3O^-$ ratio. Methyl formate ($HCOOCH_3$) is formed at low temperatures on catalysts containing potassium, evidently as a result of the interaction of the unstable $HCOO^-$ with methane. The methyl formate can then take part in the synthesis of higher alcohols.

$HCOO^-$ and CH_3O^- groups were detected[17] during the decomposition of CH_3OH on Cr_2O_3. The adsorbed formate groups are stable in a vacuum, but in the presence of $^{13}CH_3OH$ vapour the ^{13}C isotope is easily incorporated into the $HCOO^-$ surface groups and hence into the reaction products. At the same time, according to IR spectroscopic data, the concentration of formate stays constant. This shows that the decomposition of CH_3OH takes place by an associative mechanism through 'desorption at the expense of adsorption', (in Tamaru's terminology[17]).

The synthesis of CH_3OH from CO and H_2 on ZrO_2 has been studied by IR spectroscopy and temperature-programmed desorption (TPD) methods.[54,55] It is accelerated by the presence of water, but ^{18}O atoms from $H_2{}^{18}O$ water do not penetrate into the CH_3OH. The following sequence of reactions is suggested:

$$CO(ads) \xrightarrow{OH^-} HCOO^- \xrightarrow{2\,H^+} OCH_3^- \xrightarrow[-OH^-]{H_2O} CH_3OH.$$

Thus, water is needed for the desorption of the methanol. A similar sequence of reactions was proposed by Onishi et al.[56] on the basis of an IR spectroscopic investigation, but these workers stipulated the formation of a bidentate carbonate group as the first stage after the adsorption of CO:



Formate is produced (with the participation of an oxygen atom from the oxide) in the interaction of H_2 with CO on MgO, CaO, La_2O_3, ThO_2, and ZrO_2 at 200–300 °C.[57] Comparing the IR with the TPD spectra showed that the formation of $HCOO^-$ is preceded by the formation (as an intermediate) of the formyl group HCO^-. The main product of the reaction was CH_3OH on La_2O_3 and ZrO_2, and CH_2O on MgO.

On Pd or Rh catalysts supported on SiO_2, Al_2O_3, or ZrO_2 (promoted with LiCl, NaCl, or KCl) formate was observed[58,59] by IR spectroscopy after the admission of a mixture of $CO + H_2$ at 180 °C. It was found that the higher the concentration of

adsorbed $HCOO^-$, the greater is the rate of the synthesis of CH_3OH. No absorption bands could be seen in the IR spectra of nonpromoted samples. The rate of formation of C_2H_5OH on $Rh-Na-Al_2O_3$ was approximately proportional to the intensity of the CH_3COO^- bands. These results led to the suggestion that the active centres contain oxidised compounds which stabilise the acetates and formates.[58]

Studies of the mechanism of the formation reaction of CH_3OH and C_2H_5OH at 240–280 °C on platinum catalysts prepared from $Pt_9(CO)_{18}.2NEt_4$ clusters supported on MgO, ZrO_2, and Al_2O_3 revealed the CO_2^{2-}, CO_3^{2-}, and CH_3O^- fragments stabilised on the carrier.[60] They are apparently formed by the interaction of Pt–CO with the OH groups (or the O^{2-} groups) of the carrier. Their hydrogenation produces the alcohols.

The decomposition of CH_3OH into CO and H_2 on Fe, Ni, or Pd foil was studied by molecular beam relaxation spectrometry.[61] The process was divided into several stages, and the kinetic parameters of each stage were determined:

$$CH_3OH \xrightarrow{(1)} CH_3OH(ads) \xrightarrow{(2)} CH_3O(ads) \xrightarrow{(3)}$$

$$\longrightarrow CH_2O(ads) \xrightarrow{(4)} \ldots \longrightarrow CO(ads) + 2\,H(ads),$$

$$CO \rightleftharpoons CO(ads),$$

$$H_2 \rightleftharpoons 2\,H(ads).$$

The reality of some of these stages was confirmed by the XPES method. On Ni the slow step was the third, with an activation energy of 104 kJ mol^{-1}. On Pd the desorption of CH_3OH could not be observed because its conversion into the subsequent products is very fast. In this case the desorption of CO becomes the rate-limiting step. On Fe the adsorbed CH_3OH can be converted into CO and H_2 through intermediate products, but it can also pass into another, unreactive form (CH_3OH^{II}):

$$CH_3OH^{I}(ads) \begin{cases} \longrightarrow CH_3OH^{III}(ads) \longrightarrow \ldots \longrightarrow CO + H_2, \\ \longrightarrow CH_3OH^{II}(ads). \end{cases}$$

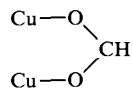
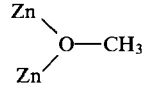
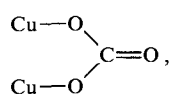
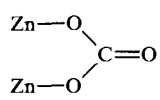
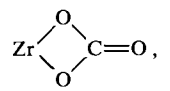
The activity of the Fe is determined by the relative probability of the reaction taking place by these two pathways. In terms of their activation energy (E_a) these metals can be arranged in the series Ni ≫ Pd > Fe, i.e. the highest E_a values are observed when the intermediates appear in the later stages of the reaction.

According to XPES and TPR data the decomposition of alkoxy groups on Fe(100) can follow one of three paths: (1) with formation of CO + H_2; (2) with formation of CH_3OH; (3) with full breaking of the C–H and C–O bonds. The last of these paths has been reported also by Benziger and Madix.[62]

Data on the intermediate compounds taking part in the synthesis and decomposition of CH_3OH are summarised in Table 2.

To conclude this section we note that, in spite of the large number of publications in which spectroscopic methods are used to study the synthesis and decomposition of CH_3OH, information on spectro-kinetic studies of these systems is almost totally absent (with a few exceptions[36,38,48,61]). The detection of the $HCOO^-$, CO_3^{2-}, CH_3O, and HCO groups on the catalyst surface is often interpreted as a proof that these species take part in the reaction as intermediates. However, direct kinetic confirmations of this conclusion are seldom put forward. Most probably the $HCOO^-$ groups contribute not to the synthesis or the decomposition of CH_3OH but to the corresponding conversion of water gas. A contribution from intermediate carbonates to the synthesis of CH_3OH is a more realistic suggestion. Furthermore, $M-CO_3$ complexes are formed simultaneously on the various phases of a complex catalyst, and it is essential to establish which of these contribute to the main reaction and which are a blind end-product or a reservoir for the former. Obviously, the spill-over phenomenon plays a very important role in the reaction mechanism. In many cases it has been established that the reaction follows an associative mechanism.

Table 2. Intermediates in the synthesis and decomposition of methanol.

Reaction, catalyst	Intermediate complex	Reliability	Ref.
Synthesis and decomposition of CH_3OH on $Cu-ZnO/Al_2O_3$	$HCOO^-$,	M	21, 29, 33–37, 39, 40, 41, 45, 50, 52
			
	CH_3O-Cu, 	M	29, 34, 35, 46, 47, 50, 51
	HCO	L	34, 36, 40, 43, 46
	CH_2O	L	47, 50
	$Cu-CO$, $Cu-H$, $Cu-HCOO$	M	36
		M	37, 38, 41, 44
			
Synthesis of CH_3OH on $Cu-ZnO-M_2O_3$	$Cu-H$, $Cu-CO$, $Cu-OH$, $Cu-HCO$	M	43
Decomposition of CH_3OH on $K-Cr-Zn-O$	CH_3O^-, $HCOO^-$	L	53
Decomposition of CH_3OH on Cr_2O_3	CH_3O^-, $HCOO^-$	L	17
Synthesis of CH_3OH on ZrO_2		L	54–56
	$HCOO^-$, CH_3O^-		
Synthesis of CH_3OH on MgO, CaO, SrO, La_2O_3, ThO_2, ZrO_2	$HCOO^-$	L	57
Synthesis of CH_3OH on Pd/SiO_2, Al_2O_3, ZrO_2	$HCOO^-$	M	58, 59
Synthesis of CH_3OH and C_2H_5OH on Pt/MgO, Al_2O_3 on ZrO_2	CO_2^{2-}, CO_3^{2-}, CH_3O^-	L	60
Decomposition of CH_3OH on Fe, Ni, Pd	CO(ads), H(ads), CH_3O(ads), CH_2O(ads)	L	61, 62

VI. Synthesis of hydrocarbons from carbon monoxide and hydrogen

The hydrogenation of CO to hydrocarbons (or Fischer–Tropsch synthesis) takes place on metals. Iron catalysts are most widely used for this reaction. However, they were studied mainly from the standpoint of their structural phase transformations under the reaction conditions. Less attention has been devoted to the forms adsorbed on the surface.

The state of the carbon on the iron surface was studied by XPES,[63–65] Raman,[66,67] and IR spectroscopy methods,[68] and also by the kinetic and the isotopic response method.[63,69–71] Three main forms of carbon were detected: graphite (which is universally known to be inactive in the Fischer–Tropsch synthesis), carbide carbon (which contributes to the synthesis of methane and of higher paraffins), and partially hydrogenated carbon CH_x (which can be hydrogenated further to give CH_4 and C_nH_m). There are also reports[64,69] of the formation of an amorphous, relatively porous form of carbon which can also be hydrogenated by hydrogen. According to Tan and Bennet[71] the real intermediate in the Fischer–Tropsch synthesis is the CH species. By using the method of 'interception' (with pyridine) of intermediate substances it was shown that alkyls can act as intermediate species of this type. Surface formates, carbonates, and carboxylates have also been detected: these are probably formed from the CO_2 produced by the disproportionation of CO.[72]

There are two contrary mechanisms for the hydrogenation of carbon monoxide by hydrogen: a dissociative and an associative mechanism.[73,74] According to the former the CO produces carbidisation of the metal (or other forms of carbon attributed to the dissociation of CO):

$$2\,Fe + CO + H_2 \longrightarrow Fe_2C + H_2O,$$

and

$$2\,Fe + 2\,CO \longrightarrow Fe_2C + CO_2,$$

and the carbide then interacts with hydrogen to give hydrocarbons

$$Fe_2C + 2\,H_2 \longrightarrow 2\,Fe + CH_4.$$

According to the associative mechanism the CO and H_2 from the gas phase react with atoms of the metal, forming complexes: for example[75]

$$H(ads) + CO(ads) \rightleftharpoons HCO(ads) \longrightarrow H_2CO(ads) \longrightarrow CH_3O(ads) \longrightarrow CH_3(ads) + O(ads).$$

The CH_3 group can be hydrogenated to methane or it can add on a CH_2 group, forming C_2 (and higher) hydrocarbons.

According to results from our laboratory[74] on iron catalysts this reaction involves oxides and carbides. The following mechanism can be proposed for the reaction at the metal–oxide boundary:

$$MO + CO = M\square_O + CO_2,$$

$$M\square_O + CO = C + MO,$$

$$2\,M + H_2 \longrightarrow 2\,M{-}H,$$

$$4\,M{-}H + C \longrightarrow 4\,M + CH_4.$$

$\square_O$ — oxygen vacancy on the catalyst surface

Here the hydrogenation of the carbon monoxide takes place mainly by a dissociative mechanism:

$$2\,CO + 2\,H_2 = CH_4 + CO_2.$$

An alternative reaction path for the hydrogenation of CO,

$$2\,CO + 3\,H_2 = CH_4 + H_2O,$$

is probably realised by an associative mechanism, involving the formation of HCO complexes in the presence of an excess of H_2 and a deficit of CO:

$$M'CO + M{-}H = M'COH + M,$$

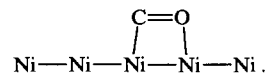
$$M'COH + 2\,M{-}H \longrightarrow M'OCH_3 + 2\,M,$$

$$M'OCH_3 + M \longrightarrow MO + M'CH_3 \xrightarrow{H_2} CH_4 + H_2O + M' + M.$$

It may be assumed that the activation of H_2 and CO takes place on different active centres: M and M'.

Nickel (unlike iron) is mainly a catalyst for the formation of methane from CO and H_2. Different forms of carbon (carbide, and hydrogenated) have been detected on a Ni surface by IR spectroscopy,[76–86] XPES,[87] and Auger spectroscopy.[88]

Bands corresponding to linear and to bridging CO groups were observed in the IR emission spectra for the interaction of CO and H_2 on 10% Ni/Al_2O_3; HCO groups were not detected.[82] It has been suggested[79] that the shift of the CO band in the IR spectra measured on Ni/SiO_2 and Ni/Al_2O_3 can be attributed to the formation of an associative HCHO complex. The preadsorption of H_2 on Ni(111) produces a shift in the bands of the adsorbed linear carbonyls (Ni–C≡O) towards the positions corresponding to the bridging C=O groups.[83] Evidently this can be explained by the formation of a surface carbonyl hydride in which the energy of the C–O bond is low and the dissociation of the carbonyl into carbide and oxide is facilitated. A possible precursor of the dissociated forms could be the 'recumbent' carbonyl



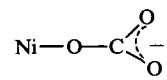
The 2050 cm^{-1} band in the IR spectrum of CO adsorbed on Ni/SiO_2 has been assigned to this form.[86]

Active carbon exists on the Ni surface in the relatively narrow temperature range between 200 and 450 °C. Above 450 °C it is rapidly converted into the inactive graphite, and below 200 °C there is no dissociation of the CO.[76,77] The following sequence of conversions of the carbon during its hydrogenation on a Ni plate has been established by in situ XPES[87] and 'absorbance-reflectance' IRS[81] methods:

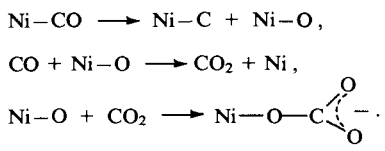
$$C \rightleftharpoons CH \longrightarrow CH_2 \rightleftharpoons CH_3 \rightleftharpoons CH_4.$$

Under reaction conditions the Ni surface is mostly covered with CH groups (Ni–CH), and their hydrogenation is probably rate-limiting.[81,87] At low temperatures we also find Ni–CH_2–Ni bridging groups, but these are lost from the surface even before the methanation temperature is reached. It is assumed[82] that under different conditions the rate-limiting step can be either the rate of formation of the CH_x species or the rate of their hydrogenation.

It has been reported[88] that the rate of methanation on Ni(100) increases with the concentration of carbon on the surface, whereas the yield of higher hydrocarbons increases with the oxygen concentration. The oxidised forms $HCOO^-$ and CH_3O^- are also found[76,77] on a Ni surface treated with a mixture of H_2 and CO, but they are hydrogenated less actively than the surface carbon. The appearance of carbonate



is apparently associated with the CO disproportionation reaction:[81]



The hydrogenation of CO to hydrocarbons on a cobalt film also includes the dissociation of CO, and probably takes place through carbide formation.[89]

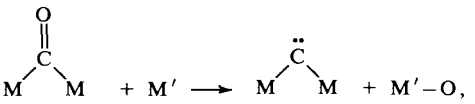
Cobalt favours the dissociative adsorption of CO more markedly than nickel.[90] This accounts for the preferential formation of methane on Ni and of methane with higher hydrocarbons on Co. However, if the Co is supported on metallic gold the rate of the hydrogenation reaction increases, the character of the CO adsorption changes, and the process takes place through the formation of HCHO complexes (or other 'associative' complexes) without dissociation of the CO.

Carbonyl groups, as well as hydrocarbons, formates, and carbonates, have been detected[91] by IR spectroscopy on Co/SiO_2 and Co/Al_2O_3 under conditions compatible with the hydrogenation of CO at 200–250 °C. The time-changes in the intensity of the bands show that these are reaction products accumulating on the surface.

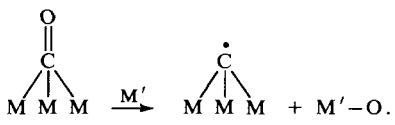
According to Loran et al.[92] the hydrogenation of CO on Ni, Ru, and Fe goes mainly via the breaking of the C–O bond in carbon monoxide, whereas on Rh and Mo it goes mainly via the breaking of the same bond in the HCHO complex.

The behaviour of bimetallic catalysts (for example, Ni–Fe and Co–Fe) towards the same reaction has also been studied.[74] The activity of the latter catalyst is attributed to the presence of cobalt, and the selectivity of the formation of olefins to the presence of iron. Obviously, the more active component contributes to the activation of H_2, and the less active to the activation of CO. It has been assumed, on the basis of IR spectroscopic data,[93] that the CO is more easily activated at the boundary between the oxidised and the reduced phase.

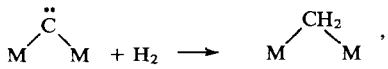
Also according to IR spectroscopic data[94] the most stable form of CO on Fe or Co is the bridging CO ($\nu_{CO} = 1800-1900$ cm^{-1}), retained until the reaction temperature is reached. Its dissociation is accompanied by the formation of carbide and oxide:



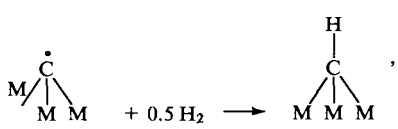
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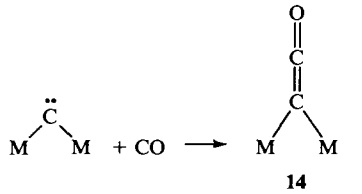


The surface carbides can then undergo hydrogenation or carbonylation.



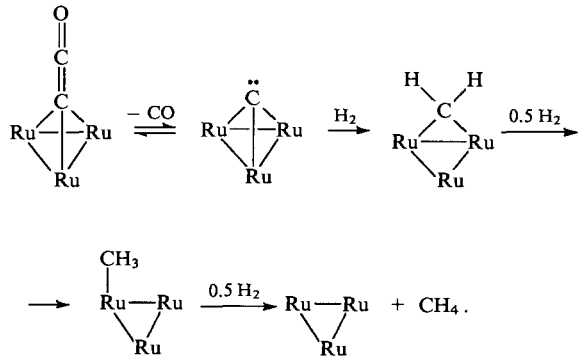
or





14

The transformations of the keten complex of ruthenium **14** supported on SiO_2 have been studied under the conditions of hydrogenation of CO at 200–300 °C:[91]



The reaction takes place by a dissociative mechanism: the associative mechanism, including (for example) the hydrogenation of the keten, is not observed.

We note that the dissociation of the C=C bond in the keten $CH_2=C=O$ added to a mixture of CO + H_2 in the hydrogenation of CO to hydrocarbons was observed by isotopic labelling more than 30 years ago.[95] The radioactivity of the hydrocarbons was found to be proportional to their carbon content. It was concluded from these results that the CH_2 species contribute to the chain initiation.

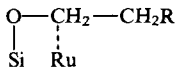
The transformation of the dissociative form of adsorption of CO into the molecular form during the carbidisation of the V(110) surface[96] is also of interest. As shown by an analysis of the EELS spectra, the C–C bond is produced during the adsorption of CO on VC, and this could be the initial stage in the subsequent synthesis of hydrocarbons.

On the platinum group metals (Ru, Rh, Pd) compounds containing oxygen are formed in addition to hydrocarbons. This is attributed to the high dissociation energy of CO on these metals.[97] On the platinum group metals (unlike iron) the energy of formation of the M–C and M–O bonds is of the same order of magnitude as the dissociation energy of CO. Many workers have studied the mechanism of the Fischer–Tropsch reaction by using a combination of physical methods. Ruthenium[97–119] and rhodium catalysts[102,120–134] were investigated most extensively.

According to IR spectroscopic measurements linear and bridging forms of CO and of the dicarbonyl $Ru(CO)_2$ are formed[97,102,104,105,108,116] on Ru/Al_2O_3. Under the catalysis conditions the linear CO groups are hydrogenated almost exclusively: the dicarbonyl groups do not contribute to the hydrogenation. Disproportionation of the CO by Boudart's reaction has also been observed.[109,123] The hydrogenation of CO takes place (apparently) through the intermediate dissociation of the linear form Ru–CO.[97,109] In the absence of H_2 the activation energy of the dissociation of CO is much higher than in its presence. The promoting action of H_2 is explained by the formation of H_2O, O(ads), and H(ads), which suppress the recombination of C and O and shift the equilibrium towards the dissociation of CO.[115] An alternative explanation of the decrease in the activation energy of the dissociation of CO in the presence of H_2 is the formation of the HCO complex.[99,117]

By using IR [97,111,114] and NMR [97,108,109] spectroscopy in conjunction with kinetic and isotopic response methods it was found that carbon is adsorbed on the surface of ruthenium in two forms: C_α and C_β. The first of these consists of adsorbed carbon atoms which are rapidly hydrogenated to CH_4 (few of these are found on a surface in a stationary state). The rate of formation of methane is directly proportional to the concentration of the C_α surface form. The C_β form consists of CH groups which accumulate on the surface and do not contribute significantly to the yield of CH_4. They are hydrogenated much more slowly than C_α CO groups are also found on the ruthenium surface, but practically no H(ads), since this is rapidly removed [98] as H_2O.

Further studies by NMR of the adsorption forms of carbon revealed the presence of four distinct forms on Ru: C_α (carbon atoms), and $C_{\beta1}$, $C_{\beta2}$, $C_{\beta3}$ (different alkyl groups). [99,101,108] The $C_{\beta1}$ form is a possible intermediate in the formation of the C_2 product. The $C_{\beta2}$ form apparently acts as a source for the formation of long hydrocarbon chains, most of which remain on the surface, and $C_{\beta3}$ is a source of branched products. The intensity of the CH_2 bands observed in the in situ IR spectra is not correlated with the rate of the reaction: evidently, these bands are due to the accumulation of reaction products on the surface. [106,107] Under the synthesis conditions (at high pressures) the hydrocarbons accumulated on the Ru surface are also bound to the support: [112]



The oxygen compounds HCO and $HCOO^-$ are also formed on the surface of supported ruthenium catalysts. [114,117] On Ru(001) promoted by potassium we find carbonate and formate:

$$CO \longrightarrow CO_2 + C,$$

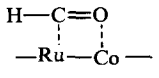
$$CO_2 + K_2O \longrightarrow K_2CO_3 \xrightarrow{H_2} KHCOO.$$

The conversion of water gas under the influence of alkaline additives also takes place through formate as an intermediate:

$$CO + H_2O \longrightarrow HCOO^- + H^+ \longrightarrow CO_2 + H_2.$$

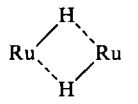
The formate is then hydrogenated to CH_4 and CH_3OH. In the absence of potassium only methane is formed.

According to calculations [94] the activation energy for the hydrogenation of HCO is smaller than for the dissociation of HCO. Therefore HCO can be hydrogenated to H_2CO(ads), CH_3O(ads), and beyond (to alcohols and hydrocarbons). As reported, the intensity of the 1584 cm^{-1} HCO band is correlated with the rate of the synthesis of oxygenated compounds. [117,134] On $Ru-Co/SiO_2$ catalysts this absorption band corresponds to the complex



The conversion of HCO into $CH_3C{=}O$ and $C_mH_nC{=}O$ groups bound to Ru and Co has been studied spectroscopically.

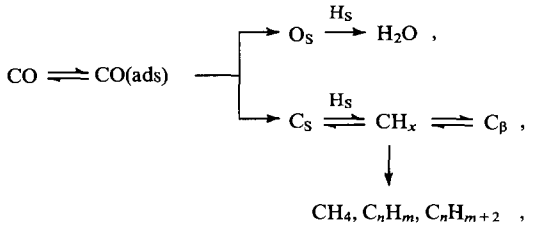
The role of carbides in the hydrogenation of CO has been studied by IR and EXAFS spectroscopic methods in the case of $[Ru_6C(CO)_{16}(CH_3)]^-$ complexes supported on MgO, ZnO, La_2O_3, TiO_2, ZrO_2, and Al_2O_3. [118,119] Whereas the carbide complex of Ru takes part in the synthesis of oxygenates, hydrocarbons and CH_4 are formed on the ordinary (carbonyl) Ru complex. It has been shown [118,119] that the central carbide atom in the cluster determines the structure of the intermediate complex, enabling it to add reversibly 8 – 11 molecules of CO onto each cluster. Under these conditions the cluster continuously expands or shrinks. The presence of a large number of adsorbed CO molecules in the bridging form (Ru_2CO) suppresses the dissociation of CO and favours the synthesis of the oxygenated compounds CH_3OH, CH_3OCH_3, and CH_2O. The expanded Ru_6C structures are more active than the compressed structures because they favour the dissociative adsorption of H_2:



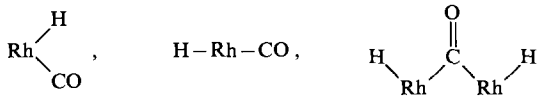
The H/D isotope exchange on the Ru_6C/MO carbide cluster is 3000 times faster than the stationary synthesis of oxygen compounds.

The low activity of rhodium towards the dissociation of CO accounts for its high activity towards the synthesis of the higher hydrocarbons (the Fischer – Tropsch reaction) and of oxygenated compounds. The Rh^0 form plays an important role in the synthesis of hydrocarbons, and Rh^+ in the synthesis of alcohols. [132] Obviously, the Rh^0-Rh^+ pairs in catalysts such as Rh/ZnO and Rh/TiO_2 can assist both the dissociation of carbon monoxide and the introduction of CO into the growing chain. [132,133]

The analysis of the IR [102,121,127] and NMR spectra [124] of the products adsorbed on supported Rh catalysts also indicates the formation of different carbonyl groups, and also of the C_α and C_β forms of carbon. The following reaction scheme was proposed: [206]

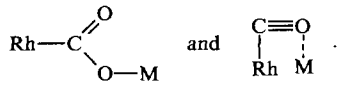


(the subscript S denoting surface atoms) according to which the form C_β does not take part in the hydrogenation of CO. The presence of H_2 assists the adsorption of CO on Rh as a result of the formation of complexes of the CH_2O type. In the methanation of CO on Rh/Al_2O_3 the formation of carbonyl hydrides has been reported: [123]

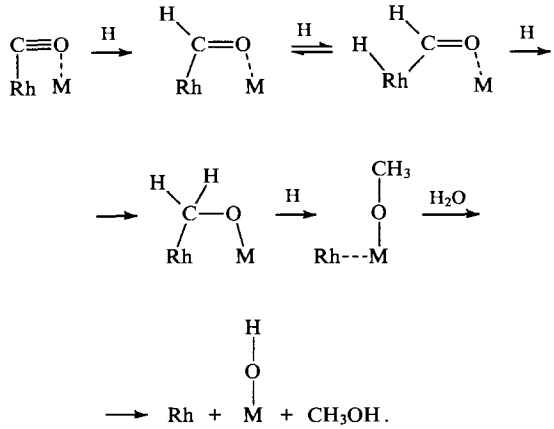


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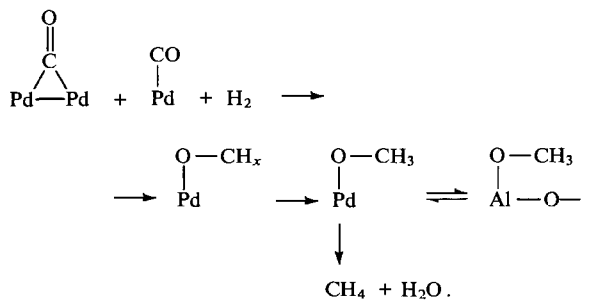
The formation of the complex **15** and the synthesis of hydrocarbons take place below the temperature of the Boudart reaction, i. e. the dissociation of CO is not observed under these conditions. The oxygenated groups OCH_3, OC_2H_5, HCOO, HCO, CH_3CO, CH_3COO, and CO_3 were detected on the rhodium surface by IR [127–130] and NMR spectroscopy. [124] The formate is produced mainly on the support: under the catalysis conditions it is fairly stable and it cannot act as an intermediate, whereas $HCOO^-$ adsorbed on metallic rhodium can play this role. [120,127] The same is true of the carbonates and acetates, which are also adsorbed mainly on the support. [128] Evidently, the active centres for the formation of oxygen compounds are on the boundary between Rh and the support. [122] Two adsorption complexes of CO, formed at the metal – support interface, have been observed [130] on Rh and Mo catalysts supported on ZrO_2:



Their dissociation is facilitated in the presence of hydrogen by the formation of the intermediate complex Rh–CHO, which is then (apparently) converted into $Rh{=}CH_2$ and methane. Methanol is obtained by the series of reactions



The properties of palladium are similar to those of Ru and Rh.[102,135–140] A scheme for the methanation of CO on Pd, involving the fully dissociated forms C(ads), H(ads), and O(ads), has been proposed.[131] The maximum coverage of the Pd/TiO_2 surface by linear carbonyls is 1%, and the maximum coverage by bridging carbonyls is 0.1%. Carbonyl groups and CH_3O, HCOO, and HCO groups, stabilised mainly on the carrier, have been observed[137] in the hydrogenation of CO on Pd/Al_2O_3. Spill-over of these species between the palladium and the Al_2O_3 was also noted. According to these workers[137] the source of the formation of CH_4 are the $CH_3–O–Pd$ groups:



According to Hindermann et al.[138] the key intermediate in the hydrogenation of CO on $Pd–MgO–SiO_2$ is the formyl group HCO. This was confirmed by the chemical interception method with dimethyl sulfate. The presence of surface formate was also noted. Its hydrogenation has been stated[140] to be the rate-limiting step.

No correlation between the catalytic activity and the concentration of CO groups on the surface was observed[141] in a study of the hydrogenation of CO on Pt/TiO_2 by IR spectroscopy. It was concluded that only a very small part of the surface CO contributes to the hydrogenation. The active centres are, apparently, the steps or kinks on the platinum crystallites, which do not appear in the spectra.

The formation of CH_3O, which is rapidly hydrogenated to methane, was observed[142] during the hydrogenation of CO on Pt/Al_2O_3. Most of the CH_3O is adsorbed on the carrier, and the H(ads) species can move from the Pt to the Al_2O_3 (and hydrogenate the CH_3O) by the spill-over effect.

According to in situ IR spectroscopic data[76] on supported iridium the reaction proceeds by the scheme

$$CO \rightleftharpoons CO(ads),$$

$$H_2 \rightleftharpoons 2\,H(ads),$$

$$CO(ads) + H(ads) \longrightarrow C(ads) + OH(ads),$$

$$2\,CO(ads) \longrightarrow C(ads) + CO_2(ads),$$

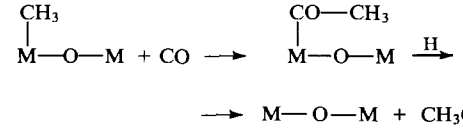
$$C(ads) + H(ads) \longrightarrow CH(ads) + CH_4,$$

$$OH(ads) + H(ads) \longrightarrow H_2O.$$

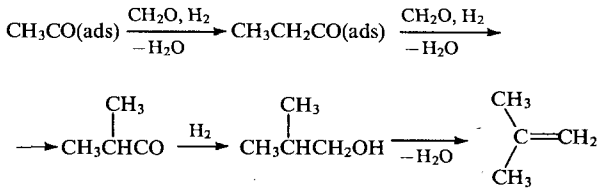
The contribution of the disproportionation of CO to the overall transformation is not substantial (only 0.8% of CO_2 is detected for a 60% conversion of the CO). The rate of hydrogenation of the adsorbed carbon is much higher than that of CO, but the adsorbed carbon is formed not by the direct dissociation of CO but by the interaction of CO with the adsorbed hydrogen (possibly through the HCO stage) by an associative mechanism.

A similar dissociative mechanism has been proposed for the hydrogenation of CO on $Ir_4(CO)_{12}$ clusters supported on α-Al_2O_3.[143] The formation of carbide, carbonyl, and oxide surface compounds has been observed by IR spectroscopy when the reaction was carried out at 250–300 °C. The rate-limiting step is the hydrogenation of the carbonyls. The formation of $Ir_xC(CO)_y$ carbide–carbonyl clusters under the reaction conditions has also been suggested, but these clusters have not been observed directly.

The hydrogenation of CO on ZrO_2 can lead to the selective synthesis of isobutene. HCOO and CH_3O groups were observed on the surface by using in situ NMR and IR spectroscopic methods.[144,145] The presence in the reaction of CH_3 and CH_2 species was also demonstrated by the kinetic interception method, using special acceptors. The introduction of the CO group into the $M–CH_3$ bond results in the formation of a new C–C bond:



The synthesis of isobutene can also take place by the aldol condensation mechanism[145]



The HCOO, CO_3, and CH_3O groups have been observed[146] by in situ IR spectroscopy at 200–400 °C on the catalyst surface during the hydrogenation of CO on Sm_2O_3. This led to the suggestion of a chain of transformations leading to the formation of methanol at temperatures below 300 °C and of hydrocarbons above that temperature.

Table 3 lists the data on the intermediate compounds which take part in the hydrogenation of CO to hydrocarbons (the Fischer–Tropsch synthesis and methanation).

In spite of the many reported studies of the CO hydrogenation mechanism by spectroscopic and kinetic methods very few truly spectroscopic investigations can be found. The best publications[97,98,104,108,109] show that the hydrogenation of CO on ruthenium catalysts takes place through the dissociative (C_α) forms of carbon. However, even these results were based on an

Table 3. Intermediates in the hydrogenation reactions of CO to hydrocarbons.

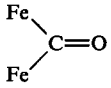
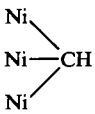
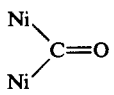
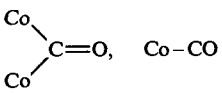
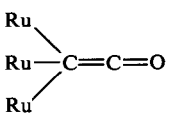
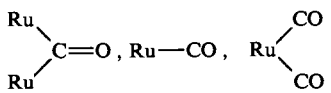
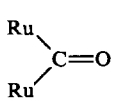
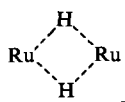
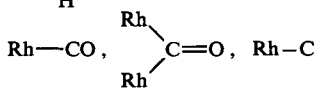
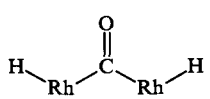
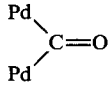
Reaction, catalyst	Intermediate complex	Reliability	Ref.
Hydrogenation of CO on Fe	FeC_x carbides	L	64–71
	$Fe-CH_x$	L	71
	Fe_5C_2, Fe–O, 	M	74
Methanation of CO on Ni (metallic or supported)	NiC_x, C(ads)	L	76–78
		L	81, 87
	Ni–CO, 	M	79, 82
		L	79, 86
Hydrogenation of CO on Co (metallic or supported)	C(ads), O(ads)	L	89
		L	74, 91
Hydrogenation of CO on Ru/SiO_2 and Ru/Al_2O_3		M	94
		M	98, 102, 104, 105, 108, 116
	C(ads), CH(ads)	M	97–99, 101, 108, 109, 111, 114
Hydrogenation of CO on Ru(001)	$HCOO^-$, CO_3^{2-}	L	113
Hydrogenation of CO on a $[Ru_6C(CO)_{16}(CH_3)]^-$ cluster supported on MgO, ZrO_2, Al_2O_3, SiO_2, etc.		M	118, 119
			
Hydrogenation of COO on Rh/SiO_2		L	106, 121, 123, 124
		M	123
	$HCOO^-$, OCH_3, OC_2H_5, CH_3COO^-, HCO	L	120, 122, 124, 127, 128

Table 3 (contd)

Reaction, catalyst	Intermediate complex	Reliability	Ref.
Hydrogenation of CO on Pd/SiO_2 and Pd/Al_2O_3	Pd–CO, Pd–OCH_3, 	M	136
	Pd–C, Pd–O, Pd–H, Pd–OH	L	102, 135–139
	HCO	L	138
Methanation of CO on Ir/SiO_2 and Ir/Al_2O_3	C(ads), OH(ads), CH(ads), O(ads), CO(ads)	L	77, 141
Hydrogenation of CO on Pt/TiO_2	Pt–CO	L	142
Hydrogenation of CO on Pt/Al_2O_3	Al–OCH_3, Pt–H	M	143
Hydrogenation of CO on Sm_2O_3	$HCOO^-$, CO_3^{2-}, CH_3O	L	146
Hydrogenation of CO on ZrO_2	$HCOO^-$, CH_3O^-, $^{\cdot}CH_3$, $:CH_2$	M	144, 145

analysis of NMR spectra, which cannot always be obtained directly under the experimental conditions because of experimental difficulties. The existence of the intermediate compound HCO seems very likely, but a direct spectroscopic proof of this assumption is still not available. The HCOO, CH_3O, and other groups observed under catalysis conditions are usually stabilised on the carrier and not on the active phase of the catalyst.

Most of the results point to a dissociative mechanism for the hydrogenation of CO, but associative mechanisms cannot be excluded.

VII. Hydrogenation of carbon dioxide

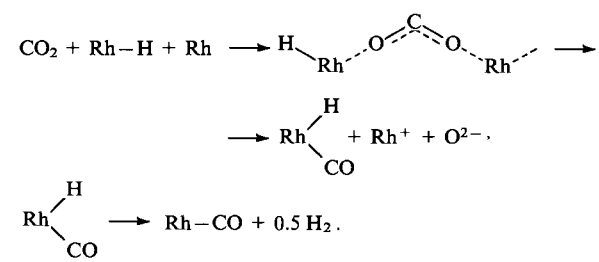
We have already discussed the hydrogenation of CO_2 as the reverse reaction of the conversion of water vapour (see Section IV), and also in connection with the synthesis of methanol on zinc–copper catalysts (see Section V). In this section we shall examine some data on the methanation of CO_2 on metallic catalysts.

The methanation of CO_2 on Rh/Al_2O_3 has been studied [147–151] by IR spectroscopy. An analysis of the IR diffuse reflectance spectra revealed HCOO groups on Rh/Al_2O_3 and HCOO and CH_3O groups on $Rh/Lu-Al_2O_3$.[147] In the first case the activation energy for the formation of CH_4 is 67 kJ mol^{-1}, and in the second case 96 kJ mol^{-1}. When CO_2 is added to the catalyst it is dissociated into CO and O(ads), and the further addition of H_2 produces formates. Stopping the addition of CO on Rh/Al_2O_3 lowers the intensity of the CO bands in the IR spectra to zero, whereas the intensity of the HCOO bands also falls but not to zero. On $Rh/Lu-Al_2O_3$ the concentration of CO groups decreases rapidly, but that of HCOO decreases slowly. From this evidence the authors conclude that the formates contribute to the conversion of water gas rather than to the synthesis of methane: the HCOO decomposes with formation of CO, which is then hydrogenated to CH_4.

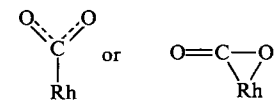
The CO, HCOO, and HCO_3 surface groups have been observed [148–151] by IR spectroscopy and EELS in the reaction of $H_2 + CO_2$ on Rh/Al_2O_3. On the unsupported catalyst HCOO groups are not formed, and on the catalyst with a carrier they appear mainly as a result of the spill-over of hydrogen from the Rh onto the carrier. The dissociation of CO_2 on Rh is assisted by the presence of H_2 because in the bent structure



an electron can be transferred from the adsorbed H_2 through the Rh to the π orbital of CO_2:



The formate group produced by the hydrogenation of Rh–CO is transferred (by spill-over) to the Al_2O_3, where it is stabilised. On the $K-Rh/SiO_2$ catalyst the band of the CO_2^- anion bound to potassium can be seen: this group is then hydrogenated to give $HCOO^-$.[151] In the absence of K or Rh no formate is produced. On massive Rh a weakly bound molecular form was observed by the EELS method during the adsorption of CO_2:



In the presence of potassium the following reactions take place:[152]

$$2\,CO_2^- \longrightarrow CO_3^{2-} + CO,$$

$$2\,CO_2^- \longrightarrow C_2O_4^{2-},$$

$$K^+ + CO_2^- \longrightarrow KO^- + CO(ads).$$

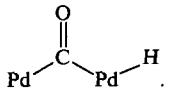
In the hydrogenation of CO_2 on $Rh-Mo/ZrO_2$ linear and bridging carbonyl forms are produced, as well as carbonate and formate, on the ZrO_2.[153]

CO(ads) and $HCOO^-$ have been detected on Ru/TiO_2 under the CO_2 hydrogenation conditions by IR diffuse reflectance spectroscopy.[154,155] The stationary concentration of CO(ads) is correlated with the rate of formation of CH_4. It was shown by the response method that the concentration of $HCOO^-$ is rapidly suppressed by the removal of H_2 from the gas mixture, but unfortunately these workers [154,155] did not provide a quantitative comparison of the concentrations of $HCOO^-$ and H_2. The formate

(or even HCOOH) produced can decompose into H_2O and CO (i. e. it can undergo a reaction which is the reverse of the conversion of water gas), or it can be hydrogenated to $CH_4 + H_2O$ in several stages. The hydrogenation of CO takes place only on a small number of Ru centres, and therefore the direct spectroscopic observation of the formation of CH_4 is experimentally difficult.

On $Ru-RuO_x/TiO_2$ the formation of various carbonyls has been observed by IR spectroscopy after the adsorption of CO_2, and after exposure to a $CO_2 + H_2$ mixture the complexes RuO_x-CO and $H-Ru-CO$ were observed.[156] Under these conditions the H or O atoms adsorbed on Ru facilitate the dissociation of the C–O bond. The much lower methanation temperature of CO_2 (as compared with CO) has been stressed: this effect is ascribed[154] to the high reactivity of the carbonyls at the instant of the dissociation of CO_2 (and also, possibly, to the formation of CO free radicals), which are subsequently converted into active carbon and methane. At high temperatures the hydrogenation mechanism of CO can include the formation of CO_2 by the Boudart reaction and its subsequent dissociation.

A study[149] of the hydrogenation of CO_2 on Pd supported on SiO_2, MgO, TiO_2, and Al_2O_3 showed that the interaction of CO_2 with Pd is facilitated in the presence of H_2 by the formation of the complex



On an iron foil the only product of the hydrogenation of CO_2 is CH_4, i. e. the process has a high selectivity.[157] On the other hand in the presence of surface oxide some CO is formed by a process which is the reverse of the water gas conversion. The high selectivity is attributed to the rapid coverage of the surface by a layer of carbon: the reaction then proceeds on the active Fe and FeC_x centres.

Magnetic studies have shown[158] that in the hydrogenation of CO_2 on Ni the carbide Ni_3C is produced by the scheme

$$CO_2 + Ni \rightleftharpoons Ni_xCO(ads) + NiO(ads),$$

$$Ni_xCO(ads) \rightleftharpoons Ni_3C + NiO(ads).$$

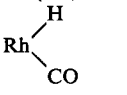
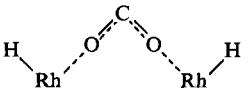
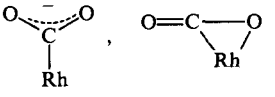
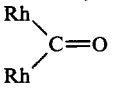
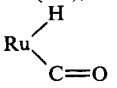
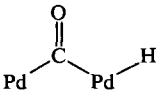
The carbide is then hydrogenated to CH_4. The methanation of CO_2 on Ni is faster than the methanation of CO.

The formates observed by IR spectroscopy during the hydrogenation of CO_2 on $La_{1-x}M_xCoO_3$ perovskites are probably intermediates in the equilibrium of the water gas conversion and of its reverse reaction. The hydrogenation of CO_2 to hydrocarbons takes place through the dissociated forms of CO_2 and H_2.[159]

Table 4 shows some data on the compounds proposed as intermediates in the hydrogenation of CO_2 to methane.

Some attempts to use spectrokinetic methods in studies of the hydrogenation mechanism of CO_2 have been reported,[154,155] but they gave ambiguous results (evidently because of the low

Table 4. Intermediates in the hydrogenation of CO_2.

Reaction, catalyst	Intermediate complex	Reliability	Ref.
Hydrogenation of CO_2 on Rh/Al_2O_3	CO(ads)	M	147–151
		L	148–150
		L	148–150
	Rh–HCOO	L	148–150
	CH_3O^-,	L	147
Hydrogenation of CO_2 on metallic Rh		L	152
Hydrogenation of CO_2 on $Rh-Mo/ZrO_2$	$Rh-CO$, $HCOO^-$, CO_3^{2-}, 	L	153
Hydrogenation of CO_2 on Ru/TiO_2	CO(ads), $HCOO^-$, RuO_x-CO, 	M	154–156
Hydrogenation CO_2 on Pd supported on SiO_2, MgO, TiO_2, Al_2O_3		L	149
Hydrogenation of CO_2 on Fe foil	C(ads)	L	157
Hydrogenation of CO_2 on Ni	Ni_3C	L	158
Hydrogenation CO_2 on spinels	C(ads)	L	159

sensitivity of the method). The only conclusion from this work was that adsorbed carbonyl is a likely intermediate in the hydrogenation reaction, whereas formate is an intermediate in the reverse water-gas formation reaction, i. e. in the reduction of CO_2 to CO.

VIII. Carbonylation and hydroformylation

The mechanism of carbonylation on heterogeneous catalysts containing rhodium or iridium is similar to the homogeneous carbonylation mechanism. In the homogeneous carbonylation on carbonyl complexes of Rh, Ru, Ir, and Co, intermediate compounds including carbonyl hydrides were detected, and in some cases CH_3OH and CH_3 species were found in the form of ligands bound to a metal atom.[160] Zeolites, which can be treated as solid quasihomogeneous systems, are mostly used as heterogeneous catalysts.

In situ IR spectra were obtained under methanol carbonylation conditions on zeolites containing rhodium at 150–200 °C.[161] On RhNaX we observe the conversion of CO under the influence of water vapour:

$$Rh^{3+} + H_2O + 3\,CO \longrightarrow Rh^{+}(CO)_2 + CO_2 + 2\,H^{+}.$$

During the interaction of CO with CH_3OH bands corresponding to CH_3COOCH_3, $(CH_3)_2O$, H_2O, CH_3O^-, and perhaps also to adsorbed CH_3COOH can be observed.

The following reaction has been studied[162] on IrNaY and RhNaY in the presence of CH_3I:

$$2\,CH_3OH + CO \longrightarrow CH_3COOCH_3 + H_2O.$$

It was found that initially the active species $[I_2Rh(CO)_2]^-$ is formed on RhNaY. The rate-limiting step of the reaction is the oxidative addition of CH_3I

$$[I_2Rh(CO)_2]^- + CH_3I \longrightarrow [I_3Rh(CO)_2CH_3]^-,$$

followed by the fast rearrangement of $[I_3Rh(CO)_2CH_3]^-$ into the rhodium acetyl derivative $[I_3Rh(CO)(COCH_3)]^-$, accompanied by the evolution of methyl acetate (in methanolysis) or of acetic acid (in hydrolysis). The rate of the reaction on rhodium catalysts is described by the equation $v = kP^{1}_{CH_3OH}P^{0}_{CO}P^{0}_{CH_3I}$, whereas in homogeneous carbonylation the rate equation is $v = kP^{0}_{CO}P^{0}_{CH_3OH}P^{1}_{CH_3I}$. On the IrNaY catalyst the rate of the reaction is described by the equation

$$v = k\frac{P_{CH_3OH}}{1 + k'P_{CH_3OH}}.$$

The rate-limiting step of the reaction is the adsorption of CH_3OH. Subsequently, under the influence of CH_3OH, the methyl group in $I-Ir(CH_3)(COOCH_3)(CO)_2$ is converted into the alkoxycarbonyl group, forming methyl acetate. The mechanism of the reaction can be described by the scheme

$$Ir + 3\,CO \longrightarrow [Ir(CO)_3] \xrightarrow{CH_3I} [I-Ir(CH_3)(CO)_3].$$

The hydroformylation or oxo-synthesis, i. e. the reaction of olefins with CO and H_2 (by which aldehydes are produced), also takes place on homogeneous and on heterogeneous catalysts. A study of the hydroformylation of C_2H_4 on Rh/SiO_2 by in situ IR spectroscopy has shown the presence of various forms of adsorbed CO. The introduction into adsorbed ethylene of the linear form of adsorbed CO produces the acyl group C_2H_5CO. The addition of CO takes place more readily than the synthesis of hydrocarbons from CO and H_2.[163–165] A study of some special features of the reaction kinetics[165] showed that acyl is not the main intermediate in the reaction.

According to in situ IR spectroscopy results[166] the CO group in the $Rh_6(CO)_{16}/SiO_2$ complex bound to the terminal Rh atom (1805 cm^{-1}) is more difficult to introduce into the Rh–C bond than the dicarbonyl group and the lienar form of CO on Rh crystallites. The low activity of this group is attributed to the absence of the rhodium centres needed for the adsorption of C_nH_{n+1}, C_2H_4, and H_2 from the surrounding of the rhodium atom. In the stationary state the rhodium is in the oxidised form Rh^+, and the limiting step is the hydrogenation of C_2H_5CO into C_2H_5CHO.

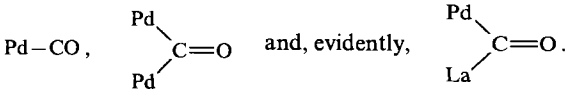
Two carbonyl complexes of rhodium, $Rh_6(CO)_{16}$ and $Rh(CO)_2$, have been detected[167] under the conditions of hydrocarbonylation of C_2H_4 on RhY. When the first complex is dissociated it is converted into CH_3CH_2CHO by the loss of several CO molecules. The second complex becomes active after lengthy exposure to a $C_2H_4 + H_2$ mixture. A likely intermediate compound in the hydroformylation of ethylene is $HRh(CO)_x$.

According to Natio and Tanimoto[168] the hydroformylation of propene on Rh/SiO_2 and Pd/SiO_2 takes place by the scheme

$$H_2 + 2\,Z \overset{(1)}{\rightleftharpoons} 2\,HZ,$$
$$CO + Z \overset{(2)}{\rightleftharpoons} COZ,$$
$$C_3H_6 + Z \overset{(3)}{\rightleftharpoons} C_3H_6Z,$$
$$C_3H_6Z + HZ \overset{(4)}{\rightleftharpoons} C_3H_7Z + Z,$$
$$C_3H_7Z + COZ \overset{(5)}{\rightleftharpoons} C_3H_7COZ + Z,$$
$$C_3H_7COZ + HZ \xrightarrow{(6)} C_3H_7CHO + 2\,Z,$$
$$C_3H_7Z + HZ \xrightarrow{(7)} C_3H_8 + Z.$$

where Z is an active surface centre. The competition between the stages (*5*) and (*7*) determines the selectivity of the reaction. On palladium step (*5*) is limiting, and on rhodium step (*6*). The activation energy of the hydroformylation is 57 kJ mol^{-1} on Rh/SiO_2 and 69 kJ mol^{-1} on Pd/SiO_2, i. e. the activation energy of step (*6*) is lower than that of step (*5*).

Bridging and linear carbonyls are observed on the surface under the conditions of the hydroformylation of propene and hex-1-ene on Pd/SiO_2 and $Pd-La/SiO_2$ at 250 °C and 10 atm:



Carbon monoxide adsorbed on La and on Pd does not contribute to the addition reaction on the $Pd-C_3H_7$ bond.[169] Spill-over of hydrogen between the Pd and the SiO_2 has been observed by the programmed temperature desorption (PTD) method. The magnitude of the spill-over is well correlated with the yield of reaction products.[169]

The hydroformylation of C_2H_4 and C_3H_6 has also been studied on the $RhFe_2$, $PtFe_2$, and $PdFe/SiO_2$ clusters.[170] A possible reaction mechanism is

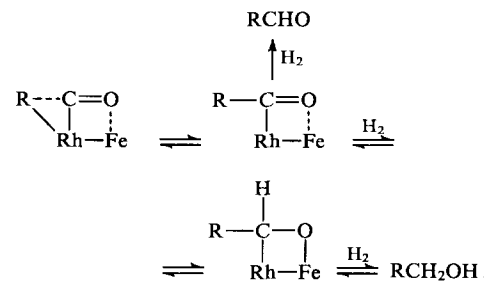
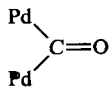
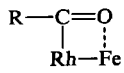


Table 5. Intermediates in carbonylation and hydroformylation reactions.

Reaction, catalyst	Intermediate complex	Reliability	Ref.
Carbonylation of methanol onRhY	$Rh^+(CO)_2$, CH_3O^-, CH_3COOH(ads)	M	161
Carbonylation of methanol on RhY	$[I_2Rh(CO)_2]^-$ $[I_3Rh(CO)_2CH_3]^-$ $[I_3Rh(CO)(COCH_3)]^-$	M	162
Carbonylation of methanol on IrY	$[Ir(CH_3)(CO)_2]^-$ $Ir(CH_3)(COCH_3)(CO)_2$	M	162
Hydroformylation of C_2H_4 on Rh/SiO_2	CO(ads), $C_2H_5CO^-$	L	163–165, 167
Hydroformylation of C_2H_4 on RhY	$Rh_6(CO)_{16}$, $Rh^+(CO)_2$	L	166
Hydroformylation of C_3H_6 and 1-C_6H_{12} on Pd/SiO_2	Pd–CO	M	168, 169
		M	169
Hydroformylation of C_2H_4 and C_3H_6 on Rh–Fe/SiO_2		L	170

A summary of the data on the intermediate compounds taking part in the carbonylation and hydroformylation reactions is shown in Table 5.

Thus definite reaction sequences have been established from IR spectroscopic data for the carbonylation and hydroformylation reactions: their reliability is confirmed (essentially) by comparing the sequences with those of the analogous homogeneous reactions. Some stages of the process can take place by associative mechanisms involving hydrogen. It is stated that the intermediates in these reactions are adsorbed carbon monoxide and the alkyl and acyl groups. Spectro-kinetic studies have not been reported.

IX. Reduction of NO_x with CO

The interaction of NO_x with CO has been widely studied by spectroscopic methods because of the high sensitivity of the C–O and N–O absorption bands in the IR spectra. This reaction is of great practical importance in relation to the problem of removing CO and NO_x from the exhaust gases of automobile engines. The reaction can follow two paths: with formation of N_2 and CO_2 or with formation of N_2O and CO_2. The first mechanism is usually predominant on metals, the second on oxides.

The NO + CO reaction on platinum foil was studied by absorbance-reflectance IR spectroscopy.[171] It was established that below 150 °C the surface is covered with CO, and that the activation energy for desorption is 14.2 kJ mol^{-1}. Above 150 °C the activation energy is governed by the dissociation of NO and is equal to 36 kJ mol^{-1}. The reaction follows a dissociative mechanism:[171]

$$CO + Z \overset{(1)}{\rightleftharpoons} COZ, \qquad NO + Z \overset{(2)}{\rightleftharpoons} NOZ,$$
$$NOZ + Z \overset{(3)}{\longrightarrow} NZ + OZ,$$
$$COZ + NOZ \overset{(4)}{\longrightarrow} CO_2 + NZ + Z,$$
$$2\,NZ \overset{(5)}{\longrightarrow} N_2, \qquad COZ + OZ \overset{(6)}{\rightleftharpoons} CO_2 + 2\,Z.$$

The rate of removal of CO (calculated from IR spectra) is determined by the kinetics of step (*4*).

On Rh(100) the reaction of NO_x with CO with studied by LEED, Auger spectroscopy, and TPD.[172] A dissociative mechanism similar to that described by Skarf and Benziger[171] was proposed. A study of the interaction of CO with NO on a Rh(331) surface has also been reported.[173] The changes in the 520 cm^{-1} absorption band (assigned to adsorbed oxygen) show that the oxygen atoms formed by the dissociation of the NO molecules are immediately removed from the surface and interact with CO molecules. The oxygen atom formed by the dissociation of the NO molecule on the surface is less active towards the adsorbed CO molecule than the oxygen atoms produced by dissociatively adsorbed O_2.

The oxygen formed on the surface by the decomposition of NO_2 under the conditions of the reaction of NO_2 with CO has properties similar to those of the oxygen formed by the decomposition of O_2. Thus, NO and CO_2 are formed on platinum at temperatures below 430 °C under the conditions of this reaction.[174] The rate of formation of CO_2 is an order of magnitude higher than the rate of interaction of CO with NO, and is almost equal to the rate of the reaction of CO with O_2.

Most of the studies have been devoted to the reaction between NO and CO on metals of the platinum group supported on SiO_2, Al_2O_3, and other carriers.[175–194] The formation of isocyanate groups (NCO) on the surface was invariably observed. For example, in the interaction of a mixture of CO and NO on Pt, Rh, and Ir supported on TiO_2, MgO, Al_2O_3, and SiO_2 carriers the IR spectrum was found to include bands at frequencies between 2180 and 2318 cm^{-1}, assigned to the NCO vibrations on the surface of both the metal and the carrier.[175] The isocyanate groups are formed by the interaction of adsorbed nitrogen atoms and CO molecules:

$$Pt–N + Pt–CO \rightleftharpoons Pt–NCO.$$

It should be noted that cyanides adsorbed on platinum or palladium absorb in the same spectroscopic region (1980–2200 cm^{-1}).[181–183] Detailed spectroscopic studies using nitrogen, oxygen, and carbon isotopes have shown that two different forms of the complex can exist on the platinum metal surface: isocyanates Rh–NCO (2172 cm^{-1}) and cyanates Rh–OCN (2225 cm^{-1}). The migration of NCO from the metal to the carrier is very fast. Its driving force is the formation of a stronger bond with the Lewis-acid centres on the carrier.

Several forms of adsorbed CO, including bridging forms (at 1875 cm^{-1}), have been observed on a binary $Pt–Rh/SiO_2$ catalyst. NCO groups are adsorbed on the Rh, but they are not observed on the Pt.[177]

Studies in situ by IR spectroscopy of the reaction of CO + NO on $Pt–WO_3/SiO_2$ at 280 °C showed that the slow step in this case is the dissociation of NO. The CO groups on Pt are rapidly replaced by NO groups, and therefore the absorption bands of the NO groups are predominant in the in situ IR spectra. Bands corresponding to CO groups are observed also on WO_x; NCO, NO_3, or NO_2 groups were seen only under the conditions of the experiment, and they were assigned[177] not to intermediates but to side-products of the reaction, because they are formed in large quantities under conditions which suppress the reaction of carbon monoxide. The active centres are located at the boundary between Pt and WO_3.

The most active of the platinum metals (rhodium) has been studied the greatest detail.[178–184] According to Hecker and Bell[178,179] the reaction of NO_x with CO on Rh/SiO_2 takes place by the scheme

$$NO + Rh \overset{(1)}{\rightleftharpoons} RhNO, \qquad CO + Rh \overset{(2)}{\rightleftharpoons} RhCO,$$
$$NORh + Rh \overset{(3)}{\longrightarrow} NRh + ORh,$$
$$NORh + NRh \overset{(4)}{\longrightarrow} N_2O + 2\,Rh,$$

$$NORh + NRh \xrightarrow{(5)} N_2 + {}^1/_2O_2 + 2\,Rh,$$

$$CORh + ORh \xrightarrow{(6)} CO_2 + 2\,Rh,$$

$$NRh + CO \overset{(7)}{\rightleftharpoons} RhNCO,$$

$$NRh + CORh \xrightarrow{(8)} RhNCO + Rh,$$

$$2\,RhNCO \xrightarrow{(9)} N_2 + 2\,CO + 2\,Rh.$$

The absorption bands of NCO on Rh (2170 cm^{-1}) appear during the catalysis; they are strongest if the reaction is carried out at 230 °C. However, there is no proof that their formation determines the rate of the catalytic reaction. The coverage of Rh by NCO groups is low as compared with the coverage by NO groups (1685 cm^{-1}) and by N atoms (1610 cm^{-1}). A high concentration of NCO is found on SiO_2 (2300 and 1960 cm^{-1}); the CO groups are observed on the carrier as a result of migration from the metal. Under the reaction conditions these groups are stable, and apparently do not contribute to the catalysis. The exposure of Rh/SiO_2 to a mixture of $N_2 + H_2 + CO$ also produces bands corresponding to the NH and NH_2 groups.[180] The activation energy for the reduction of NO in the presence of H_2 is very substantially lowered (from 34 to 23 kJ mol^{-1}). An intermediate compound [urea, $(NH_2)_2CO$] is formed on the reduced catalyst, probably by the reaction

$$HNCO + NH_3 \longrightarrow NH_4OCN + (NH_2)_2CO.$$

HNCO is formed on an oxidised catalyst.

When the reaction of NO_x with CO is carried out on Rh/Al_2O_3 Rh–NCO complexes are not formed, but Rh(CO)(NO) groups have been observed[186] and suggested as the source of the reduction of NO. The formation of dicarbonyls suppresses the reaction. However, Dictor[181] has noted the formation of $Rh(CO)_2$, but was unable to detect Rh(CO)(NO) groups. The $Rh-NO^-$, Rh–NO, $Rh-NO^+$, Rh–CO, Rh_2CO, Rh–CN, and a large number of NCO groups adsorbed mainly on the Al_2O_3 were also detected. It is suggested that NO dissociates on the reduced Rh and easily oxidises the catalyst. The NCO groups are probably formed at the Rh – carrier boundary (but not on the Rh^+).

It has also been shown[182] that the stability of NCO increases in the presence of O_2, and therefore isocyanate could be an intermediate in the catalytic reaction of NO + CO + O_2.

The NO + CO + O_2 reaction has been studied[186] on Pt/SiO_2. At low coverages of the surface by CO groups the CO + O_2 reaction takes place much more readily than the CO + NO reaction. A dissociative mechanism is suggested, with the dissociation of chemisorbed NO as the rate-limiting step.

The forms $NO-Ru^{2+}$ and NO_2-ZnO have been observed[188] on the Ru/ZnO catalyst. Carbon monoxide adsorbed on Ru reacts with NO when the latter is dissociated, forming NCO and CO_3. As a result of spill-over the NCO and CO_3 species move from the metal to the carrier, where they are stabilised even for temperatures above the catalysis temperature.[188]

Under catalytic conditions the formation of NCO groups and their migration towards the carrier have been observed[185] on Ir catalysts supported on SiO_2, Al_2O_3, TiO_2, or MgO. As reported, the dissociation of NO takes place on reduced iridium centres by the scheme

$$Ir(CO)(NO) \longrightarrow IrN + CO_2.$$

NNO groups, which are intermediates in the formation of N_2O, are formed in parallel with NCO:

$$IrN + NO \longrightarrow IrNNO \longrightarrow Ir + N_2O.$$

On an oxidised Ir surface no interaction between NO and CO was detected.

The only systematic spectroscopic investigation of the interaction of CO and NO on supported platinum group metals appears to be a group of studies from our laboratory.[189–194] This work involved the simultaneous measurement of the rate of conversion of the surface compounds [CO(ads), CO_2^{2-}, and NCO] and of the rate of formation of the reaction products (N_2, N_2O, and CO_2). As a result we were able to establish the following series of steps in the interaction of CO with NO:

$$CO + M \overset{(1)}{\rightleftharpoons} M-CO,$$

$$NO + M \overset{(2)}{\rightleftharpoons} M-NO,$$

$$M-NO + M \xrightarrow{(3)} M-N + M-O,$$

$$M-N + M-CO \xrightarrow{(4)} M-NCO + M,$$

$$M-NCO + M-NO \xrightarrow{(5)} M-CO_2 + N_2 + M,$$

$$M-CO + M-O \xrightarrow{(6)} M-CO_2 + M,$$

$$M-CO_2 \xrightarrow{(7)} CO_2 + M,$$

$$M-N + M-NO \xrightarrow{(8)} N_2O + 2\,M,$$

$$O_2 + 2\,M \xrightarrow{(9)} 2\,MO.$$

I: $2\,CO + 2\,NO = 2\,CO_2 + N_2$,

II: $CO + 2\,NO = N_2O + CO_2$,

III: $2\,CO + O_2 = 2\,CO_2$.

It was found that this sequence is identical for all the catalysts examined.[189–194]

The NO + CO reaction was studied on a Ni/SiO_2 catalyst by IR spectroscopy and microgravimetrically.[195] The adsorbed NO [mainly in the form of $Ni(NO)_2$] reacts with CO, giving NiNCO + CO_2. The stoichiometry of the reaction corresponds to the equation

$$4\,NO(ads) + 3\,CO \longrightarrow$$
$$\longrightarrow NCO(ads) + 2\,O(ads) + 3\,N(ads) + 2\,CO_2.$$

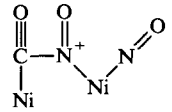
Weakly adsorbed CO is formed also by the interaction

$$NiNCO + Ni \longrightarrow NiN + NiCO.$$

In the absence of CO the following reaction takes place;

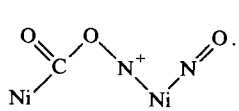
$$Ni + Ni(NO)_2 \longrightarrow 2\,NiNO \longrightarrow 2\,N(ads) + 2\,O(ads).$$

A correlation between the decomposition of NO and the formation of NCO is established 10 min after the beginning of the reaction. The possible formation of associative intermediate complexes has been suggested:[195]



16

or



17

The formation of NCO in the reaction of surface nitride NiN (after the dissociation of NO) with CO has not been observed.

The same reaction (NO + CO) has been studied on a reduced copper catalyst (Cu/Al_2O_3) by in situ IR spectroscopy and TPD.[196] The products (CO_2 and N_2) are formed in a single elementary step. The adsorption of CO groups on Cu^0 and Cu^+ centres has been observed. The action of NO on the reduced

surface leads to the reoxidation of the copper and subsequently to the formation of NCO, probably on the carrier. The following reaction mechanism has been suggested:

$$NO \rightleftharpoons NO(ads) \longrightarrow N(ads) + O(ads),$$

$$N(ads) + N(ads) \longrightarrow N_2,$$

$$N(ads) + NO(ads) \longrightarrow N_2O,$$

$$NO(ads) + NO(ads) \longrightarrow N_2O + O(ads),$$

$$O(ads) + 2\,Cu^0 \longrightarrow Cu_2O,$$

$$Cu_2O + CO \longrightarrow 2\,Cu + CO_2,$$

$$N(ads) + CO(ads) \longrightarrow NCO(ads),$$

$$NCO(ads) + NO(ads) \longrightarrow N_2 + CO_2.$$

The last step is rate-limiting. The possible spill-over of N particles from the copper towards the carrier and their interaction with CO on the carrier have also been suggested.[196]

Absorption bands corresponding to the complexes $Cu^{2+}-NCO$, $Cu^{+}-NCO$, $Cu^{+}-NO$, $Cr^{2+}-NO$, $Cu^{2+}-CO$, $Cu^{2+}-NO$, and $Cu^{+}-CO$, and also absorption bands from carbonates, carboxylates, nitrites, and nitrates, have been observed in the IR spectra obtained under reaction conditions on a $Cu-Cr/Al_2O_3$ catalyst.[197,198] The NCO group is formed by the NO + CO reaction, and also by the sequential exposure of the catalyst first to NO and then to CO. However, not all the NCO takes part in the catalysis. Its formation and decomposition on the copper are also possible:

$$Cu^{+}-N + CO \longrightarrow Cu^{+}-NCO,$$

$$Cu^{+}-NCO + NO \longrightarrow Cu^{+} + N_2 + CO_2.$$

NCO groups are obtained also in the CO + NO reaction on oxide catalysts, for example on Cr_2O_3 [199] and on $LaMO_3$, where M = Cr, Mn, Fe, Co, or Ni.[200]

The interaction of CO and NO has also been studied[201,202] on CuO supported on Al_2O_3. Bands from carbonate–carboxylate complexes (1200–1650 cm^{-1}), from adsorbed CO_2 (2350 and 2370 cm^{-1}), and from CO bound to the reduced copper ions ($Cu^{+}-CO$, 2130 cm^{-1}) have been observed in the spectra for the adsorption of CO on Cu/Al_2O_3. The adsorption of NO produces nitrate–nitrite structures (1200–1660 cm^{-1}) and NO complexes bound to the Cu^{2+} ions (1880 cm^{-1}). $Cu^{+}-NO$ complexes (1740–1780 cm^{-1}) can also be formed. After the adsorption of a CO + NO mixture bands at 2130 ($Cu^{+}-CO$), 1880 ($Cu^{2+}-NO$), and 1780 cm^{-1} ($Cu^{+}-NO$), were observed in the spectra, and also bands at 2270, 2240, and 2140 cm^{-1} which were assigned to vibrations of the isocyanate complex. The role of the latter in the reaction was not examined. A scheme for the interaction of CO and NO in which $Cu^{+}-NO$ is the intermediate complex was proposed on the basis of spectroscopic data.

A quantitative proof that the surface carbonyl $Cu^{+}-CO$ is the intermediate complex in the interaction of CO and NO was produced[203,204] by simultaneous measurements of the diffuse reflectance spectra in the IR region and of the reaction rate on CuO/Al_2O_3.

Reports of simultaneous measurements of the rate of transformation of surface compounds and of the rate of the reaction on copper catalysts are few. In particular, one investigation of this type on CuO/SiO_2 has been described.[205,206] Comparing the spectroscopic and the kinetic results produced a scheme in which the adsorbed NO form acts as an intermediate in the formation of nitrogen. Under the reaction conditions weak adsorption bands from the isocyanate complex were observed. This suggests the possibility of the dissociative adsorption of NO:

$$Cu + NO \rightleftharpoons CuNO,$$

$$CuNO + Cu \longrightarrow CuN + CuO,$$

$$CuNO + NO \longrightarrow Cu + N_2O,$$

$$Cu^{+} + CO \rightleftharpoons Cu^{+}-CO,$$

$$Cu + N_2O \rightleftharpoons CuONN,$$

$$CuONN \rightleftharpoons CuO + N_2,$$

$$Cu_2O + CO \longrightarrow Cu^{+} + CO_2,$$

$$CuO + CO \longrightarrow Cu + CO_2,$$

$$CuN + CO \rightleftharpoons CuNCO.$$

The existence of centres of different types on the surface has been proposed: Cu, Cu^{+}, and Cu^{2+}. The dissociation and the formation of the isocyanate complex take place on the reduced centres.

A similar study was carried out on Cr_2O_3/SiO_2.[207] The activity of the catalyst was measured in a gradient-free reactor which also allowed simultaneous spectroscopic measurements. A correlation was observed between the rate of formation of CO_2 and the intensity of the absorption band at 1735 cm^{-1}, corresponding to the vibrations of NO adsorbed in the dinitrosyl form.

The interaction of NO and CO with formation of N_2O and CO_2 was studied[208] on an Au–ZSM-5 catalyst at 70 °C. Under the reaction conditions the $Au^{+}-CO$, $Au^{+}-NO$, $Au^{+}-(NO)_2$, and $Au^{+}-NO_2$ bands were observed.

It should be noted that studies in which the measurements of the reaction rate were accompanied by simultaneous measurements of the rate of conversion of surface complexes were more generally reported than in previous work.

The N_2O + CO reaction on MgO was studied by IR emission spectroscopy and by the response method.[209] An intermediate formate complex was observed, and found to be removed by the reaction

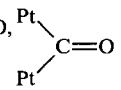
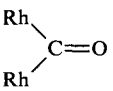
$$HCOO^{-} + N_2O \longrightarrow CO_2 + N_2 + OH^{-}.$$

On oxidation-reduction catalysts the N_2O + CO interaction follows a different path, involving an alternation of oxidation and reduction processes.

Table 6 lists the intermediate compounds observed in the study of the CO + NO reaction on different catalysts. Compounds such as **16** or **17**, which were proposed but not experimentally observed, are not included in the table.

To conclude the present section we note that many surface species have been considered in in situ studies of the CO + NO reaction by IR spectroscopic methods, but few direct kinetic confirmations of the reality of their contribution to the catalysis have been put forward. Both a dissociative mechanism (with dissociation of the CO and NO molecules) and an associative mechanism [with formation of NCO, NNO, and M(CO)(NO) species] have been suggested by different workers. There have been extended discussions of the participation in the catalysis of the NCO isocyanate species, which can be adsorbed on both the metal and the carrier. The most widely held view is that NCO adsorbed on the carrier does not contribute to the catalysis whereas NCO adsorbed on the metal. The rate of its transformation on the metal is fairly high, and after the reaction this species is not usually observed. There are also assumptions of the formation of more complex associative complexes such as **16** and **17**.

Table 6. Intermediates in the NO + CO reaction.

Catalyst	Intermediate complex	Reliability	Ref.
Pt foil	CO(ads), NO(ads)	H	171
Rh(100)	CO(ads), NO(ads)	H	172
Pt, Rh, Ir on TiO_2, MgO, Al_2O_3, SiO_2	M–NCO, carrier–NCO	M	173
Pt–Rh/SiO_2	Rh–NCO, 	M	177
Pt–WO_3/SiO_2	Pt–CO, Pt–NO, WO_x–CO, NCO	L	176
Rh/SiO_2	Rh–NCO, SiO_2–OCN, Rh–NO, Rh–CO	M	178–180
Rh/Al_2O_3		L	186
	$Rh-(CO)_2$, $Rh-NO^+$, Rh–NO, $Rh-NO^-$, Rh–CO, Rh–CN, Al_2O_3–OCN,	L	181, 182
			
Pt/SiO_2	NO(ads)	L	186
Ru/ZnO	Ru^{2+}–NO, ZnO–NO, Ru–CO, Ru^{2+}–CO, NCO, CO_3	L	188
Ir on SiO_2, Al_2O_3, TiO_2	 , Ir–NCO	M	185
Pt, Pd, Rh, Ru on Al_2O_3	M–NCO, M–CO, $M-CO_2^{2-}$	H	190–194
Ni/SiO_2	$Ni-(NO)_2$, Ni–CO, $Ni-NO_2$	M	195
Cu/Al_2O_3	Cu^+–CO, Cu^0–CO, NCO	L	196
Cu–Cr–O/Al_2O_3	Cu^{2+}–NCO, Cu^+–NCO, Cu^+–NO, Cr^{2+}–NO, Cu^{2+}–CO, Cu^+–CO,	L	197, 198
Cr_2O_3, $LaMO_3$	NCO	L	199, 200
CuO/Al_2O_3	Cu^+–NO	L	202, 203
Cr_2O_3/SiO_2	$Cr-(NO)_2$	M	205
CuO/Al_2O_3	Cu^+–CO	H	206, 207
Au–ZSM-5	Au^+–CO, Au^+–NO, $Au^+-(NO)_2$, Au^+-NO_2	M	208

X. Reduction of NO_x with other reducing agents

The reduction of NO_x with other reducing agents has been studied intensively in recent years with the aim of removing nitric oxide impurities from oxygen-containing exhaust gases from industry and transport. Ammonia is often used as a reducing agent to purify industrial gases and gases from electrical power stations, and the $V_2O_5-TiO_2$ system usually provides the catalyst.

On pure V_2O_5 the mechanism of the reduction of NO_x was first studied by Takagi et al.[210] An analysis of the IR spectra recorded at room temperature showed that in the absence of oxygen NO is not adsorbed on V_2O_5, but in the presence of oxygen it is adsorbed [as NO_2(ads)]. Upon adding ammonia they observed NH_4(ads). From these results they proposed the following reaction mechanism:

$$NO + {}^1/_2O_2 \longrightarrow NO_2(ads),$$

$$ZOH + NH_3 \longrightarrow ZO^- + NH_4^+(ads),$$

$$ZO^-...NH_4^+(ads) + NO_2(ads) \longrightarrow N_2 + 2\,H_2O + ZO^-,$$

$$ZO^- + H_2O \longrightarrow 2\,ZOH.$$

On TiO_2 the following forms of adsorbed NO_x were observed by IR spectroscopy: NO on Ti^{4+} ions (Lewis centres), N_2O on Ti^{3+} (through the reduction of NO), and NO_3^- on Ti^{3+} (through the oxidation of NO).[211] In the adsorption of NO_2 nitrates are formed, and in the adsorption of NH_3 we find coordinatively bound ammonia (on the Ti^{4+} Lewis centres), which is stable up to 300 °C. The ammonia displaces NO from the surface, but does not react with it.

Another communication from the same authors[212] describes a study of the reaction between NO_x and NH_3 on the $V_2O_5-TiO_2$ system. In the adsorption of NO the surface is rapidly covered with nitrosyl groups and slowly with NO_3 and NO_2. NH_4^+ and coordinatively bound ammonia are formed on the V–OH centres as a result of the adsorption of ammonia. At 250 °C the intensity of the coordinated ammonia bands in the IR spectra decreases, and the NH_4^+ bands disappear, but they are replaced by NH_2 bands. Heating a surface covered with ammonia in an NO atmosphere leads to the reaction

$$VO^{2+} + NH_3 \longrightarrow [HO-V-NH_2]^{2+},$$

$$NO + [HO-V-NH_2]^{2+} \longrightarrow \underset{\textbf{18}}{[HO-V-NH_2-NO]^{2+}},$$

$$[HO-V-NH_2-NO]^{2+} \longrightarrow N_2 + H_2O + [VOH]^{2+},$$

$$[VOH]^{2+} + {}^1/_4O_2 \longrightarrow VO^{2+} + {}^1/_2H_2O.$$

The overall reaction is

$$NH_3 + NO + {}^1/_4O_2 = N_2 + 1\,{}^1/_2H_2.$$

Thus the reaction of NO_x with NH_3 on V_2O_5 takes place through the decomposition of the associative complex **18**. NO or NO_2 can contribute to the reoxidation stage instead of O_2:

$$[VOH]^{2+} + {}^1/_2NO \longrightarrow VO^{2+} + {}^1/_2\,H_2O + {}^1/_4\,N_2,$$

$$2\,[VOH]^{2+} + {}^1/_2NO_2 \longrightarrow 2\,VO^{2+} + H_2O + {}^1/_4\,5\,N_2.$$

Data obtained[213] by Fourier transform IR spectroscopy and by electrical conductivity methods lead to a similar conclusion:

$$3\,V_2O_5 + 2\,NH_3(ads) \longrightarrow N_2 + 3\,H_2O + V_2O_4,$$

NH_3 reduces the V^{5+} by the reaction

$$2\,V_2O_4 + NO \longrightarrow N_2 + 2\,V_2O_5.$$

and NO reoxidises the V^{4+} to V^{5+}:

At 200 °C the formation of the intermediate complex $V^{5+}-ONH_4$ was observed:

$$2\,V^{5+}-ONH_4 + V^{5+}-O-V^{5+} + 2\,NO \longrightarrow$$

$$\longrightarrow 2\,N_2 + 3\,H_2O + 2\,V^{5+}-OH + V^{4+}\square V^{4+}$$

A study of the reaction[214] by Auger spectroscopy and by TPD showed that NH_3 is adsorbed on both TiO_2 and V_2O_5, but NO is adsorbed only on TiO_2.

Ammonia reduces V_2O_5 by a reaction which produces N_2O. In the presence of N_2O, NO, and O_2 the V_2O_5 surface is reoxidised, and N_2 is evolved. NO and NH_3 molecules adsorbed on TiO_2 do not interact, but they interact on $V_2O_5-TiO_2$. The reaction apparently takes place near the Ti–V interface. Of all the possible intermediates the NH_2 groups are adsorbed on the V_2O_5:

$$V_2O_{5-x} + x\,NH_3 \longrightarrow V_2O_5 + 1^1/_2\,x\,(NH_2)_x + {}^1/_2\,x\,H_2O,$$

$$V_2O_5 + 1^1/_2\,x\,(NH_2)_x + x\,O_2 \longrightarrow V_2O_{5-x} + {}^1/_2\,x\,N_2O + H_2O,$$

$$V_2O_{5-x} + x\,N_2O \longrightarrow V_2O_5 + x\,N_2.$$

The interaction of NO with NH_3 has been studied also on metallic catalysts. On Pt(111) at low temperatures the IR spectra include a band at 1280 cm^{-1} assigned[215] to the associative complex NH_3NO. Upon being heated to 350 °C the system again breaks down into NH_3 + NO. Absorption bands due to adsorbed NO and NH_3 have also been observed. The NH_3 + NO reaction begins only at temperatures above 400 °C, stimulated by the dissociation of NH_3 into NH_2 and H.

When the NO + NH_3 reaction was carried out on FeY zeolite the bands corresponding to NH_3(ads) and NH_4^+ appeared in the IR spectra.[216] Contributions to the catalysis from HNO and N_2O species have also been suggested.

Several papers have dealt with the mechanism of the reduction of NO by hydrogen on metals, including the faces of Pd,[217] Rh,[218] and Ru monocrystals.[219]

An analysis of the EELS spectra obtained uring the reaction of NO with H_2 on Pt(III) under stationary conditions (100–350 °C, pressure $10^{-9}-10^{-8}$ Torr) showed[220] that with an excess of NO the main product of the reaction is N_2, whereas with an excess of H_2 it is NH_3 (in the temperature range 20–200 °C) or N_2 (at higher temperatures). The same precursor appears in both reactions. The NH_3NO complex which is observed (a wide band at 1280 cm^{-1}) inhibits the reaction; when heated it dissociates into NH_3 and NO. At low temperatures the Pt surface is covered with linear and with bridging NO groups, but the NO apparently contributes to the reaction in its dissociated form.

The reaction of NO + H_2 on Pt(111) under the same conditions ($10^{-9}-10^{-8}$ Torr) was studied by EELS and thermosorption methods.[221,222] Two forms of linear NO and two of bridging NO were detected in the low-temperature adsorption of NO: on the (111) plane and on defects (atomic steps). The α form of NO is desorbed at temperatures close to 100 °C, and the β form dissociates at 200–250 °C with formation of N_2. The HNO, N, NH, NH_2, and NH_3 groups are also observed on the surface.

The following mechanism is proposed for the reduction:

$$NO \xrightarrow{(1)} \alpha_1\text{-}NO(ads),$$

$$H_2 \xrightarrow{(2)} 2\,H(ads),$$

$$H(ads) + \alpha_1\text{-}NO(ads) \xrightarrow{(3)} HNO(ads),$$

$$HNO(ads) + H(ads) \xrightarrow{(4)} N(ads) + H_2O,$$

$$N(ads) + 3\,H(ads) \xrightarrow{(5)} NH_3,$$

$$2\,N(ads) \xrightarrow{(6)} N_2.$$

The NO + H_2 reaction has been studied also on supported metal catalysts. A mechanism in which the first stage is the adsorption of NO and the dissociation of H_2 was proposed[223] for the reaction on Rh/SiO_2. Nitrogen is formed by the interaction of N(ads) and NO rather than by the recombination of adsorbed N atoms. On other centres this interaction leads to the formation of N_2O:

$$NO \overset{(1)}{\rightleftharpoons} NO(ads),$$

$$H_2 \overset{(2)}{\rightleftharpoons} 2\,H(ads),$$

$$NO(ads) + H(ads) \xrightarrow{(3)} N(ads) + OH,$$

$$NO(ads) + N(ads) \xrightarrow{(4)} N_2O,$$

$$NO(ads) + N(ads) \xrightarrow{(5)} N_2O + O(ads),$$

$$O(ads) + H(ads) \xrightarrow{(6)} OH(ads),$$

$$OH(ads) + H(ads) \xrightarrow{(7)} H_2O,$$

$$N(ads) + H(ads) \xrightarrow{(8)} NH(ads),$$

$$NH(ads) + H(ads) \xrightarrow{(9)} NH_2(ads),$$

$$NH_2(ads) + H(ads) \xrightarrow{(10)} NH_3.$$

The Rh–NO and Rh–N=O···Sn complexes, and also Rh–O–Sn, were observed by IR spectroscopy and XPES under the conditions of the reaction of NO with H_2 at 100 °C on a $Rh-Sn/SiO_2$ catalyst. Their interaction with hydrogen produced N_2, N_2O, and H_2O.[224]

A study of the reaction of NO with H_2 on Au/SiO_2 and Au/MgO by in situ Fourier transform IR spectroscopy[225] revealed a wide band at 2400–2700 cm^{-1}, which could not be identified. It was assumed that the reaction includes the intermediate dissociation of NO and involves adsorbed atomic nitrogen.

With one exception[223] none of the studies mentioned above was spectroscopic, amd therefore the proposed mechanisms must be treated as tentative. Obviously, associative and dissociative steps are combined in the mechanism of the NO reduction reaction: the NO molecule takes part (as a whole) in the interaction with NH_3 or with H_2. The formation of the $NO{\cdot}NH_3$ complex assists the formation of N–N bonds and the dissociation of the NO molecule.

Reactions leading to the selective reduction of NO_x to nitrogen by using the hydrocarbons contained in the 'lean' mixtures (i.e. mixtures with an excess of oxygen)[226] characteristic of the exhaust gases of Diesel engines were recently discovered on the Cu–ZSM-5 zeolite catalyst. These have stimulated a new series of studies[227–231] aimed at establishing the mechanism of this reaction and the mechanism of the decomposition of NO_x on zeolites.

The state of the copper in the zeolites was studied by ESR (including under reaction conditions[227–229]), XPES, Auger spectroscopy,[230] and IR spectroscopy.[231] All these workers point out that the zeolite contains bivalent and univalent copper, but that the Cu^+ is predominant under the reaction conditions. As reported,[227,231] the reaction

$$2\,Cu(OH)^+ \rightleftharpoons [Cu-O-Cu]^{2+} + H_2O$$

takes place on Cu–ZSM-5. However, the formation of paired copper clusters raises some doubts, since the H^+ ions in the H–ZSM-5 zeolite are located too far from each other to allow a paired cluster to be retained near these centres. A mechanism for the autoreduction of Cu^{2+} with formation of free-radical centres has been proposed:[229]

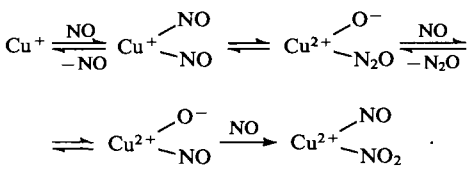
$$Cu(OH)^+ = Cu^+ + \dot{O}H,$$

$$Cu(OH)^+ + \dot{O}H = CuO + H_2O,$$

$$2\,Cu(OH)^+ \rightleftharpoons Cu^+ + CuO + H_2O.$$

According to this scheme the water oxidises the Cu^+ centres. We know[232] that water acts as a catalyst poison in the reaction between NO and hydrocarbons in the presence of oxygen. Therefore it follows that the Cu^+ centres are the active centres under the catalysis conditions.

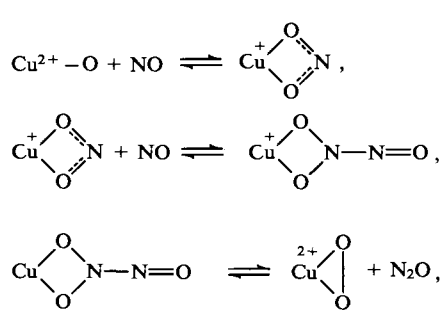
The decomposition of NO on Cu–ZSM-5 takes place at the same temperatures as its reduction by hydrocarbons. Therefore the decomposition of NO has been widely studied by spectroscopic methods.[227–229,232–234] In almost every case the formation of dinitrosyl complexes $Cu^+(NO)_2$ was observed. The following sequence of these complexes, leading to the formation of N_2O, has been proposed:[236]



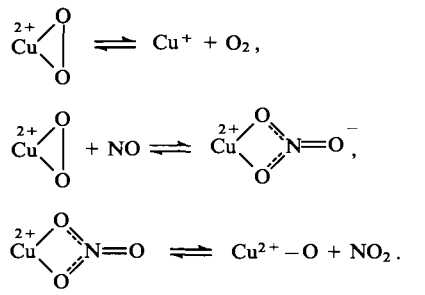
N_2 and O_2 are evolved during the dissociation of the last of these complexes. Complexes of the species $NO^{\delta+}$, $NO^{\delta-}$, $(NO)_2^{\delta-}$, and $NO_2^{\delta-}$ with Cu^{2+} have been detected.[233] During the decomposition of NO the intensity of the $NO^{\delta-}$ and $(NO)_2^{\delta-}$ bands decreases, and that of $NO^{\delta+}$ increases. The decomposition accompanied by the formation of nitrate ($NO_3^{\delta-}$), nitrite ($NO_2^{\delta-}$), and associative ($NO_2 \cdot NO$) complexes:[234]

$$NO_2(ads) + NO(ads) \longrightarrow [NO_2 \cdot NO] \longrightarrow O(ads) + N_2 + O_2.$$

Many different complexes have been observed in an analysis[229] of the IR spectra of the products of the reaction of NO with H_2. Bands corresponding to the following complexes were found after the adsorption of NO on Cu–ZSM-5 at room temperature: $Cu^{2+}-N=N$ (2156 cm^{-1}), $Cu^{2+}-NO$ (1910 cm^{-1}), Cu^+-NO (1811 cm^{-1}), $Cu^+(NO)_2$ (1734, 1827 cm^{-1}), and $Cu^{2+}-O-N=O$ (1631 cm^{-1}). At higher temperatures, and under conditions corresponding to the onset of the decomposition of NO, bands assigned to the following complexes were observed: $Cu^{2+}-NO_2$ (2130 cm^{-1}), $Cu^{2+}-NO$ (1910 cm^{-1}), Cu^+-NO (1811 cm^{-1}), $Cu^{2+}-O-N=O$ (1616, 1590, 1574 cm^{-1}) and $Cu^{2+}-NO_3$ (1502 cm^{-1}). The following scheme for the transformations of these complexes during their adsorption and decomposition was proposed:[229]



$$Cu^+ + N_2O \rightleftharpoons Cu^{2+}-O + N_2,$$



The mechanism of the interaction of hydrocarbons with NO in the presence of O_2 has been studied by spectroscopic methods.[235–241] In most cases propene was used as the reducing agent, but propane[237] and isobutane[241] were also used. Ideas on the intermediate forms of the hydrocarbons taking part in the reaction are not so definite as the ideas on the forms of NO. According to one suggestion, based on experiments in a TAP (temporal analysis of products) reactor,[236] the product obtained from the hydrocarbons is coke, which is a reducing agent for NO_x on Cu–ZSM-5 in the presence or in the absence of oxygen. The zeolite has a positive effect on both the formation of coke and on keeping the copper in the Cu^+ state.

Some workers have observed the formation under the reaction conditions of isocyanate[238–240] and of cyanide complexes.[240] The isocyanate groups can be bound both to the Cu and to an Al atom in the zeolite. As reported,[239] the process takes place by the following scheme:

$$C_xH_y \rightleftharpoons C_xH_y(ads),$$

$$C_xH_y(ads) + O_2 \longrightarrow C_mH_nO + CO_2 + H_2O,$$

$$C_mH_nO + m\,NO \longrightarrow m\,NCO + z\,H_2O,$$

$$NCO + NO \longrightarrow N_2 + CO_2 \text{ (rate limiting)},$$

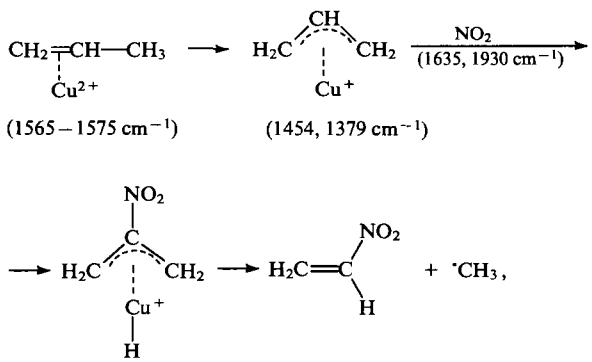
$$2\,NCO + O_2 \longrightarrow N_2 + 2\,CO_2,$$

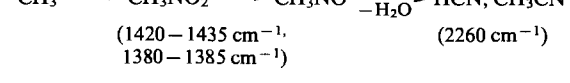
$$C_xH_y(ads)\,(\text{or } C_mH_nO) + NO \longrightarrow N_2O + CO_2 + H_2O,$$

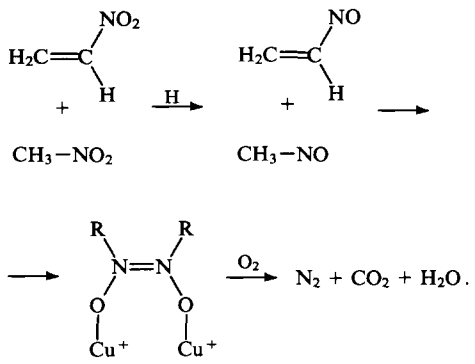
$$C_xH_y(ads) + O_2 \longrightarrow x\,CO_2 + y/2\,H_2O,$$

$$C_mH_nO + O_2 \longrightarrow m\,CO + n/2\,H_2O.$$

There is also a more detailed scheme, based on in situ IR spectroscopic studies:[240]







In this scheme cyanides are dead-end compounds, and isocyanates are not formed.

The interaction of NO with hydrocarbons in the presence of O_2 was studied by spectroscopic methods also on other zeolites of the ZSM-5 type (containing ion-exchange cations). The reaction of $C_3H_6 + NO + O_2$ on Ce–ZSM-5 was studied by in situ spectroscopy combined with the kinetic response method using gas-phase analysis.[242, 243] The absorption bands of the NO_2, NO_3, NCO, and CH_3NO_2 species adsorbed on the surface were detected in the IR spectra under the catalytic conditions. According to these workers[242] the reaction takes place by the mechanism

$$CH_3NO_2 + NO \longrightarrow N_2 + CO_2 + H_2O\,.$$

The Ga–ZSM-5 catalyst was found to be very selective in the processes associated with the interaction of NO with methane and ethane.[242–244] Its unique properties are attributed to the dissociative adsorption of methane on Ga–ZSM-5 (in contrast to its adsorption on Cu–ZSM-5. This was confirmed, in particular, by isotope exchange experiments between CH_4 and CD_4 on Ga–ZSM-5.

The reduction of NO_x by hydrocarbons in the presence of O_2 has been studied also on other catalysts. Thus, in particular, the $C_3H_6 + NO + O_2$ reaction takes place on Rh/Al_2O_3.[247] According to published data NO_2^- and NO_3^- are formed in an excess of O_2, and they subsequently react with C_3H_6 giving the $^{\cdot}C_3H_5$ radical and HNO_x. The weakly bound $^{\cdot}C_3H_5$ radical is rapidly oxidised to CO_2 by nitrates and nitrites.

The species $R-NO_x$, NO_x, NCO, nitrate, and nitrite were detected[248] spectroscopically in a study of the reduction of NO by hydrocarbons on various zeolites, and also on modified ZrO_2 and on complex oxides supported on γ-Al_2O_3.

We should stress that studies of the reduction of NO_x by hydrocarbons began only 2 or 3 years ago. Nevertheless there are already numerous reports of the spectroscopic detection of various surface forms, though only few spectro-kinetic studies could be traced. The existence of adsorbed intermediate forms of NO is most convincingly established, that of the complexes of NO with hydrocarbons is still arguable. The NCO species observed by several workers may play a key role in the reduction of NO both by CO and by hydrocarbons, though detailed schemes are still to be developed.

Table 7 gives a summary of data on the intermediate compounds which take part in the reduction of NO by ammonia, hydrogen, and hydrocarbons.

Table 7. Intermediates in the NO_x reduction reactions.

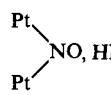
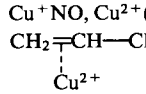
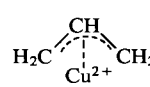
Reaction, catalyst	Intermediate complex	Reliability	Ref.
Reduction of NO with NH_3 on V_2O_5	NO_2(ads), NH_4^+	L	210
Interaction of NO with NH_3 on TiO_2	$NO-Ti^{4+}$, N_2O-Ti^{3+}, $NO_3^- - Ti^{3+}$, NH_3-Ti^{4+},	L	211
Interaction of NO with NH_3 on $V_2O_5-TiO_2$	$V^{5+}ONH_4$, $[HOVNH_2]^{2+}$, $V^{5+}OH$, NO, NO_2^-, NO_3^-, NH_3-Ti^{4+}	L	212, 213
	NH_3-V^{5+}, $NO-Ti^{4+}$, NH_2-V	L	214
Interaction of NO with NH_3 on FeY	NH_3(ads), NH_4^+	M	216
Interaction of NO with NH_3 on Pt(111)	NH_3(ads), NO(ads), NH_3NO, NH_2	L	215
NO + H_2 reaction on Pt(111)	 NO, HNO, N(ads)	L	220–222
NO + H_2 reaction on Rh/SiO_2	NO(ads), NH_2(ads)	M	223
NO + H_2 reaction on Au/SiO_2, Au/MgO	NO(ads), N(ads)	L	225
Decomposition of NO on Cu–ZSM-5	O(ads)	M	227
	Cu^+NO, $Cu(NO_2)$, $Cu(NO_2)^-$	M	228
	$(Cu-O-Cu)^{2+}$, $CuOH^+$	L	230, 231
	CuNO, $Cu(NO)_2$	M	232
	$Cu^+NO^{\delta+}$, Cu^+NO^{2-}, $Cu^+(NO)_2^{\delta-}$, $Cu^{2+}NO^{\delta+}$	M	233
	$Cu^{2+}-N=N$, $Cu^{2+}-NO$, Cu^+-NO, $Cu^+(NO)$, $Cu^{2+}-O-N=O$, $Cu^{2+}-NO_2$, $Cu^{2+}-NO_3$	H	229
$C_3H_6 + NO + O_2$ on Cu–ZSM-5	Cu^+NO, $Cu^{2+}(NO)(NO_2)$	M	236
		M	240
			
	NO_2(ads), $H_2C=CH-NO_2$, CH_3NO_2, HCN, CH_3CN, $-CN$, $-NCO$	M	238
	$Cu^{2+}(NO)_2$, Cu^+O(ads)	L	235
	NCO, C_mH_n, C_xH_y	M	239

Table 7 (contd)

Reaction, catalyst	Intermediate complex	Reliability	Ref.
$C_3H_8 + NO + O_2$ on Cu – ZSM-5	NO_2(ads), C_xH_yO	L	237
i-$C_4H_8 + NO + O_2$ on Cu – ZSM-5	C_x, NO(ads)	L	241
$C_3H_6 + NO + O_2$ on Ce – ZSM-5	NO_2^-, NO_3^-, CH_3NO_2, NCO	H	242, 243
$CH_4 + NO + O_2$ on Ga – ZSM-5	CH_3(ads)	L	244, 246
$C_3H_6 + NO + O_2$ on Rh – Al_2O_3	C_3H_5(ads), HNO_x	L	247
$C_3H_6 + NO + O_2$ on ZrO_2	R – NO_x, NO_x, NCO, NO_2, NO_3^-	M	248

XI. Conclusion

The reactions discussed in this review had been more carefully studied than those which were examined in our previous article.[1] This is because the extinction coefficients of the C – O, N – O, O – H, and N – H bonds are substantially higher than those of the C – H and C – C bonds. As a result, in reactions involving CO and NO (and sometimes also hydrogen) the sensitivity of the spectrokinetic measurements is higher, but the measured characteristic times of the elementary processes are lower. However in this case, as can be seen from the above tables, the confidence level of the great majority of the reported studies is only moderately high. We consider the studies of the catalytic reduction of NO by carbon monoxide, ammonia, and hydrocarbons to be the most reliable. These reactions began to be studied relatively late, but for this reason the methods used for the detection of surface compounds were more sensitive and up-to-date than the methods used in the earlier work.

In many cases the observed surface compounds (carbonates, formates, NCO) were stabilised on the carrier rather than on the active phase. They could be dead-end compounds, but they could also take part in the catalytic reaction as a result of their migration (spill-over) towards the active surface or towards the phase separation boundary.

A generalising analysis of all the reactions so far considered will be given in the third (closing) part of the present series of reviews.

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The radical polymerisation of acrylamide and its derivatives in the presence of complexing salts

V F Gromov

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Abstract. The results of studies of the radical polymerisation of acrylamide and of its derivatives in the presence of inorganic salts (Lewis acids) in various solvents are correlated. It is shown that the effect of inorganic salts on the polymerisation of acrylamide depends to a large extent on the nature of the solvent. During polymerisation in water the addition of Lewis acids has no effect on the rate of the process. The effect of Lewis acids is most marked when the reaction is carried out in organic solvents of relatively low polarity. It is shown that the change in the overall rate of the process in the presence of Lewis acids is due to a change in the rate constants of the chain growth and chain breaking reactions, induced by the formation of a complex between the amide group of the propagating radicals and/or monomers and the inorganic salt. The introduction of substituents into the acrylamide suppresses the formation of a complex with the salt, and therefore the effect of the salt on the polymerisation of substituted acrylamides is less marked than in the polymerisation of acrylamide itself. The bibliography includes 52 references.

I. Introduction

Studies reported during the past 15–20 years have convincingly established that in the radical polymerisation of vinyl monomers the nature of the reaction medium has a strong influence on the overall rate of the process, on the rate constants of the elementary propagation and termination reactions of the polymer chains, and on the molecular characteristics of the resulting polymers. Changing the nature of the solvent or introducing various complexing additives into the reaction mixture can significantly affect the kinetic parameters of the homogeneous radical polymerisation reaction.

Solvent effects are especially marked in the polymerisation of water-soluble monomers. Thus, in the polymerisation of monomers such as acrylamide, acrylic acids, *N*-vinylpyrrolidone, and the tertiary salts of the aminoesters of (meth)acrylic acid the chain propagation rate constant (k_p) is increased 50–100-fold[1–6] when the homogeneous polymerisation in organic solvents is replaced by polymerisation in an aqueous solution. The nature of the solvent has a smaller effect on the polymerisation of nonpolar and moderately polar vinyl monomers such as styrene and methyl methacrylate. But even in this case the overall rate of the reaction can be varied by a substantial factor by changing the nature of the solvent, and the k_p value for the homogeneous polymerisation of styrene varies by 50%–70% depending on the nature of the solvent. These effects have been discussed in depth in several monographs and reviews (see, for example, Refs 1 and 7–14). An analysis of published data suggests that the principal causes of the influence of the nature of the solvent on the kinetic parameters of the homogeneous radical polymerisation of vinyl monomers are the formation of specific complexes between the reacting species (the monomer, and the polymeric radicals) and the solvent molecules, the hydrophobic interactions stimulated by the polymerisation of water-soluble monomers in aqueous solutions, and also the change in the quality of the solvent as compared with the growing polymer. In the case of low-polarity hydrocarbon monomers of the styrene type the factor which mainly determines the effect of the solvent on k_p is the formation of donor–acceptor complexes between the solvent molecules and the growing polymer radicals, leading to a decrease in the activity of these radicals.

The formation of donor–acceptor complexes between the vinyl monomers and/or their radicals (on the one hand) and inorganic salts acting as Lewis acids (on the other) can also affect the radical polymerisation of the vinyl monomers. Detailed analyses of the reported studies of polymerisation in the presence of Lewis acids can be found in several publications.[15–22] Their results, correlated in those reviews, show that the addition to the reaction system of Lewis acids such as zinc chloride, aluminium bromide and chloride, stannic chloride, lithium chloride, and also various organoaluminium compounds leads to marked changes in the kinetics of the homopolymerisation of vinyl monomers (acrylonitrile, methacrylonitrile, methyl acrylate, methyl methacrylate, etc.) and of the copolymerisation of these monomers. Under these conditions substantial changes in the molecular masses of the polymers also take place. Most of the authors explain the observed kinetic effects in terms of complex formation between the components of the reaction mixture and of the influence of these complexes on the rate constants of the elementary propagation and termination reactions of the polymer chains. The formation of complexes in systems containing vinyl monomers and various Lewis acids has been established experimentally by spectroscopic methods: in many cases the complexes between the monomer and the Lewis acids were isolated in a pure state. A study of the effect of the complexing

V F Gromov Radiation Polymerisation Laboratory of the L Ya Karpov Physicochemical Research Institute, ul. Vorontsovo pole 10, 103064 Moscow, Fax (7-095) 975 24 50

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agent on the radical polymerisation of (meth)acrylonitrile and methyl(meth)acrylate[23] showed that (depending on the strength of the Lewis acid, its concentration, and the donor–acceptor properties of the monomer) the complex-forming salts can both accelerate and inhibit this process.

Thus we have very extensive and convincing evidence of the effect of the nature of the solvent and of added complexing salts on the radical polymerisation of a large number of vinyl monomers. One of the sources of the observed effect is the formation of various types of complex between the components of the reaction system. Furthermore, the nature of the resulting complexes and their influence on the polymerisation kinetics may be different if the polymerisation is carried out in different solvents or in the presence of Lewis acids. Therefore information on the effect of the nature of the solvent on the radical polymerisation in the presence of complexing salts could be useful in establishing the mechanism by which the composition of the reaction medium affects the kinetic parameters of the polymerisation. The aim of the present review is to generalise the results of studies of this problem.

Studies of the influence of the nature of the solvent on the polymerisation in the presence of complex-forming salts were carried out mainly on acrylamide and on some of its derivatives. The polymers of acrylamide offer a wide range of important properties for practical applications.[24–26] They are used as efficient flocculants in the purification of potable water and of effluents from metallurgical, mining, and other industrial plants, to improve the performance of petrol engines, to decrease the hydrodynamic resistance to the motion of water along pipelines and to the motion of various objects in water, in the textile and the food industry, etc. Therefore studies of the polymerisation mechanism of acrylamide and its derivatives in the presence of salt additives are of great interest not only in establishing the fundamental rules governing the radical polymerisation process but also for practical purposes.

II. Polymerisation of acrylamide and its derivatives in the presence of Lewis acids

We know that the amide group has a planar configuration, the *trans* form being the most favourable:[27,28]



In the absence of metal ions the amide group is almost neutral; in an acid medium it can add on a proton, the protonation taking place mainly at the oxygen atom.[28,29]

Complex formation with metal ions lengthens the C = O bond and shortens the C–N bond. Experimental and theoretical studies have identified an increase in the double-bond character of the carbon to nitrogen bond, due both to metallisation and to the protonation of the amide group in an acid medium.[27]

These results suggest that in the polymerisation of amide monomers a specific interaction should exist between the amide group of the monomer (and/or the polymeric radical) and the metal atoms of the Lewis acid, leading to a change in the reactivity of the reacting species and therefore also of the kinetic parameters of the polymerisation of these monomers. A partial confirmation of these changes is provided by data on the copolymerisation of acrylamide with other vinyl monomers in the presence of Lewis acids. Thus, in the copolymerisation of acrylamide with acrylic acid the addition of zinc chloride strongly influences both the copolymerisation constant and the overall rate of the process.[30] Whereas in the absence of the salt the copolymerisation of these monomers in benzene produces a random copolymer, and the system is characterised by the copolymerisation constants $r_1 = 1.38$ and $r_2 = 0.36$, the addition of zinc chloride (at all concentrations of the initial mixture of monomers) produces an alternating copolymer of equimolar composition. The changes in the copolymerisation constants of acrylamide with vinyl acetate and methacrylic acid in the presence of a Lewis acid are also confirmed by independent results.[31]

Several studies of the complex formation of acrylamide and some of its derivatives with the halides of various metals (in particular, with zinc chloride and bromide) in the solid state and of the polymerisation of these solid complexes were reported in the early 1980s.[32–35] The polymerisation of several *N-tert*-alkylacrylamides in solution under the influence of zinc chloride was also studied. The formation of solid complexes of acrylamide, methacrylamide, and their *N*-substituted analogues with zinc, cadmium, and mercury halides has been investigated.[32] The ability of these systems to form complexes depends both on the structure of the amide and on the nature of the salt. The presence of bulky *tert*-alkyl substituents near the nitrogen atom of the amide group strongly suppresses the complex-forming properties of the monomer. Furthermore methacrylamide is less effective in complex formation than acrylamide. A study of the structure of the *N-tert*-butyl- and *N-tert*-amylacrylamide complexes with zinc chloride in dioxan showed that in this case the electrophilic attack of zinc chloride takes place at the oxygen atom of the carbonyl group in the amide.[33]

The complex formation of *N-tert*-butyl- and *N-tert*-hexylacrylamide with zinc chloride increases the rate of radical polymerisation of these amides in the solid state. In most cases the formation of complexes of these amides with zinc bromide is accompanied by a decrease in the reactivity of the monomers.[34] At a given polymerisation temperature an increase in the size of the alkyl substituent on the nitrogen atom increases the rate of solid-phase polymerisation of the complexed monomer. However, at a given reduced temperature (i.e. for a fixed $T:T_m$ ratio) we observe the opposite activity sequence of the complexed monomers. It is important to note that the activation energy for the polymerisation of the complexed monomers is higher than the value for the free amide monomers.

In the presence of zinc chloride *N-tert*-alkylacrylamides (*N-tert*-butyl- and *N-tert*-amyl-) are polymerised at 60 °C even without a radical initiator if the reaction is carried out in solvents of low polarity (benzene, dioxan).[35] The yield of the polymers depends on the strength of the interaction between the salt and the solvent (Table 1). When this interaction is very strong (with polar solvents like pyridine, ethyl acetate, and especially water) the influence of the Lewis acid on the reactivity of the monomer is slight, and the rate of polymerisation is low. Adding water to a solution of the monomer in dioxan breaks the bond between the monomer and the salt and thus lowers the yield of polymer.

Table 1. Polymerisation of *N-tert*-butylacrylamide (I) and *N-tert*-amylacrylamide (II) under the influence of zinc chloride.[35]

Solvent	Yield of polymer (%)	
	I	II
Water	—	0.85
Pyridine	0.81	1.80
Dioxan	45.80	23.57
Ethyl acetate	0.81	2.52
Benzene[a]	60.00	40.00
Methanol	0	0
Acetone	0	0

Note. Reaction conditions: concentration of amide 0.2866 M, of salt 0.1433 M; temperature 60 °C; polymerisation time 1 h.
[a]During the polymerisation in benzene the polymer is partially precipitated as a separate phase.

The effect of Lewis acids on the polymerisation of acrylamide has been examined in much greater depth. The polymerisation of this monomer was studied in detail in various solvents and in the presence of inorganic salts of different types, thus allowing a well founded mechanism of the process to be developed.

1. Effect of the nature of the solvent on the polymerisation of acrylamide in the presence of Lewis acids

The radical polymerisation of acrylamide in water and in various organic solvents and water–organic mixtures in the presence of Lewis acids has been studied in our laboratory.[36–40] In every case the reaction was carried out under UV radiation in the presence of the dinitrile of azoisobutyric acid (DAA) as a photosensitiser. The polymerisation of acrylamide (AA) in an aqueous solution in the presence of lithium bromide has also been discussed.[36,39] It can be seen from the results in Fig. 1 that at relatively low rates of initiation the addition of the salt (lithium bromide) produces a marked decrease in the overall rate of the reaction. However, at higher rates of initiation the effect of the salt becomes less marked and the reaction no longer depends on the additions of salt. An analysis of these results (and in particular the study of the effect of the salt on the order of the polymerisation reaction with respect to the initiator, which varies from 1 to 0.5 as the salt concentration is increased) leads to the conclusion that the lithium bromide additive has no effect on the rate constants of the chain propagation and chain termination reactions in the polymerisation of acrylamide in aqueous solution.[36,39] On the other hand the decrease in rate observed at low rates of initiation is entirely due to the presence of additives in the system. The conclusion that additions of Lewis acids have no effect on the rates of the propagation and termination reactions of the chains during the polymerisation of amide monomers (and also of acrylonitrile) in aqueous solutions is also consistent with other results.[35,41]

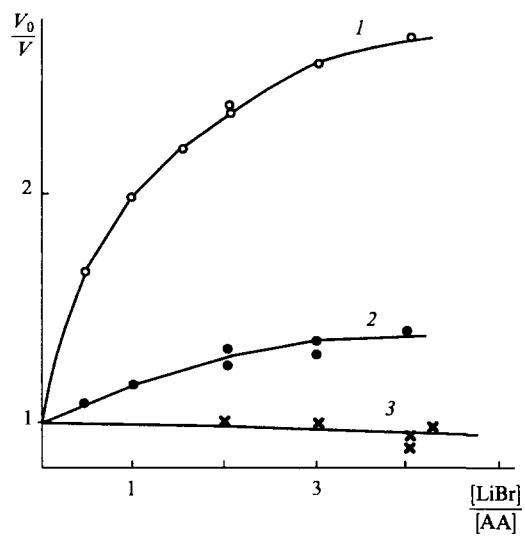


Figure 1. Dependence of the relative rate of polymerisation of acrylamide in water on the concentration of lithium bromide. Concentration of acrylamide 0.5 M; $T = 20$ °C; V_0 and V are the reaction rates in the absence and in the presence of the salt respectively. Concentration of DAA, M: 0.5×10^{-4} (*1*), 0.8×10^{-3} (*2, 3*); intensity of incident UV light, arbitrary units: 1 (*1, 2*), 2.5 and 4.0 (*3*).

It should be noted that some studies have revealed a change in the rate of polymerisation of acrylamide under the influence of several oxidation–reduction initiating systems after the addition of sodium, potassium, iron, manganese, and other salts (see, for example, the monograph by Finch[26]). However, this effect is fully explained by the influence of those salts on the rate of the oxidation–reduction initiation, and is not dependent on any interaction of the salts with the monomer and/or the growing radicals.

A different state of affairs is found in the polymerisation of acrylamide in less polar solvents. The addition of lithium bromide to a solution of acrylamide in dimethyl sulfoxide (DMSO) leads to an increase in the total rate of polymerisation, which reaches a maximum at a molar ratio of [salt] : [monomer] = 1.5, followed by a slight decrease when the salt concentration is increased beyond this value (Fig. 2). The order of the reaction with respect to the initiator is 0.5, both in the absence of salt and in the presence of a [salt] : [monomer] ratio of 1.5. When the concentration ratio of salt to monomer is kept constant the order of the reaction with respect to the monomer increases from 1.0 (in the absence of the salt) to 1.96 (at a ratio of 1.5). Increasing this ratio to 2.0 produces a decrease in the order of the reaction with respect to monomer.[37,39]

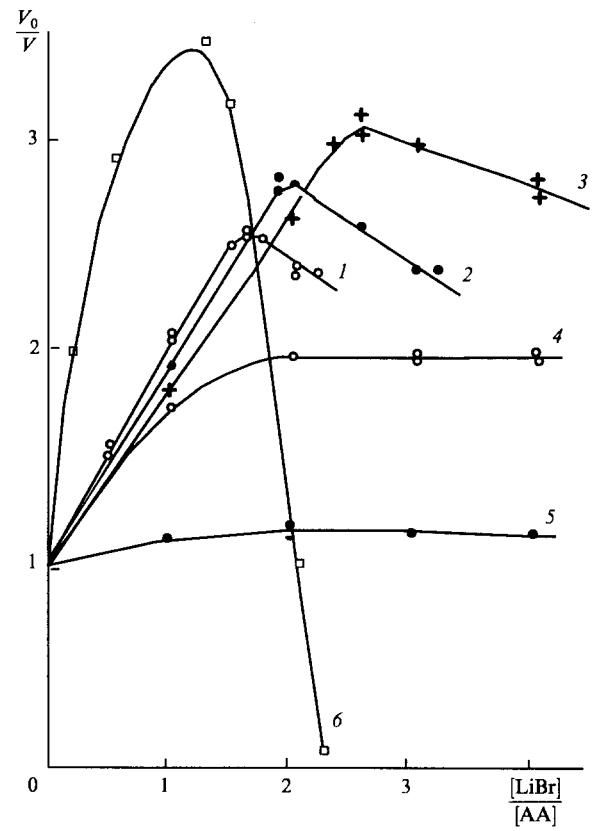


Figure 2. Dependence of the relative rate of polymerisation of acrylamide in DMSO (*1*), in a water–DMSO mixture (*2–5*), and in tetrahydrofuran (THF) (*6*) on the concentration of lithium bromide. Concentration of acrylamide 0.5, concentration of DAA 3×10^{-3} M; $T = 30$ °C; concentration of water in the mixture with DMSO mol %: (*2*) 8.4, (*3*) 20, (*4*) 65, (*5*) 85.

Adding water to the DMSO produces a gradual decrease in the effect of the salt on the rate of polymerisation of acrylamide. For small additions of water (8.4 and 20 mol% of the DMSO) the plots of the overall rate of polymerisation (V) against the concentration of the salt show a maximum at higher concentrations than in the polymerisation in the absence of water (Fig. 2, curves *2* and *3*). Under these conditions the effect of the salt on the rate of polymerisation (i.e. the ratio V/V_0, where V_0 is the rate of polymerisation in the absence of water) is greater in the presence of water than when the polymerisation takes place in dry DMSO. For higher water concentrations in the mixed solvents (65 and 85 mol%) the maximum effect of the salt is less marked than in pure DMSO (Fig. 2, curves *4* and *5*). Furthermore at high

water contents there is practically no decrease in the reaction rate beyond the lithium bromide concentration at which the maximum value is reached.

The effect of lithium bromide on the polymerisation of acrylamide is strongest in THF. In this solvent the reaction takes place with precipitation of the polymer from solution, and therefore the rate of photopolymerisation was determined in the earliest stages of the process, when the loss of transparency of the reaction system produced by the precipitation of the polymer was not too serious, i.e. the rate of photoinitiation was practically constant. The results in Fig. 2 show that, as in DMSO, in the polymerisation in THF (curve *6*) the reaction rate reaches a maximum at a well defined concentration of the salt, and that in this case the maximum V/V_0 ratio is much higher than in the polymerisation in DMSO and the maximum is observed at a lower concentration ratio of the salt and the monomer. However, at higher concentrations of lithium bromide the rate of polymerisation of acrylamide falls off steeply.

The addition of saturated acetamide to a reaction system containing lithium bromide and acrylamide lowers the rate of polymerisation in DMSO, and this effect increases with the concentration of acetamide.[39, 40] In the absence of the salt, adding acetamide has no effect on the rate of polymerisation of acrylamide. When acrylamide is polymerised in DMSO in the presence of acetamide, salt additions increase the rate of the reaction but in this case the accelerating effect of lithium bromide is less marked than in the absence of acetamide (Fig. 3).

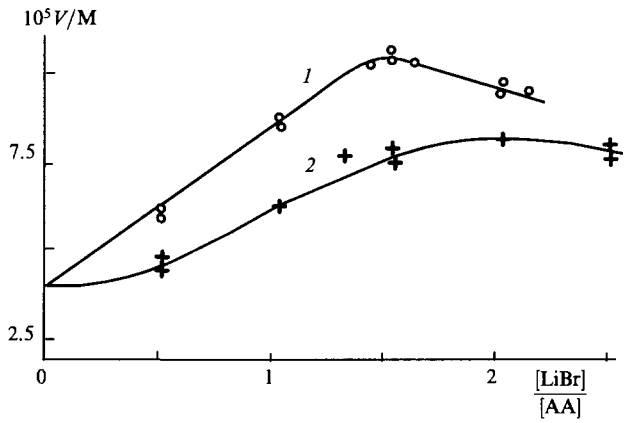


Figure 3. Effect of the concentration of lithium bromide on the rate of polymerisation of acrylamide in DMSO in the presence (*1*) and in the absence of 1.0 M of acetamide (*2*). Concentration of acrylamide 0.5, of DAA 3×10^{-3} M, $T = 30$ °C.

2. Effect of the nature of the inorganic salt on the polymerisation of acrylamide

The effect of the nature of the Lewis acid on the polymerisation of acrylamide has been studied for the reaction in DMSO.[38-40]

Lithium, calcium, and zinc chlorides were used as the Lewis acids. The reaction was carried out under the conditions used in the presence of lithium bromide. In every case the reaction proceeds (without a period of induction) with a constant initial rate. The polymerisation in the presence of lithium and calcium salts produces a maximum in the plot of the overall rate of the process against the concentration of the salt (Fig. 4). However, the position of the maximum varies with the nature of the salt. With respect to their influence on the overall rate of polymerisation of acrylamide the salts can be arranged in the following series: LiBr < LiCl < $CaCl_2$. The rate of polymerisation of monomers such as acrylonitrile and methyl methacrylate,[42] and also *N*-alkylacrylamides,[35] increases markedly in the presence of zinc chloride, but the addition of this salt has

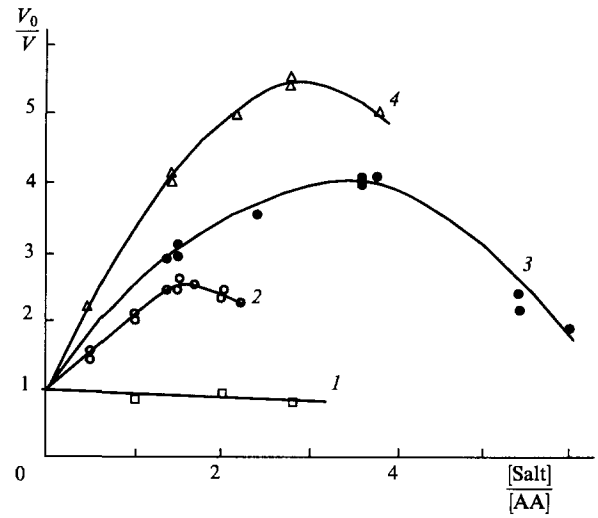


Figure 4. Dependence of the relative rate of polymerisation of acrylamide in DMSO on the salt concentration. Concentration of acrylamide 0.5, concentration of DAA 3×10^{-3} M; $T = 30$ °C; salt (*1*) $ZnCl_2$, (*2*) LiBr, (*3*) LiCl, (*4*) $CaCl_2$.

almost no effect on the rate of homogeneous polymerisation of acrylamide under the conditions of these experiments.

The rate of polymerisation of acrylamide in the presence of lithium bromide or calcium chloride depends on the nature of the solvent in which the reaction is carried out: the accelerating effect of small additions of salt on the polymerisation process increases as the polarity of the solvent decreases (Fig. 5).[40] It should be noted that (as in the polymerisation of *N-tert*-alkyl substituted acrylamides in a low-polarity medium[35]) the polymerisation of acrylamide in *N*-methylpyrrolidone (the least polar of the solvents used in that work[40]) with [salt]:[monomer] ratios between 0.35 and 0.40 takes place even in the absence of radical initiators. The spontaneous polymerisation of acrylamide (in the

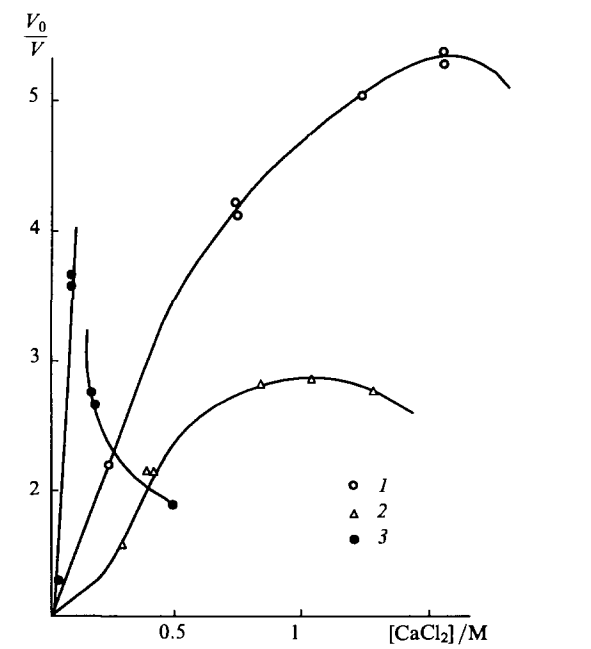


Figure 5. Dependence of the relative rate of polymerisation of acrylamide in DMSO (*1*), formamide (*2*), and *N*-methylpyrrolidone (*3*) at 30 °C (*1*) and 20 °C (*2, 3*) on the concentration of calcium chloride. Concentration of acrylamide 0.5, concentration of DAA 3×10^{-4} M.

Table 2. Order of the reaction with respect to the monomer in the polymerisation of acrylamide in DMSO for different concentration ratios of salt to monomer.[38,39]

Salt	[Salt]:[Monomer]	n	Relative viscosity of salt solution in DMSO	n' (see [a])
LiBr	0.5	1.3	1.4	1.3
	1.0	1.6	1.6	1.3
	1.5	1.9	2.0	1.7
LiCl	0.5	1.4	1.4	1.2
	1.5	2.2	2.0	1.9
$CaCl_2$	1.5	2.8	4.0	2.2
	3.0	3.6	19	2.5

Notes. Reaction conditions: concentration of acrylamide 0.5, of DAA 3×10^{-3} M; $T = 30$ °C.
[a] n' was calculated from the rates of polymerisation reduced to a fixed viscosity of the reaction system equal to the viscosity of DMSO.

absence of UV radiation) was not observed at other salt concentrations in *N*-methylpyrrolidone.

The kinetic order with respect to the initiator in the polymerisation of acrylamide in DMSO is 0.5 in the presence of lithium and calcium chlorides (as it is in the presence of lithium bromide). On the other hand the order of the reaction with respect to the monomer (n) at a constant ratio between the salt and the monomer varies with this ratio between 1.3 and 3.6 (Table 2). The addition of salts to a solution of acrylamide in DMSO produces a large increase in the viscosity of the reacting solution. Thus, at a salt concentration of 0.75 M the viscosity of the solution increases 2-fold with lithium chloride and bromide and 4-fold when calcium chloride is added. As was pointed out,[43] an increase in the viscosity of the reaction medium should be accompanied by an increase in the overall rate of polymerisation. Therefore the reaction rates were recalculated for a fixed viscosity of the reaction solution, equal to the viscosity of DMSO, and the order of the reaction with respect to the monomer was then redetermined (n'). It was assumed that the rate of the reaction was proportional to the viscosity of the reaction system to the power 0.5. The results (see Table 2) show that the order of the reaction with respect to the monomer was greater than 2.0 in the presence of calcium chloride at high [salt]:[monomer] ratios, whereas it approached this value during polymerisation in solutions containing lithium chloride or bromide.

Additions of inorganic salts (Lewis acids) affect not only the overall rate of polymerisation but also the molecular mass of the polymers, which is much greater than the molecular mass of the polyacrylamide synthesised in the absence of salts.[38-40] Thus, the intrinsic viscosity of the polymer produced in DMSO at a monomer concentration of 0.5 M is 0.88 dL g^{-1}, whereas the polymers synthesised in the presence of 1.0 M of lithium bromide or chloride or of calcium chloride have an intrinsic viscosity of 2.9, 3.5, and 4.1 dL g^{-1} respectively.

The change in reactivity of acrylamide and/or its radical in the presence of Lewis acids also results in changes in the overall rate of the process and in the copolymerisation constants of acrylamide with styrene in DMSO. It has been shown[40] that the rate of polymerisation of acrylamide decreases rapidly with small additions of styrene, the effect depending on the presence of a Lewis acid in the reaction system. Thus, adding 5 mol% of styrene lowers the rate of polymerisation in the absence of the salt by a factor of 17, whereas in a system containing lithium bromide ([salt]:[acrylamide] = 1.5) the rate falls by a factor of 32, and in the copolymerisation under similar conditions but in the presence of lithium chloride it falls by a factor of 40. The copolymerisation constants of acrylamide with styrene in DMSO are $r_1 = 0.21$ and $r_2 = 2.35$ in the presence of lithium chloride and $r_1 = 0.40$ and $r_2 = 2.0$ in the absence of the salt.[44]

3. Mechanism of the effect of salts on the polymerisation of acrylamide

The results discussed above denote a specific interaction between the reacting species and the salts (Lewis acids) in the polymerisation of acrylamide. The IR and PMR spectra of acrylamide–salt systems in DMSO were analysed in order to confirm the presence of this interaction.[38-40] In the IR spectra the absorption band which characterises the NH group of the monomer is shifted towards lower frequencies in the presence of lithium bromide (Fig. 6). The PMR spectrum also reveals a small shift of the signal due to the protons of the NH_2 group towards lower energies.[36,40] A more substantial shift is observed when lithium chloride is added to a solution of acrylamide in DMSO, and an even stronger shift when calcium chloride is added. On the other hand the addition of zinc chloride to the acrylamide–DMSO system does not produce a significant shift of this signal. Thus the spectroscopic results point to the formation of a complex between the amide group of acrylamide and the inorganic salts (except zinc chloride). The C=C vinyl group does not take part in complex formation. A similar result was obtained in a study[45] of the interaction between methyl methacrylate and Lewis acids. The formation of complexes between the amide group of acrylamide and the salt is confirmed by kinetic data on the effect of acetamide on the polymerisation of acrylamide in DMSO in the presence of lithium bromide. If the vinyl group had contributed to the formation of a complex between acrylamide and the salt, the rate of polymerisation of the acrylamide would not have been affected by the addition of acetamide. Evidently acetamide (like acrylamide) forms a complex with lithium bromide, and the addition of a saturated amide to the reacting system creates a competition between the acrylamide and the acetamide for the formation of a complex, which lowers the rate of polymerisation. The fact that even small additions of acetamide (as compared with the acrylamide) produce a marked decrease in the rate of polymerisation is evidence that the formation of a complex between the salt and a saturated amide has a higher probability than the same reaction with the unsaturated acrylamide. PMR spectroscopy results[36,40] lead to the same conclusion: under otherwise identical conditions the signal which characterises the protons of the amide group is shifted by the addition of lithium bromide by 0.30 and 0.23 ppm for acetamide and acrylamide respectively.

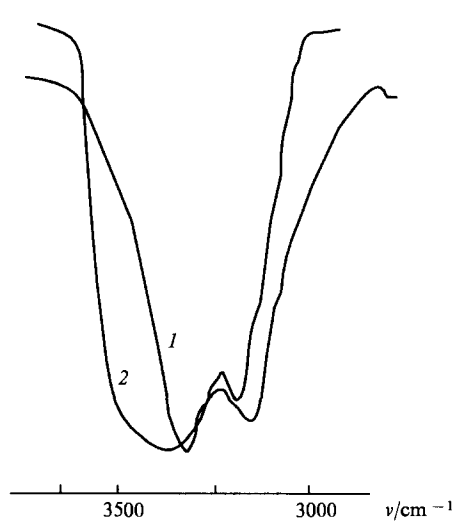


Figure 6. IR spectra of solutions in DMSO (*1*) and in DMSO + LiBr (*2*). Concentration of acrylamide 0.5 M, of salt 0.75 M.

The PMR spectroscopy data indicate an increase in the double-bond character of the C–N bond in acrylamide after the addition of the Lewis acid. It may be assumed that the presence of a C=C double bond undergoing conjugation with the C=O bond of the amide lowers the probability of complex formation between the acrylamide and the salt as compared with acetamide.

According to the IR and PMR spectroscopy data the amount of monomer complexed in the reaction mixture is small. Therefore we may assume that the complexed radicals (which have a high activity) and not the complexed acrylamide play the key role in the change in the rate of polymerisation of acrylamide in the presence of Lewis acids.

The stability constants of the complexes formed by acrylamide with salts (K) in various solvents have been calculated[36,38–40] from PMR data. The K values for 27 °C calculated by the Hildebrand–Benes method[46] from the dependence of the shift of the PMR signal at 7.50 ppm on the concentration of acrylamide at constant salt concentration are shown below:

Solvent	DMSO	DMSO	THF	Water
Salt	LiBr	$CaCl_2$	$CaCl_2$	LiBr
K/L mol^{-1}	0.066	0.14	0.23	0

As in the case of lithium bromide, in systems containing lithium chloride or calcium chloride the complexed radicals play the main part in the polymerisation process. However, at high salt concentrations the contribution from the complexed monomer cannot be ignored. This is specially true of polymerisation in a DMSO solution of calcium chloride, since the power to form complexes with acrylamide is highest in this salt.[36–40]

The following kinetic scheme for the formation of a complex between the reacting species (monomer and radical) and the salt and also for the polymerisation of acrylamide in the presence of Lewis acids was derived[36–40] from the reported kinetic and spectroscopic data.

If $R_c^{\cdot}$ radicals bound in a complex take part in the polymerisation process their concentration in the reaction system is determined by the reaction

$$\text{Salt} + R^{\cdot} \xrightarrow{K} R_c^{\cdot}.$$

If the concentration of the salt is much greater than the concentration of the radicals we have

$$[R_c^{\cdot}] = K[\text{Salt}]([R^{\cdot}]_0 - [R_c^{\cdot}]).$$

and

$$[R_c^{\cdot}] = \frac{K[\text{Salt}][R]_0}{1 + K[\text{Salt}]}.$$

On the assumption that the chain propagation reaction is characterised by the constant k_p when the participating radicals are not complexed and by the constant k_p' in the case of complex-bound radicals we can write the following equation for the overall rate of polymerisation in the presence of a complex-forming salt:

$$V = [M]\{k_p([R^{\cdot}]_0 - [R_c^{\cdot}]) + k_p'[R_c^{\cdot}]\}. \quad (1)$$

After substituting for $R_c^{\cdot}$ we find

$$V = [M][R^{\cdot}]_0\left(\frac{k_p}{1 + K[\text{Salt}]} + \frac{k_p'K[\text{Salt}]}{1 + K[\text{Salt}]}\right). \quad (2)$$

If $K[\text{Salt}] \ll 1$ the overall rate of polymerisation is

$$V = [M][R_0^{\cdot}](k_p + k_p'K[\text{Salt}]). \quad (3)$$

For a polymerisation process involving not only radicals bound in a complex but also complexed monomer molecules the following rate equation for the polymerisation has been obtained:

$$V = [M][R^{\cdot}]_0(k_p + k_1[\text{Salt}] + k_2[\text{Salt}]^2). \quad (4)$$

Here k_1 and k_2 are constants which characterise the rate of the chain propagation reaction of the corresponding complexed species and the stability constant of the complex. The term $k_2[\text{Salt}]^2$, which does not appear in Eqn (3), results from allowing for the interaction of complexed radicals with the monomer.

It follows from Eqn (4) that the overall rate of polymerisation should increase linearly with the concentration of the monomer, and that the order of the reaction with respect to the salt as a function of the relative values of k_p, $k_1[\text{Salt}]$, and $k_2[\text{Salt}]^2$ should vary from 0 to 1 if only complexed radicals contribute to the polymerisation [see Eqn (3)], or from 0 to 2 if both complexed radicals and the monomer bound in a complex are involved. Therefore the overall order of the polymerisation reaction with respect to the monomer and the salt (i.e. when the concentrations of the salt and of the monomer are both changing, but the ratio of these components of the reaction mixture is held constant) should increase from 1 to 2 or from 1 to 3 respectively with the salt concentration. The experimental data shown in Table 3 agree satisfactorily with these predictions. They also confirm the participation of the complexed monomer in the polymerisation of acrylamide in a DMSO solution containing calcium chloride. This is not surprising, since the concentration of complexed acrylamide in this system is approximately 15%–20% of the total concentration of monomer under the conditions corresponding to the maximum rate in curve *4* of Fig. 4.

In order to explain the mechanism of the effect of inorganic salts on the radical polymerisation of acrylamide the absolute values of the rate constants of the elementary reactions for the propagation and termination of the polymer chains were determined for the reaction in DMSO in the presence of various salts.[38–40] It was found that the changes in the rate of polymerisation of acrylamide can be attributed almost entirely to changes in the rate constants for the propagation (k_p) and termination (k_t) of the chains, and are not dependent on changes in the rate of initiation produced by the addition of salts (see Table 3 and Fig. 7). A similar state of affairs was observed in the polymerisation of acrylonitrile in the presence of Lewis acids.[42]

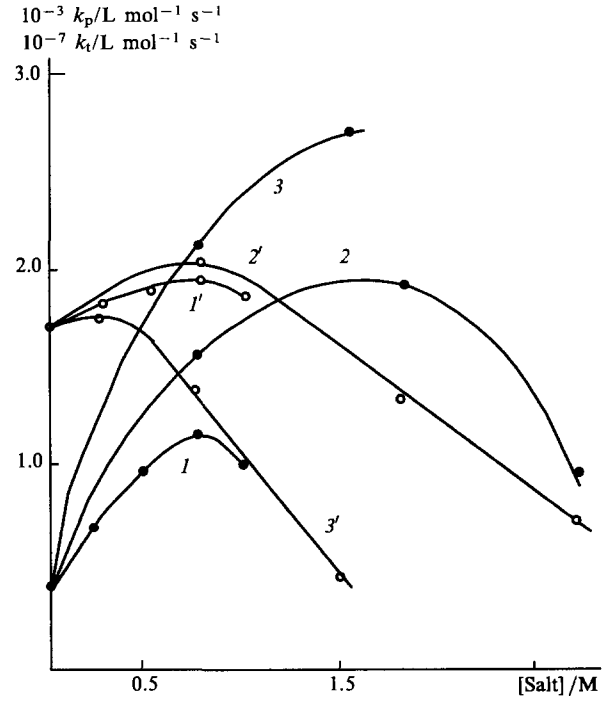


Figure 7. Dependence of the rate constants for the propagation (*1*–*3*) and for the termination of the chains (*1′*–*3′*) on the salt concentration during the polymerisation of acrylamide in DMSO at 30 °C. Salt: (*1*) LiBr, (*2*) LiCl, (*3*) $CaCl_2$.

Table 3. Rate constants of the chain propagation (k_p) and termination reactions (k_t) in the homogeneous polymerisation of acrylamide in DMSO in the presence of complexing salts (acrylamide concentration 0.5 M).[36]

[LiBr]/ M	T/ °C	10^{-3} k_p/ L mol^{-1} s^{-1}	E_p/ kcal mol^{-1}	10^{-7} A_p/ L mol^{-1} s^{-1}	10^{-7} k_t/ L mol^{-1} s^{-1}	E_t/ kcal mol^{-1}	10^{-8} A_t/ L mol^{-1} s^{-1}
0	20	2.5	6.0	7.8	16.7	0.3	2.8
	30	3.7			16.9		
	40	5.0			17.3		
0.25	20	4.6	5.4	5.3	17.7	0.3	3.0
	30	6.8			18.1		
	40	9.0			18.4		
0.50	20	7.0	4.7	2.5	18.7	0.3	3.1
	30	9.7			19.0		
	40	12.5			19.3		
0.75	20	8.5	4.3	1.5	19.0	0.4	3.8
	30	11.6			19.4		
	40	14.5			19.8		
1.0	20	7.0	4.8	2.8	18.2	0.6	5.1
	30	10.0			18.8		
	40	12.9			19.4		

The changes in the overall rate of polymerisation observed after the addition of lithium bromide to a solution of acrylamide in DMSO are due mainly to changes in k_p (since the changes in k_t are only slight). Additions of this salt lower the activation energy of the chain propagation reaction, and this effect is associated with a decrease in the complex formation constant with temperature. Thus an increase in temperature is accompanied by a decrease in the stability constant of the complex, and therefore also in the concentration of complexed radicals, and this leads to a less steep temperature dependence of the rate of chain propagation.

The complex formation constant decreases as the polarity of the solvent increases. This accounts for the influence of the nature of the solvent on the polymerisation of acrylamide in the presence of lithium bromide or calcium chloride. The effect of the salt on the polymerisation is greatest in tetrahydrofuran ($K = 0.23$ L mol^{-1}), whereas in an aqueous solution no acceleration is produced by the salt (the stability constant of the complex in water is zero).

In the presence of complexing salts the constant k_p varies in the same sense as the change in the overall rate of polymerisation (see Table 3). The experimentally observed dependence of the chain termination rate constant on the salt concentration is due to the diffusion control of the polymer chain propagation reaction. We know[43] that the chain termination rate constant is directly proportional to the fluidity of the reaction system. Therefore we used the formula[40]

$$k_t' = \eta k_0$$

(where k_t' is the experimental value, and η is the viscosity of the initial reaction mixture relative to DMSO) to calculate the k_t' values for a viscosity equal to that of pure DMSO. It was shown that the k_t' values are directly proportional to the salt concentration (Fig. 8), which suggests an increase in the reactivity of the polymeric radicals with increasing salt concentration and confirms the concept of complex formation by polymeric radicals.[36-40]

The difference in the chain propagation rate constants observed in the homogeneous polymerisation of acrylamide in DMSO containing various salts can be attributed to different degrees of complex formation between the active centres and the salt. It should not be forgotten that free radicals both bound and not bound in a complex contribute to the polymerisation. An increase in the complex formation constant results (not surprisingly) in an increased number of complexed active centres and therefore in an increase in the effective rate coefficient of the chain propagation reaction. Since the complex formation constant for potassium chloride with acrylamide in DMSO is higher than for lithium bromide we may suggest that the complex formation constants of these salts with polymeric radicals vary in the same sequence. Therefore the propagation of chains should have its highest specific rate in the presence of calcium chloride and its lowest in the presence of lithium bromide, as is indeed observed experimentally. It follows from PMR spectroscopy data that zinc chloride does not form a complex with acrylamide in a DMSO solution. Therefore the addition of this salt to a solution of acrylamide in DMSO does not affect the overall rate of polymerisation.

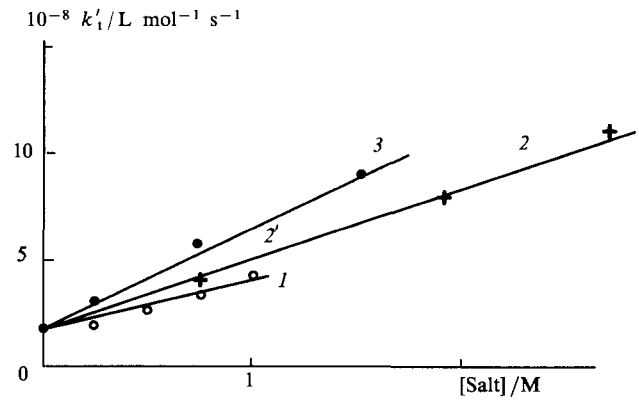
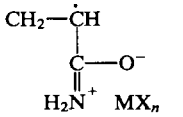


Figure 8. Plots of the rate constant of the chain termination reaction reduced to a single viscosity for the polymerisation of acrylamide in DMSO at 30 °C against the salt concentration. Salt: (*1*) LiBr, (*2*) LiCl, (*3*) $CaCl_2$.

The formation of a complex between the acrylamide molecules and the salts is accompanied by an increase in the distance between the signals in the PMR spectra which characterise the protons of the amide group in the monomer. Whereas the signal at 7.0 ppm is almost unaffected by the addition of salts the signal at 7.5 ppm is shifted towards lower

energies, indicating an increase in the double-bond character of the C–N bond in acrylamide as a result of the formation of a complex with the salt.[36,38]

The higher reactivity of the complexed acrylamide radical, which produces an increased rate of polymerisation of acrylamide in the presence of Lewis acids, can be attributed to the formation of the structure



whose most important feature is the localisation of an unpaired electron on the carbon atom.

In the PMR spectrum the distance between the signals which characterise the protons of the amide group in acrylamide decreases at higher temperatures, and both signals (at 7.0 and 7.5 ppm) become broader. At a well defined temperature the two signals merge together. This temperature is determined by the energy of the rotation round the C–N bond, and depends on the degree of double-bond character between these two atoms. The merging temperature of the singlets is strongly dependent on the nature of the complexing salt, and increases on changing from lithium bromide (80 °C) to lithium chloride (92 °C) and to calcium chloride (106 °C) (Fig. 9). This sequence shows that the double-bond character of the C–N bond is more marked in acrylamide complexed with calcium chloride than in acrylamide complexed with lithium salts.

The presence of a single signal in the PMR spectrum of acrylamide denotes free rotation round the C–N bond. In this case the presence of a Lewis acid in the system does not affect the reactivity of the acrylamide radical, and therefore also the rate of polymerisation of acrylamide. Thus, in the polymerisation of acrylamide in the presence of lithium bromide in DMSO at 80 °C, i.e. under conditions which produce only one signal from the protons of the amide group in the PMR spectrum of acrylamide, the addition of salt (in the region of the maximum in curve *1* of Fig. 2) does not affect the rate of polymerisation as compared with the polymerisation of acrylamide without the salt.

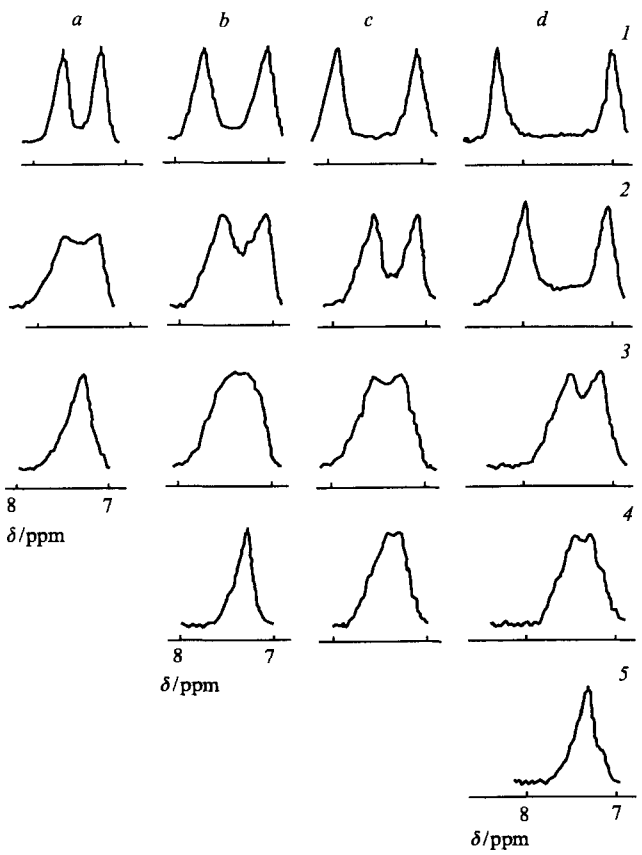


Figure 9. Effect of temperature on the shape of the PMR spectrum of acrylamide in DMSO in the presence of various salts. Salt: (*a*) none, (*b*) LiBr, (*c*) LiCl, (*d*) $CaCl_2$; *T*, °C: (*1*) 27, (*2*) 50, (*3*) 70, (*4*) 90, (*5*) 106.

The decrease in the overall rate of polymerisation and in the rate constants of the chain propagation and termination reactions beyond their maxima may be due to a change in the conformational characteristics of the macromolecules in the solution at high salt concentrations. The addition of a large quantity of salt probably degrades the thermodynamic quality of the solvent, and therefore it lowers the rate coefficients of the propagation and growth of the chains (as is found in the homogeneous radical polymerisation of acrylamide in the absence of salts[6,47,48]). Therefore the maximum in the plots of the overall rate of polymerisation and of the rate coefficient for the growth of the chains against the concentration of the salt is probably due to the competing effects of complex formation (leading to an enhanced rate of polymerisation and to an increased rate coefficient for the propagation) and of the conformation of the macromolecules (i.e. of the salting-out effect of the salts). The greater complex-forming capacity in lithium chloride and in calcium chloride (as compared with lithium bromide) produces a shift in the maximum rate towards higher salt concentrations (see Fig. 4).

We know that in the radical polymerisation of hydrocarbon monomers the reactivity of the radicals and that of the monomers change in opposite directions.[23] Therefore the decrease in the rate of polymerisation in the presence of high concentrations of salt could also be due to the participation in the polymerisation reaction of monomer molecules bound in a complex, whose activity may be lower than the activity of noncomplexed acrylamide molecules. This approach was proposed earlier to account for the maxima on the plots of the overall rate of the process against the salt concentration in the polymerisation of methyl methacrylate.[23] The participation of complexed monomer molecules in the reaction can make a substantial contribution, since at high salt concentrations (and in spite of a relatively low complex formation constant) the number of complexed monomers should be appreciable. Thus, at 30 °C and a molar ratio of 4.0 between the calcium chloride and the acrylamide the fraction of complexed monomer should be ~30%. However, if allowance is made only for the change in reactivity of the complexed monomer and for its relative concentration the maximum in the dependence of the overall rate of polymerisation on the salt concentration should be found at lower concentrations for calcium chloride than for lithium bromide, since the complex formation constant of acrylamide is lower for the lithium salt than for calcium chloride.

III. Polymerisation of *N*-substituted acrylamides in the presence of calcium chloride

These ideas on the effect of the complex formation by the amide group of the monomer with the complexing Lewis acids on the polymerisation kinetics were confirmed by studies of the polymerisation of derivatives of acrylamide (methacrylamide and *N-tert*-butylacrylamide) in various solvents in the presence of calcium chloride. The photopolymerisation of *N-tert*-butylacrylamide in *N*-methylpyrrolidone and that of methacrylamide in formamide have been studied.[49] The polymerisation of these monomers takes place under homogeneous conditions both in the absence of a salt and in the presence of calcium chloride. In every case the initial rate of the polymerisation becomes constant immediately after the application of UV light. The dependence of the overall rate of the polymerisation on the salt concentration is shown in Fig. 10. For comparison the figure also shows data for

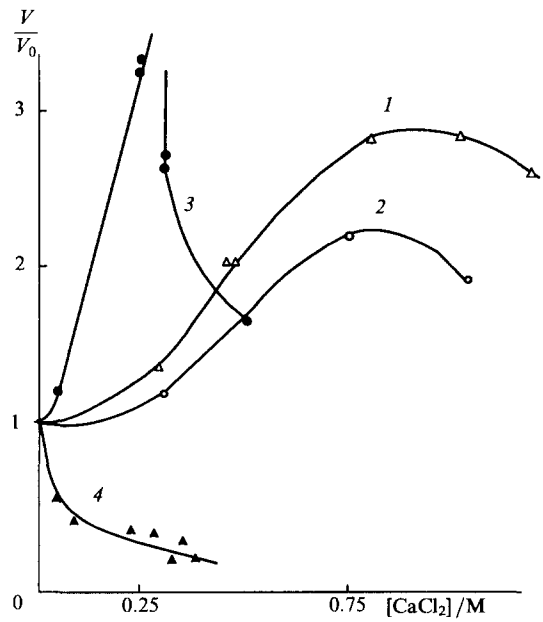


Figure 10. Dependence of the relative rate of polymerisation of acrylamide and its derivatives in various solvents on the concentration of calcium chloride at 20 °C. Concentration of monomer 0.5, concentration of DAA 3×10^{-3} M. System: (*1*) acrylamide in formamide, (*2*) methacrylamide in formamide, (*3*) acrylamide in *N*-methylpyrrolidone, (*4*) *N-tert*-butylacrylamide in *N*-methylpyrrolidone.

the polymerisation of acrylamide in formamide and in *N*-methylpyrrolidone. It follows from these results that in the polymerisation of acrylamide in both these solvents and in the polymerisation of methacrylamide in formamide additions of calcium chloride initially produce a large increase in the reaction rate, which goes through a maximum at a definite concentration of the salt before falling off again. The initial rate of polymerisation in these systems is proportional to the square root of the rate of initiation; the order of the reaction with respect to the monomer is close to unity. The $k_p/k_t^{1/2}$ ratios were calculated from the overall rate of polymerisation and from the rate of initiation, determined by measurements in the presence of an efficient radical polymerisation inhibitor (2,2,6,6-tetramethyl-4-oxopiperidine-*N*-oxyl). In the polymerisation of acrylamide this ratio increases from 0.61 in the absence of the salt to 2.0 when calcium chloride is added ($[CaCl_2]:[\text{acrylamide}] = 1.8$). In the case of methacrylamide the parameter $k_p/k_t^{1/2}$ increases from 0.06 to 0.14 when the same amount of salt is added. Comparing the overall rates and the $k_p/k_t^{1/2}$ values for these systems shows that the changes in the rate of polymerisation produced by the addition of calcium chloride are almost wholly due to changes in the rate of the chain propagation and termination reactions.

The effect of calcium chloride on the polymerisation of methacrylamide in formamide is less marked than in the case of acrylamide. This difference is due partly to a decrease in the complex formation constant between methacrylamide and its radical, and partly to a decrease in the same parameter for calcium chloride. PMR spectroscopy data also confirm that the complex formation of methacrylamide with lithium bromide is weaker than the corresponding reaction of acrylamide. The addition of lithium bromide (0.75 M) to a solution of acrylamide in DMSO (0.5 M) increases by 0.30 ppm the spacing of the signals which characterise the protons of the amide group. On the other hand with methacrylamide the increase in the spacing of the signals from the protons of the amide groups is 0.20 ppm under similar conditions. Other results[32] also confirm that methacrylamide is less reactive towards the formation of complexes with Lewis acids.

In contrast to acrylamide and methacrylamide no increase in the rate of the process is observed when calcium chloride is added to *N-tert*-butylacrylamide. Conversely, the addition of even small amounts of this salt (0.04 M at a monomer concentration of 0.5 M) markedly lowers the rate of homogeneous polymerisation of this monomer in *N*-methylpyrrolidone. An increase in the salt concentration produces a further decrease in the rate of polymerisation of *N-tert*-butylacrylamide (see Fig. 10). Most probably, the formation of a complex between the amide group and the salt is seriously hindered (if not completely suppressed) by the presence of a bulky *tert*-butyl substituent on the nitrogen atom of *N-tert*-butylacrylamide. As a result the addition of calcium chloride to a solution of *N-tert*-butylacrylamide does not increase the rate of polymerisation but only produces a 'salting-out' effect which degrades the thermodynamic quality of the solvent and is accompanied by a decrease in the overall rate of polymerisation. It should be noted that the results published from our laboratory[49] are consistent with the report[35] that in polar solvents the spontaneous polymerisation of *N-tert*-butylacrylamide in the presence of Lewis acids takes place slowly or not at all.

IV. Complex-radical polymerisation of acrylamide in the presence of zinc chloride

It is of interest to examine the causes of the difference in behaviour of salts such as lithium chloride and bromide, and calcium chloride (on the one hand) and zinc chloride (on the other) in the homogeneous polymerisation of acrylamide in DMSO. Zinc chloride is a Lewis acid of moderate strength, and it effectively accelerates the polymerisation of several other vinyl monomers such as acrylonitrile, methyl methacrylate, and other esters of acrylic and methacrylic acid. Since metal ions are involved[27,28] in complex formation between inorganic salts and amides it could be suggested that the different effects of salts on the polymerisation of acrylamide in DMSO are related to differences in their degree of dissociation in the relatively basic solvent DMSO.[36-40]

In order to test this hypothesis the dissociation of various salts in DMSO was measured, and the polymerisation of acrylamide in the presence of zinc chloride was also studied in another solvent.[50] The dissociation of the salts was determined by studying the dependence of the electric conductivity of their solutions in DMSO on the salt concentration, and the equivalent conductivity at infinite dilution (λ_∞) was obtained. To simplify the calculation all the salts were treated as 1:1 electrolytes. The λ_∞ values found in this way for lithium chloride and bromide and for calcium chloride lie in the range of 33–39 Ω^{-1} cm^2 (g-equiv)$^{-1}$, in good agreement with published data.[51] The degree of dissociation of the salts (α) was calculated as in the case of weak electrolytes: from the ratio of the specific to the equivalent conductivity. The results thus obtained showed that at concentrations of lithium salts and of calcium chloride between 0.2 and 0.3 M their dissociation is not less than 30%.

The conductivity of zinc chloride solutions in DMSO was almost constant at salt concentrations between 0.01 and 0.32 M, and did not exceed 1.0 Ω^{-1} cm^2 (g-equiv)$^{-1}$. Therefore the dissociation of this salt in the concentration range examined is ~1%–2%. It appears that the interaction of DMSO with zinc chloride produces an adduct which suppresses the dissociation of this salt in a solution of DMSO.

We know[52] that zinc chloride is partially dissociated in a mixed solution of water and tetrahydrofuran containing 77.5 mol% of water. The dissociation of the salt in that solution at concentrations of 0.1–0.5 M is 30%–12%, i.e. it is close to the dissociation of lithium salts and of calcium chloride in DMSO. The photopolymerisation of acrylamide in a mixture of THF and water was therefore studied in the presence of various concentrations of zinc chloride.[50] As can be seen from the results in Fig. 11 these polymerisation conditions produce a

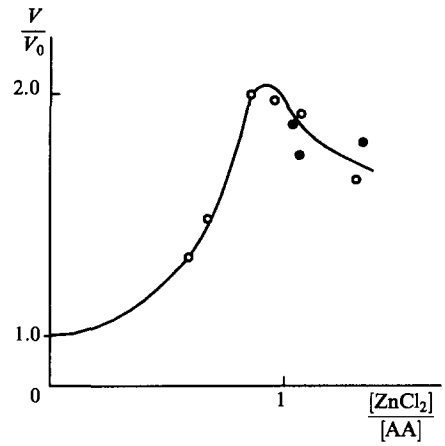


Figure 11. Dependence of the relative rate of polymerisation of acrylamide in a mixture of tetrahydrofuran and water containing 77.5 mol% of water on the concentration of zinc chloride at 20 °C. Concentration of acrylamide 0.5 M.

dependence of the overall rate of polymerisation on the concentration of the salt similar to the dependences observed in the polymerisation of acrylamide in DMSO in the presence of lithium salts or of calcium chloride (see Figs 2 and 4).

As in the case of the other salts, the changes in the kinetic parameters of the polymerisation of acrylamide in the presence of zinc chloride are due to complex formation between the reacting species and the salt. The formation of a complex between the monomer and zinc chloride in a mixture of water and tetrahydrofuran is confirmed by IR spectroscopy results: the 1695 cm^{-1} absorption band, characteristic of the C=O group in acrylamide, is shifted by 10 cm^{-1} towards lower frequencies by the addition of the salt.

The largest change in the overall rate of polymerisation of acrylamide in the presence of zinc chloride is somewhat smaller than for the polymerisation in DMSO in the presence of the other salts which have been studied. The lower effect of the salt during polymerisation in a mixture of water and tetrahydrofuran may be due (at least partially) to the influence of the water on the complex formation between the salt and the acrylamide, and/or its growing radical. Thus the addition of water should markedly lower the formation constant of the complex between the amide group and the salt.

Further evidence of the participation of the salt in an ionised state in the complex formation process was obtained during the study of the acrylamide–tetrahydrofuran–zinc chloride system. Additions of zinc chloride to a solution in tetrahydrofuran do not affect the IR spectrum of acrylamide, showing that in this solvent no complexes are formed between zinc chloride and the monomer.

The participation of lithium chloride (in an ionised form) in the complex formation with acrylonitrile radicals, leading to an increase in their reactivity and therefore also to an increase in the overall rate of polymerisation of acrylonitrile in the presence of lithium chloride, was first suggested by Bamford.[19] We may therefore assume that the influence of the nature of the solvent on the complex-radical polymerisation of vinyl monomers in the presence of inorganic Lewis acids is determined by the effect of the solvent on the dissociation of the Lewis acid, and also on the constant which defines the formation of a complex between the metal ions and the reacting species (the monomer and the polymeric radicals).

V. Conclusion

Available data show that (as in the polymerisation of vinyl monomers) inorganic Lewis acids have a substantial influence on the polymerisation of acrylamide and its derivatives. In every case the effect of inorganic salts such as metal halides is the result of their formation of a complex in the ionic form with the monomer, and also with the growing polymeric radicals, and of the change in the reactivity of the reacting species produced by this complex formation. The formation of complexes between the salts (Lewis acids) and the functional groups of the monomers and/or the growing polymeric radicals is strongly dependent on the polarity of the solvent in which the reaction is carried out. The acid–base characteristics of the solvent also have a definite effect. For this reason the Lewis acids show their strongest kinetic effect in polymerisations carried out in solvents having a relatively low polarity and no basic properties. In the radical polymerisation of acrylamide in aqueous solutions the addition of Lewis acids does not affect the kinetic parameters of the process or the molecular characteristics of the resulting polyacrylamide.

The results discussed in this review show that (as in the radical polymerisation of vinyl monomers such as acrylonitrile, methyl methacrylate, and the vinylpyridines) the addition of various Lewis acids to the reaction system can be used to control the radical polymerisation of acrylamide and its derivatives. In this way a change in the composition of the reaction medium can be used to carry out the polymerisation of acrylamide at different rates and to obtain polymers having different molecular masses and the required operational properties.

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1,6-Electrocyclic reactions

V A Bakulev

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Abstract. New data on the thermal and photochemical reactions between hexa-1,3,5-trienes and cyclohexadienes as well as their heteroanalogues are surveyed. The bibliography includes 283 references.

I. Introduction

Electrocyclic reactions include the rearrangement of linear alkenes with a conjugated system of π-bonds accompanied by the formation of a new σ-bond and ring closure as well as the reverse rearrangements involving the dissociation of a σ-bond in a cyclic unsaturated compound and the formation of compounds with a conjugated system of π-bonds. The study of such reactions began as early as the beginning of this century.[1–3] Among them, an important place is occupied by 1,6-electrocyclic reactions (1,6-ER), which are six-electron electrocyclic processes. These include the cyclisation reactions of hexatriene, its derivatives, and its heteroanalogues as well as the ring opening in cyclohexadiene. The cyclisation of hexatriene to cyclohexadiene was first achieved in 1964.

After the theory of pericyclic processes had been developed,[1–3] these studies began to develop vigorously. The details of the mechanism of the cyclisation of hexatriene were investigated and numerous theoretical studies of 1,6-electrocyclic reactions involving quantum-chemical calculations were published.

More than 800 communications on 1,6-ER have now been published and half of them appeared during the last decade. They include a series of reviews devoted to individual questions of 1,6-ER or problems associated with these reactions. Marvell's book,[4] in which the literature on thermal ER published up to 1979 is surveyed, appeared in 1980. Unfortunately it does not include photochemical electrocyclic reactions, which are of enormous interest for the understanding of the characteristic features of electrocyclic processes.

Among the latest advances in this field, mention should be made of the development of a new approach to the synthesis of cyclic systems: electrocyclic and other pericyclic reactions, occurring successively, making it possible to obtain a whole series of highly effective antibiotics; a series of investigations demonstrating that the 1,6-ER of trienes is one of the stages in the mechanism of the action of a series of highly active antitumour preparations; the development of new photochromic systems on the basis of the ER of hexatriene hetero-analogues.

The present review deals with the continuation of the present author's investigations[5,6] and contains data on thermal and photochemical 1,6-ER.

V A Bakulev Laboratory for Problems of Physiologically Active Compounds, Department of Technology of Organic Synthesis, Ural State Technical University, ul. Mira 19, 620002 Ekaterinburg, Russian Federation. Fax (7-343) 244 04 58. Tel. (7-343) 244 88 18

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II. Theoretical investigations

There have been relatively few studies on the cyclisation of hexa-1,3,5-trienes and their hetero-analogues. Lewis and Steiner[7] calculated the activation parameters for this reaction by the method of Evans and Polanyi.[8] Marvell[9] used a modified Hendrickson method for the determination of the influence of substituents on the rate of reaction.

Attempts have been made to predict and explain the reactivity of hexa-1,3,5-trienes by Hückel's method[10] and by various semiempirical methods: PPP,[11] MINDO/2,[12] MINDO/3,[13–16] MNDO,[17] CNDO/2S,[18] and AM1,[19] as well as ab initio methods with the 3-21G, 6-31G, and 6-31G + MP2 basis sets.[20]

The activation energies for the thermal cyclisation of hexa-1,3,5-triene, determined by the MINDO/2 and MINDO/3 methods, are 24.6 kcal mol^{-1},[12] and 33.2 kcal mol^{-1},[16] respectively, which are close to the experimental value (29.4 kcal mol^{-1}).[1–3]

It has been shown that true transition states (TS) correspond to both the 'allowed' and 'forbidden' paths in the thermal reaction.[16] However, the transition state corresponding to the conrotatory path is asymmetric.[16] The authors[16] showed that, when the hydrogen atoms at the C(2) and C(5) atoms of the hexatriene system are located on one side of the molecular plane, a disrotatory transition state is indicated, while their location on each side of the molecular plane is evidence for a conrotatory transition state.[16]

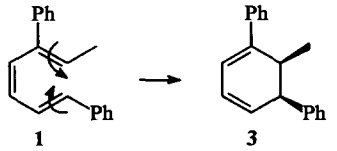
Gatti et al.[21] used the topological theory of molecular structures to investigate the reactions of cyclic systems. Baldwin et al.[22] calculated the kinetic isotope effect in the cyclisation of hexa-1,3,5-triene with the aid of semiempirical calculations in terms of the 6-31G basis set. The values obtained proved to be close to the experimental data.[22]

Bock et al.[23] presented data on the interconversion of benzene oxide and oxepine—the oxa-analogues of cyclohexadiene and hexa-1,3,5-triene. The calculations were performed by the AM1 and ab initio methods in terms of the 6-21G, 6-31G, and 6-31G + MP3 basis sets.[23] The authors showed that the best agreement between the calculated and experimental data is attained when third-order perturbation theory is used to perform the calculations.[23]

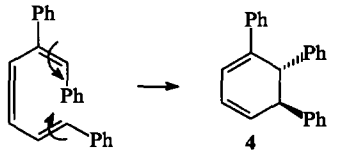
Calculations have been performed for the photochemical isomerisation of cyclohexadiene to hexatriene by means of the MRDCI method.[24]

III. Stereochemical characteristics of 1,6-electrocyclic reactions

According to the rules for the conservation of orbital symmetry, the cyclisation of hexa-1,3,5-trienes should be disrotatory in the ground state and conrotatory in the excited state.[1-3] This conclusion has been confirmed by numerous theoretical and experimental studies.[1-3] According to MINDO/3 calculations, the disrotatory path to the cyclisation of hexa-1,3,5-triene is preferred to the conrotatory path to the extent of 14.5 kcal mol^{-1}.[13] Padwa et al.[25] showed that, on heating in toluene, the trienes **1** and **2** undergo disrotatory cyclisation to the cyclohexadienes **3** and **4**. The products of the conrotatory cyclisation were not detected under these conditions.

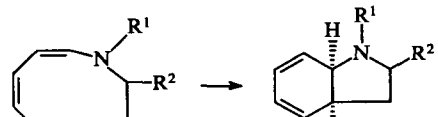


1 **3**



2 **4**

In a study of the thermolysis of *cis*-5,6-dimethylcyclohexadiene and 1-phenylhepta-1,3,5-triene, it was shown that the yield of the products of the conrotatory cyclisation is less than 0.5%.[4] The cyclic trienes **5** give rise to the bicyclic compounds **6** with a *cis*-disposition of the substituents at the bridging carbon atoms, which is also evidence for a disrotatory process.[26,27]



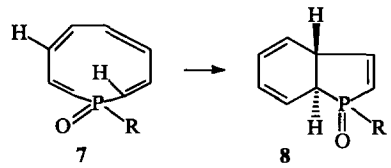
5a,b **6a,b**

R^1 = CO_2Me, R^2 = CH_2Ph (**a**);

R^1 = Ph, R^2 = CH_2Ph (**b**).

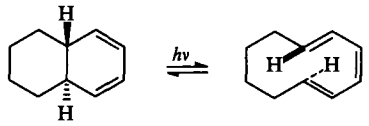
However, it is essential to note that experiments indicating disrotatory cyclisation of compound **5** are not very convincing, since the bicyclic compounds **6** are formed from initial compounds having a specific geometry.

The experiment of Quin et al.[28] is especially interesting in this connection. They showed that the tetraene **7**, the geometry of which should promote conrotatory cyclisation, actually cyclises to the bicyclic product **8** with a *trans*-disposition of the hydrogen atoms at the bridging carbon atoms.[28]

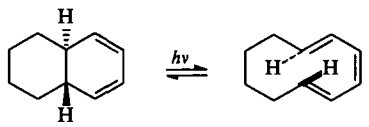


7 **8**

The most striking examples confirming the conrotatory mechanism of the photocyclisation of the cycloala-1,3,5-trienes[21] is provided by experiments with the optically active dienes **9**. When the dienes **9** are irradiated, the ring opens with retention of the chirality and the photocyclisation of the resulting trienes **10** leads to the exclusive formation of the initial enantiomers.[29]



(−)-**9** (+)-**10**



(+)-**9** (−)-**10**

IV. Thermodynamic and kinetic investigations

The energy of activation for the formation of cyclohexa-1,3-diene from *cis*-hexa-1,3,5-triene is 29 kcal mol^{-1}.[4] Thermochemical determination of the heats of formation of cyclohexa-1,3-diene and *cis*-hexa-1,3,5-triene (25.38 and 40.58 kcal mol^{-1}) has made it possible to calculate the heat of formation of the transition state in this reaction (69.6 kcal mol^{-1}) and the energy of activation for the opening of the cyclohexa-1,3-diene ring (44.2 kcal mol^{-1}).[4]

The difference between the allowed disrotatory and forbidden conrotatory paths is 5 kcal mol^{-1} according to the authors' estimate[4] and 14.5 kcal mol^{-1} according to calculations by the MINDO/3 method.[13]

Kinetic studies have been carried out on the cyclisation of acyclic[4] and cyclic[4,29-39] hexatrienes as well as their heteroanalogues.[37-39]

Kinetic data have been published recently for photochemical 1,6-ER.[40,41] The most complete set of activation parameters for 1,6-ER has been presented in a monograph.[4] Treatment of the experimental data with the aid of CAMEO† programs permitted the following generalisations:[42]

1. When the triene system is incorporated in a ring, the activation energy diminishes by 2 kcal mol^{-1}.

2. *cis*-Substituents in the terminal positions of the conjugated systems increase the corresponding activation energy, apparently as a result of the deviation from planarity by 2 kcal mol^{-1}.

3. The activation energy for the cyclisation of trienes in which the terminal atom is part of a cumulene system is reduced by 10 kcal mol^{-1}.

4. The activation energy for the ER involving cyclic π-systems should be apprreciably lower than in the case of acyclic analogues. If the triene is part of a ring in which the number of atoms is more than six, then E_a diminishes by 10 kcal mol^{-1}.

5. If the cyclisation of trienes results in the formation of a three- or four-membered ring, then E_a increases by 10 kcal mol^{-1}.

6. If the cyclisation disturbs or generates aromaticity, E_a increases or diminishes by 8 kcal mol^{-1}.

† CAMEO = Computer-assisted mechanistic evaluation of organic reactions.

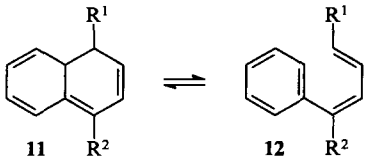
Unfortunately, the authors [42] did not include all the literature data then available in the information which they interpreted. Because of this, the well established fact that the cyclisation of 1,3,5-trienes is accelerated by the introduction of substituents in the 2- or 5-position remained outside the limits of their assessment. [4] Marvell [4] explained this effect by the decrease in the steric interactions of the substituent with the triene system in the transition state having the *cis*-(*Z*)-*cis*-conformation, compared with the initial compound which exists predominantly in the *cis*-(*Z*)-*trans*-form. [4]

V. Thermal processes

1. Reactions of acyclic compounds

It has been already noted that cyclohexadienes are more stable than hexatrienes, but if the opening of the cyclohexadiene ring results in the formation of an aromatic ring then this may alter and facilitate the process.

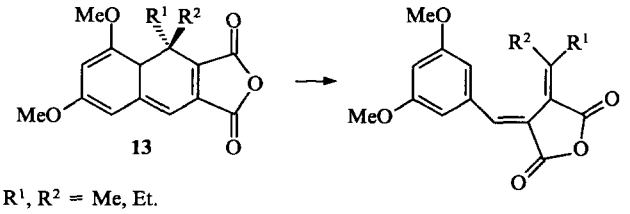
With the aid of deuterium labels, Lamberts and coworkers [43–45] showed that the flash thermolysis of the dihydronaphthalenes **11** results in the opening of the cyclohexa-1,3-diene ring and the formation of the butadiene derivatives **12**. The authors [45] established that only compounds where the recyclisation leads to the formation of an aromatic ring enter into the reaction.



11 **12**

R^1, R^2 = H, Ph, 4-MeC_6H_4.

The formation of an aromatic ring may be the cause of the ready opening of the cyclohexadiene ring in the tricyclic compound **13**. The reaction takes place even at 28 °C. [46]

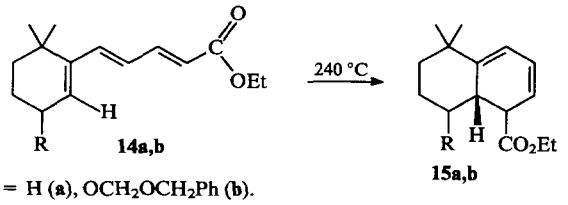


13

R^1, R^2 = Me, Et.

Trienes cyclise to hexadienes as a rule at elevated temperatures. [4] This is associated with the high energy barrier in the isomeric interconversions between the *cis*- and *trans*-isomeric forms of hexatriene. Thus compounds **14** cyclise only at temperatures above 240 °C. [47]

It has been shown [47] that the cyclisation of compound **14b** results in the formation of only one diastereoisomer **15b**, which indicates an effective stereocontrol by the OCH_2OCH_2Ph group. This implies the possibility of carrying out asymmetric syntheses of compounds **15**, which are the starting materials for the synthesis of forskolin — an oxygen-containing diterpene exhibiting a broad spectrum of physiological activity. [47]



240 °C

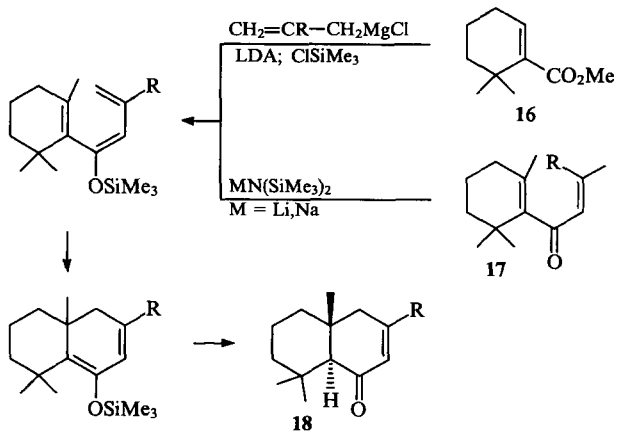
14a,b **15a,b**

R = H (**a**), OCH_2OCH_2Ph (**b**).

The introduction of the electron-accepting carbamoyl groups in the 2- and 5-positions in the hexatriene system greatly facilitates the cyclisation and the process takes place smoothly already at 200 °C. [4]

The photochemical reaction involving the opening of the cyclohexadiene ring is frequently employed to obtain trienes with a *cis*-(*Z*)-*cis*-configuration. [4]

An interesting method for the generation of trienes by the Grignard reaction from methyl β-cyclogeranate **16** or by the deprotonation of the enone **17** has been described. [48]



16 **17** **18**

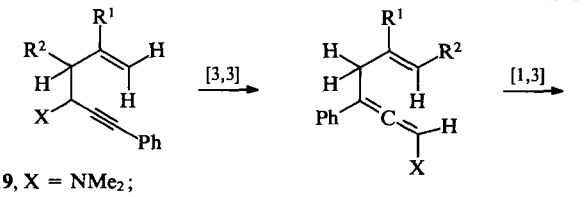
R = H, Me;

LDA = $(Pr^i)_2NLi$.

This process and the subsequent electrocyclisation constitute a new method of synthesis of the cyclic enone **18**.

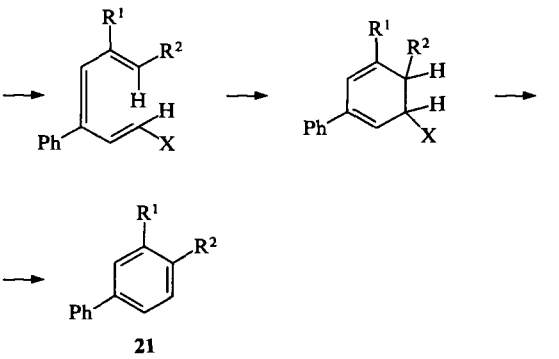
It has been shown [49] that the ynamine **19** and the thioether **20** can serve as sources of hexatrienes. Moderate thermolysis of these compounds leads to the formation of the benzene derivative **21** (Scheme 1).

Scheme 1



19, X = NMe_2;

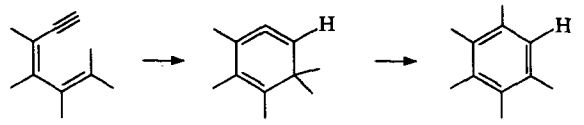
20, X = SMe.



21

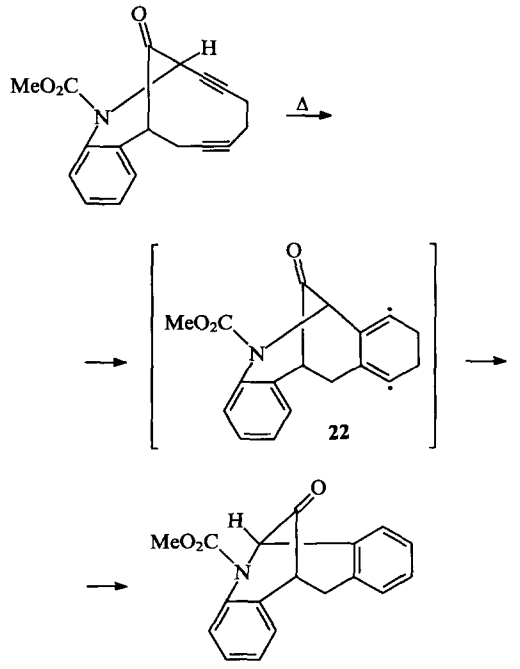
The substitution of one or both terminal double bonds in the hexa-1,3,5-triene by triple bonds does not prevent the cyclisation. [4]

The thermal cyclisation is carried out at elevated temperatures (~300 °C), but in the presence of strong bases it is possible to carry out this reaction at 80 °C. The rate-limiting stage is apparently the migration of hydrogen, but it has been shown that other groups can also migrate. [50]

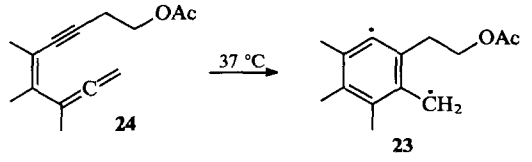


Systems of conjugated multiple bonds enter into the composition of the molecules of daunomycin, neocarzinostatin, and esperamicin–antibiotics with a high antitumour activity.[51–55]

It has been suggested[53,54] that the mechanism of the biological action of these compounds is associated with the formation of the tricyclic biradical **22**, which can abstract hydrogen from DNA and thus damage its helix. It has been demonstrated by kinetic investigations that the rate of cyclisation of such systems increases with decrease in the distance between the terminal atoms of the conjugated π-system.[51,52]

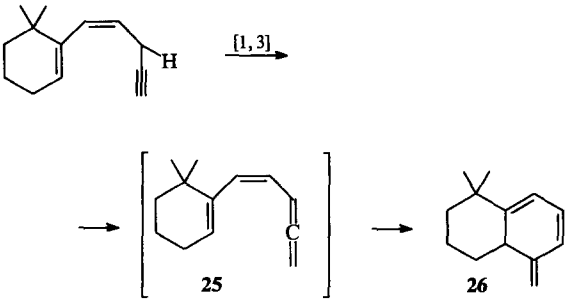


Ethynyldienes in which the terminal π-bond is part of an allene group are also biologically important. They are part of the molecules of antibiotics of the enediyne series.[56,57] It has been suggested that Bergman type electrocyclisation of these compounds, which leads to the biradical **23**, plays an important role in the cleavage of the DNA helix by antibiotics of the enediyne series.[56]



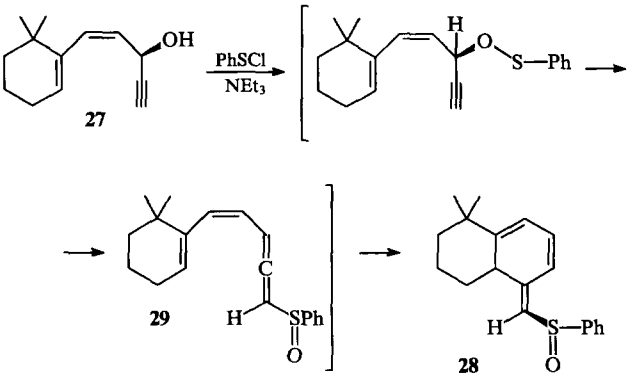
The activation energies E_a have been determined[56] for the cyclisation of a series of type **24** compounds and it has been shown that steric factors affect its rate to a greater extent than electronic factors.

The trienes **25**, in which one π-bond enters into the composition of an allene group, are unstable and are readily transformed into compounds **26**.[58]

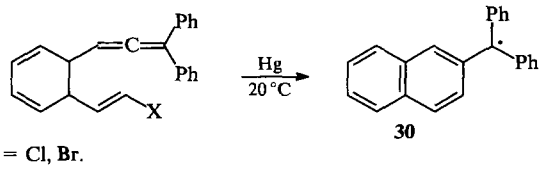


It has been demonstrated[58] that the electrocyclic reaction takes place with a lower value of E_a than the 1,3-sigmatropic shift of hydrogen.

The interaction of the optically active *cis*-propargyl alcohol **27** with benzenesulfenyl chloride leads exclusively to the diastereoisomer **28**.[58] The authors[58] claim that this reaction is a stereospecific tandem centre–axis–centre transfer and that the cyclisation of compound **29** takes place via a disrotatory mechanism.



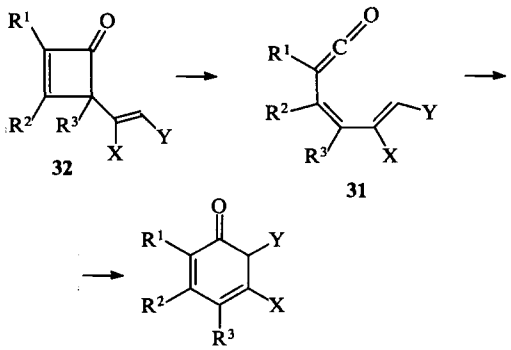
It is of interest to note that the cyclisation of butadienylallenes in the presence of elemental mercury leads to the stable triarylmethyl radical **30**.



X = Cl, Br.

When one double bond of the 1,3,5-triene system is part of a ketene group, the rate of electrocyclisation increases greatly.[4]

The butadienylketenes **31** can be generated in the vacuum flash thermolysis of 5-(3-indolinylmethylene)-2,2-dimethyl-1,3-dioxane-4,6-dione[60] and on opening the ring in the cyclobutenes **32** having a vinyl group in the 3-position[60–67] including the case where the group forms part of the composition of the benzene system[65,66] or a heterocyclic system.[65,67]

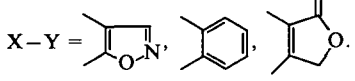


32 31

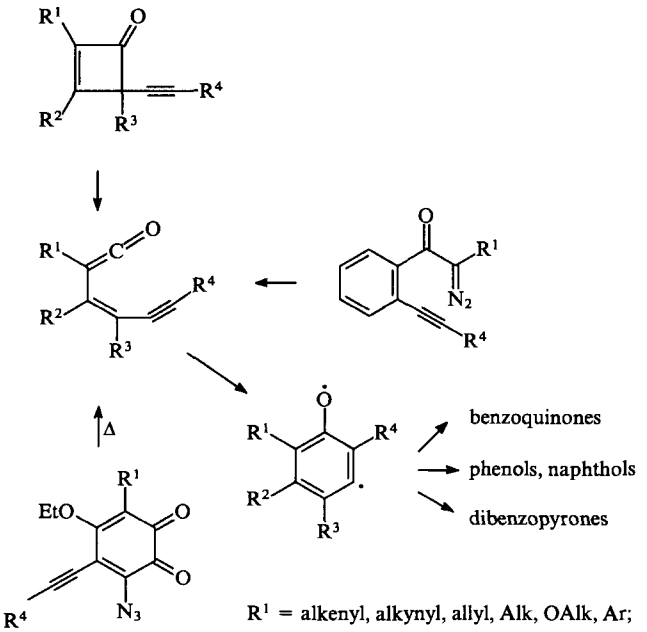
R^1 = Alk, Ar, alkynyl; X = H, Me_3Si;

R^2 = OAlk; Y = OMe, H;

R^3 = H, Cl, OAlk, OH, SPh;

X–Y = 

The replacement of the vinyl group by the ethynyl group does not prevent cyclisation.[61,65,68–73]



R^1 = Cl, R^4 = Ar.

R^1 = alkenyl, alkynyl, allyl, Alk, OAlk, Ar;

R^2 = Alk, OAlk, Ar;

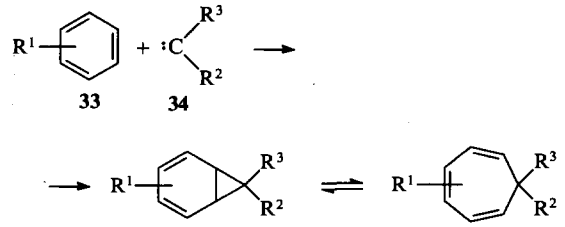
R^3 = OH, OAlk, CN;

R^4 = Alk, Ar.

The reactions of cyclobutenes described constitute general and flexible methods of synthesis of benzoquinones, phenols, naphthols, and related compounds, which are constituents of many biologically important substances. Thus the methods have been used in the synthesis of a nonsteroid antiinflammatory agent—(±)-naproxen.[74]

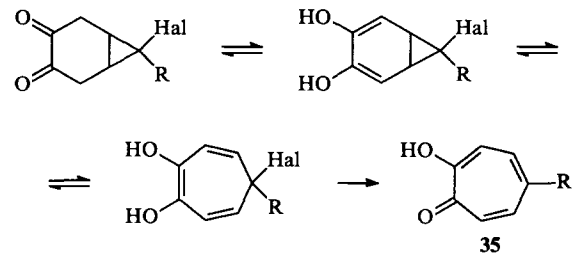
2. Reactions of cyclic compounds

In the general case, ER in cyclic systems are facilitated compared with acyclic systems. As a consequence of the high strain energy of the three-membered ring, the interconversions between cycloheptatrienes (CHT) and norcaradienes (NC) occupy a special place in this series. The opening of the norcaradiene ring is one of the stages in the syntheses of cycloheptatrienes from the benzene derivatives **33** and from the carbenes **34**[4,75,76] and of the hydroxytrienes **35**[77] and also in the rearrangements of the cycloheptatrienes **36** and **37**.[78,79]



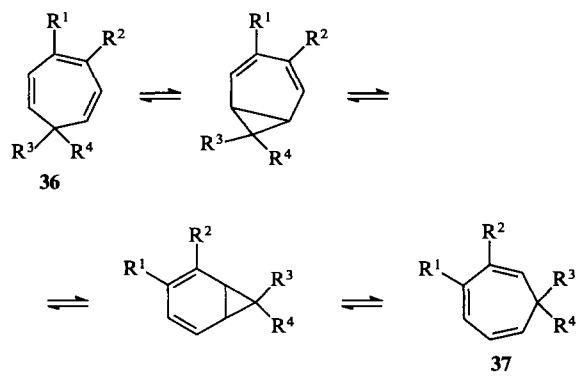
33 34

R^1, R^2, R^3 = H, Alk, Ar, CO_2Alk, CN.



35

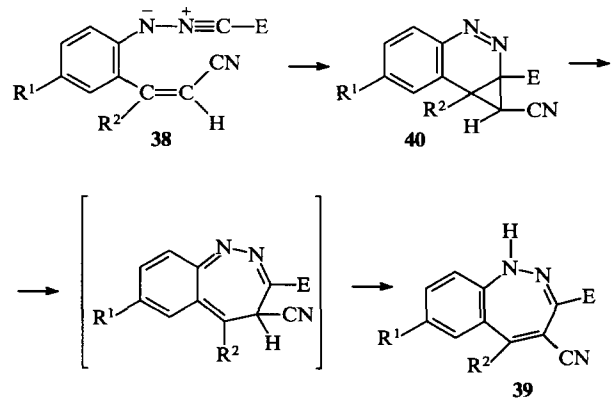
Hal = Cl, Br; R = Hal, H, Me_3Si.



36 37

R^1 = CO_2Me; R^2 = H, D; R^3 = Me, R^4 = CH_2OMe.

The rearrangement of the nitrile imines **38** to the benzodiazepines **39** also involves the 1,6-ER involving the opening of the norcaradiene ring.[80] The 2,3-diazanorcaradiene **40** formed in this reaction is stable; it is converted fully into the benzodiazepine **39** only on refluxing in benzene.[80]



38 40 39

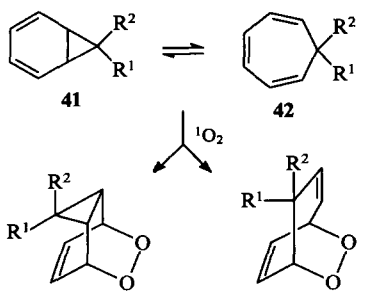
R^1 = H, R^2 = H;

R^1 = Cl, R^2 = Ph;

E = electron-accepting group.

The equilibrium between the norcaradienes and the cycloheptatrienes is as a rule appreciably displaced towards the latter and the concentration of the norcaradienes‡ in the mixture is low. Therefore, a very sensitive method is essential for the determination of the influence of the substituents on the equilibrium in the system.

The limitations in the use of NMR spectroscopy for these purposes have been noted by Adam et al.[82] At the same time, the method which they proposed for the determination of the position of equilibrium between the norcaradiene **41** and the cycloheptatriene **42** by using cycloaddition of singlet oxygen is inapplicable to the determination of equilibrium constants. It is in essence a variant of the method of competing reactions and makes it possible to determine the influence of substituents on the relative reactivities in the cycloaddition of the norcaradiene and the cycloheptatriene.[83,84]

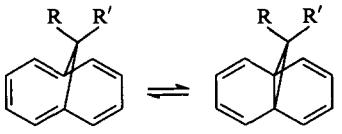


41 **42**

R^1, R^2 = H, Me, CO_2Me, Ph, 4-$MeO_2CC_6H_4$.

Kinetic studies have been made and quantum-chemical calculations of the activation parameters for this reaction have been performed.[85,86] According to kinetic data, the activation energy is only 7.7 kcal mol^{-1}.[83] Ab initio calculations in terms of the 4-31G basis set yield 7.3 and 2.3 kcal mol^{-1} for the forward and reverse reactions respectively in the cyclisation of the annulenes **43** to the norcaradienes **44**.[86]

The conversions of compounds **43** into compounds **44** are of great theoretical interest in connection with the aromatic properties manifested by the annulenes **43**, which contain 10 π-electrons.

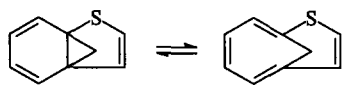


43 **44**

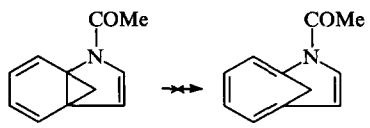
A topological approach has been applied to the study of the properties of 11-R, 11-R'-1,6-methano(10)annulenes.[21]

The existence of a critical bonding point in the 11,11-dicyano-derivative of compound **44** and in the β-phase of the crystals of the 11-cyano-11-methyl derivative of this annulene indicates a tricyclic structure for these substances. The authors[21] showed that the crystals are made up of two molecules; one has the norcaradiene structure **44** but with a low bond order, while the other has the annulene structure **43**. It is of interest to note that the bonds of the cyclopropane ring in compound **44** and the bridging bonds in compound **43** have an appreciable π-character and are conjugated with the π-system.[95]

The data concerning the influence of substituents on the equilibrium position between cycloheptatrienes and norcaradienes have been compiled by Marvell[4] and in subsequent publications.[87-92] The introduction of electron-accepting substituents in the 7-position, the inclusion of the π-bonds of the norcaradiene structure in the aromatic rings, and the introduction of bulky substituents in the 3- and 5-positions are all factors stabilising the structure of the norcaradiene. It has been shown that the insertion of yet another bridge between the 1- and 6-positions increases the stability of the norcaradiene form.[4,93-96] This feature is illustrated particularly clearly by the heteroatomic systems **45** and **46** incorporating sulfur and nitrogen atoms.[95,96] Thus the content of the tricyclic compound **45** in the equilibrium mixture is 84%, while that of compound **46** is 100%.



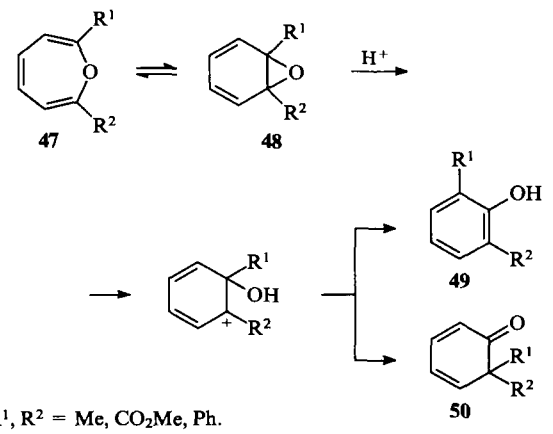
45



46

The interconversions of the heteroanalogues of the norcaradienes and cycloheptatrienes containing nitrogen,[97] oxygen,[98-100] sulfur,[101] phosphorus,[102] and boron[103] atoms instead of the methylene group have been described. The reactions of the oxygen-containing analogues have been most thoroughly investigated. It has been shown that arene oxides are the products of the metabolism of monocyclic and polycyclic aromatic compounds in plants, animals, and microorganisms[104,105] and that the reverse ring opening reaction to give oxepines is associated with their carcinogenic activity.[104,105]

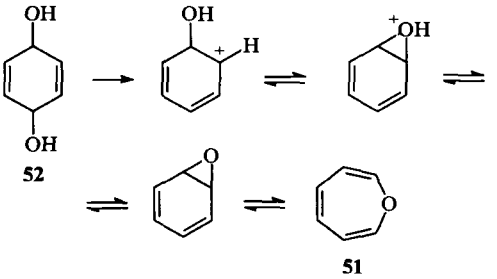
The conversion of the oxepines **47** into arene epoxides **48** is the first stage of the rearrangement of the oxepines **47** into the phenols **49** and the cyclohexadienones **50**[106,107] and also in the reactions of the aza-analogues of these compounds.[107]



47 **48** **49** **50**

R^1, R^2 = Me, CO_2Me, Ph.

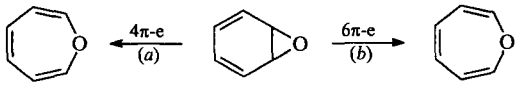
Conversely the retro-ER of the arene epoxides into oxepines is the last stage in the synthesis of type **51** compounds from compounds **52**.[108]



52 **51**

‡ The presence of the norcaradienes has been confirmed by NMR spectroscopy at low temperatures[81] and by X-ray diffraction of the xylene derivatives of this series.[93]

Benzene epoxide was first synthesised by Vogel et al.[109] about thirty years ago. It was shown that benzene epoxide is a little more stable than oxepine. The arene epoxide–oxepine equilibrium position is influenced by various factors: temperature, conjugation with the aromatic ring, the nature of the substituents, protonation, or complex formation. In the main, an analogy can be traced with the reactions of norcaradienes and cycloheptatrienes. The influence of various factors on the equilibrium between arene epoxides and oxepines has been examined in detail in a number of studies.[97,110–112] Two possible mechanisms of the conversion of aromatic arene epoxides into oxepines have been demonstrated[106] — the conrotatory opening of the oxirane ring (*a*) and the disrotatory opening of the cyclohexadiene ring (*b*).

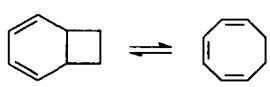


The choice in favour of the disrotatory 1,6-ER was made on the basis of the positive entropy of activation for the process determined from kinetic measurements and the lower activation energy than for the opening of the ring in oxiranes§ to give carbonyl ylides.[110–112] Kinetic studies on the 1,6-ER of arene epoxides and oxepines have been performed only for several compounds. This is associated mainly with the difficulty of determining the rates of fast reactions. The method for the determination of the rates of isomerisation of arene epoxides and oxepines involving the study of the degenerate racemisation of chiral arene epoxides at low temperatures, proposed by Jennings et al.,[112] is therefore a major achievement.

The relative stabilisation energies of arene epoxides and oxepines have been calculated with the aid of perturbation theory. The calculations explained the differences between the rates of racemisation of optically active polynuclear arene epoxides.[113]

Calculations for arene epoxides and oxepines by the AM-1 method and ab initio methods with various basis sets have been published quite recently. It has been shown that only the ab initio calculations in terms of the 6-31G basis set and involving the use of the third-order perturbation theory yield satisfactory heats of formation of benzene epoxide and oxepine.[23]

As a result of the lower strain energy of the cyclobutane ring compared with the cyclopropane ring, bicyclooctadienes are much more stable than bicycloheptadienes. The equilibrium between the bicyclooctadienes **52** and the octatrienes **53** and the rate of ER are influenced by various factors: electronic[4–35] and steric properties of the substituents,[114] the strain energy of dienes and trienes with cisoid double bonds, conjugation of double bonds with aromatic π-systems,[32] etc.



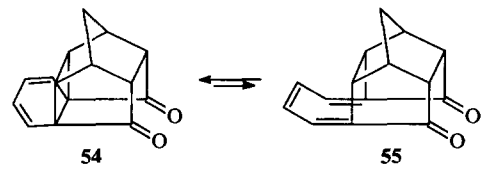
52 **53**

Apart from their theoretical interest, the 1,6-ER of cyclic trienes have also a considerable practical importance. Thus they have been used in the synthesis of vitamin A[115] and of endiandric acids.[116,117]

An increase in the size of the ring condensed with the cyclohexadiene leads to a greater stability of the bicyclic form compared with the monocyclic form,[4] which promotes the cyclisation of isomeric trienes. Thus compound **5a** cyclises at 75 °C,[26] while compound **5b** cyclises at room temperature.[27,28] The transoid trienes **10** cyclise even more readily (at −55 °C).

§ The isomerisation of the optically active *trans*-2-phenyl-3-(*p*-tolyl)-oxirane (conrotatory opening of the oxirane ring) takes place at high temperatures (180–247 °C) and has E_a = 35.9–41.1 kcal mol^{-1} and ΔS = −2 to +2 kcal mol^{-1} K^{-1}.

In conclusion of this section, we may note that in a later study[118] the authors were able to observe the 1,6-ER in the propellane systems **54** and **55**.



54 **55**

VI. Photochemical processes

It has been shown by means of a large number of examples that the interconversions between cyclohexa-1,3-dienes and hexa-1,3,5-trienes are effected photochemically as conrotatory processes.[4] However, it is claimed[16] that the cyclisation process does not involve the retention of the C_2 symmetry axis. The transition state on the potential energy surface (PES) in the ground state and the state corresponding to the minimum on the PES for the excited state are asymmetric.

It has been shown that these processes proceed via a ππ* excited state and are photochemical singlet reactions.[1–3,14,40,41] Kinetic[40,41] and quantum-chemical studies[14,41] permitted the conclusion that the photochemical opening of the ring in cyclohexadienes does not take place adiabatically and constitutes a more complex process. The first stage involves photoexcitation and transition from the ground state ($1A_1$) to the excited state ($1B_2$), in the second stage there is a transition (with a small energy barrier) to the next excited state ($2A_1$), then there is a nonadiabatic transition onto the potential surface for the conrotatory reaction, and the final stage involves the formation of the triene in the ground state (Fig. 1).

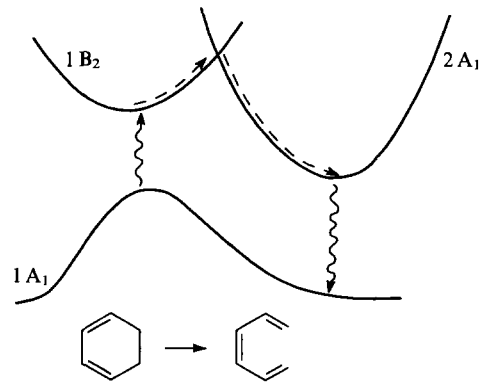
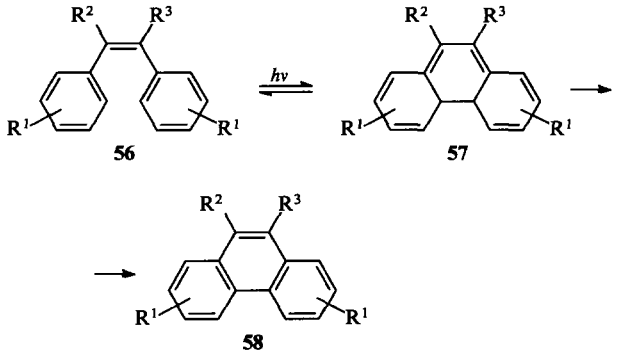


Figure 1. The mechanism of the photochemical opening of the ring in cyclohexadienes. The potential surfaces for the $1A_1$, $2A_1$, and $1B_2$ states are shown.

The photochemical reactions of simple cyclohexadienes and hexatrienes described by Havinga and coworkers[119–121] and also by their successors[122–124] have been the subject of a series of reviews[4,124–126] and we shall therefore not consider them in detail.

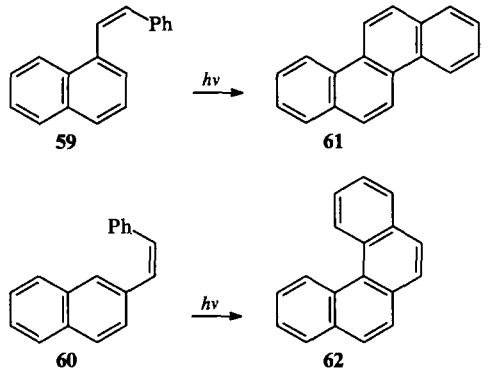
In describing thermal 1,6-ER, it was noted that the processes proceeding with breakdown of the aromaticity of the rings incorporating the double bonds of the triene or hexadiene system are hindered. In contrast to the thermal reactions, the opening of the cyclohexadiene rings and the cyclisation of hexatrienes are readily effected photochemically also in the case when one of the double bonds enters into the composition of an aromatic cyclic system.[17]

The photocyclisation of the substituted *cis*-stilbenes **56** to 4*a*, 4*b*-dihydrophenanthrenes **57**, which are unstable and are converted into the polynuclear arenes **58** in the presence of atmospheric oxygen or iodine, has been thoroughly investigated and is widely used in organic synthesis.[4]



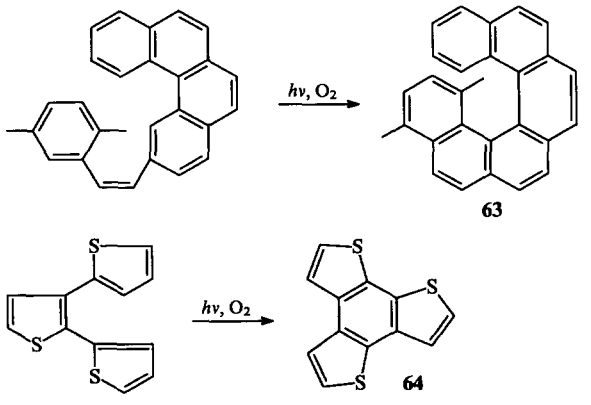
R^1, R^2, R^3 = H, Alk, Ar, OAlk, and others.

This reaction has been extended also to other arylhexatrienes. Thus the cyclisation of α- or β-(phenylvinyl)naphthalenes **59** and **60** leads to the formation of chrysene **61** and benzo[*c*]phenanthrene **62**.

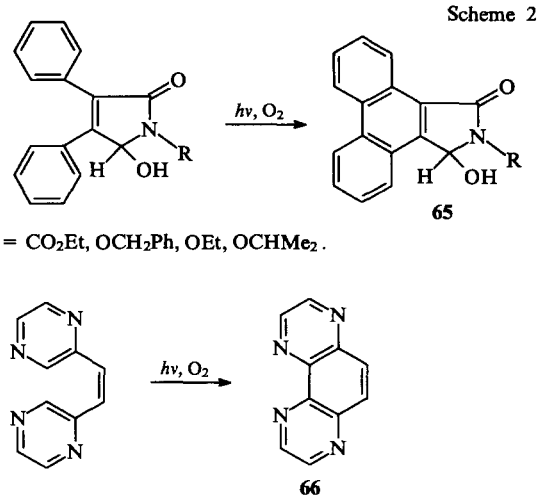


Photocyclisation is used to obtain the helicenes **63** (including the optically active compound),[127] the heterocyclic compound benzotrithiophene **64**,[128] the phenanthropyrrolines **65**, and 1,4,5,8-tetraazaphenanthrene **66** (Scheme 2).[129,130]

Scheme 2

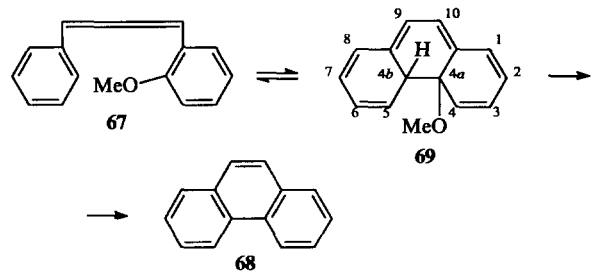


Scheme 2 (cont.)



R = CO_2Et, OCH_2Ph, OEt, $OCHMe_2$.

Mallory et al.[131] note that *meta*-substituted stilbenes give rise to mixtures of isomers which are difficult to separate into their components. They showed that the introduction of the methoxy-group leads to the regioselective cyclisation of compound **67** with participation of the substituted atom; the subsequent elimination of methanol, which is facilitated by the addition of a solution of sulfuric acid in *tert*-butyl alcohol, gives the individual phenanthrene **68**.

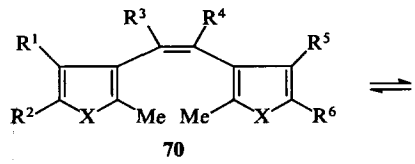


When amines are used in the absence of oxygen, aromatic dihydro-compounds of type **69** are obtained.[132] It has been shown that the amine behaves as a base and interacts with the 4*a*, 4*b*-dihydrophenanthrene formed initially, promoting proton transfer from the C(4*a*) atom to the C(4) atom. Propanethiolate promotes proton transfer to the 9-position, whilst sodium methoxide promotes such transfer to the 2-, 4-, and 9-positions, which leads ultimately to the formation of 1,4- and 9,10-dihydrophenanthrenes.[133]

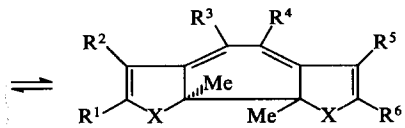
In connection with the discovery of the photochromic properties of 1,2-diheteroarylethenes, a number of studies on the synthesis of a wide variety of compounds of this series have been carried out.[16,134-137] It has been shown that 1,2-diheteroarylethenes **70** undergo a photoinduced thermally irreversible cyclisation to the coloured compound **71**. It is interesting to note that the acquisition of a colour–decolorisation cycle may be repeated more than 10 000 times without appreciable loss of efficiency.[116]

In contrast to other representatives of this series, compounds **71** [X = NMe; R^1, R^2 = $-(CH{=}CH)_2-$; R^3 = R^4 =CN; R^5 = R^6 = Me] have no thermal stability, like dihydrophenanthrenes,[4] while compounds of type **72**, containing imidazo[1,2-*a*]-pyridine residues, do not cyclise, undergoing the photoinduced *Z*–*E* isomerisation to compounds **73**[135] and are therefore of no interest as photochromic materials of this type.

The replacement of one imidazopyridine fragment in compound **72** by a thiophene fragment facilitates the 1,6-electrocyclic reaction.[135]



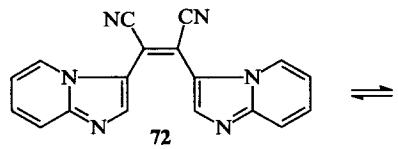
70



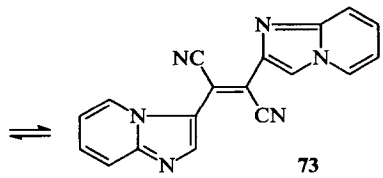
71

$R^1+R^2 = R^5+R^6 =$ 

R^3, R^4 = CN,  ; X = S, Se.



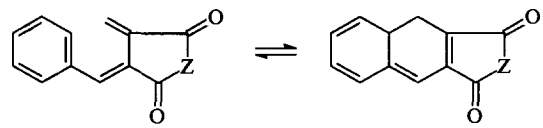
72



73

Nakamura and Irie[17] analysed the results of semiempirical calculations in terms of the MNDO approximation carried out for 1,2-di(3-furyl)-, 1,2-di(3-thienyl)-, 1,2-di(3-pyrrolyl)-, and 1,2-diphenyl-ethenes and showed that the energy barrier in the ring opening reaction is correlated with the difference between the energies of the ground states of the cyclic and open-chain forms; the smaller this difference, the higher the barrier.[17] The difference between the energies of the cyclic and open-chain forms is in its turn correlated with the aromatic stabilisation energy of the cyclic substituents. Thus the higher thermal stability of 1,2-diheteroarylethenes compared with 1,2-diarylethenes can be explained by the lower aromaticity of the heterocyclic compounds compared with benzene.[17]

The phenomenon of photochromism in the fulgides **74** and fulgimides **75** is also due to the 1,6-ER of hexatrienes.

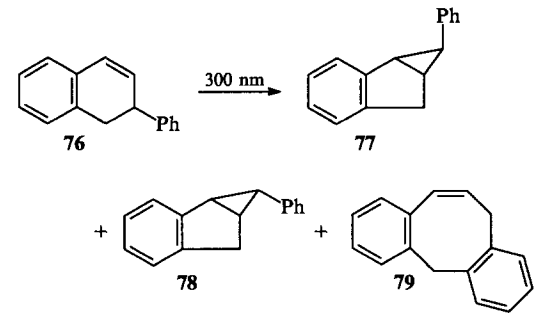


74, Z = O. **75**, Z = NR (R = Ph, Bz, Alk).

Reactions of this type have been described in a review[138] and those of the hetero-analogues of fulgides and fulgimides have been described in a number of other communications[139-144] and are therefore not considered here.

The ring opening reaction of cyclohexadienes, which occurs on UV irradiation, is used to synthesise trienes in the *cis*-(*Z*)-*cis*-conformation.[4] The ring-opening process is usually accompanied by side reactions — *Z*–*E* isomerisation, sigmatropic shifts of hydrogen atoms, and also 1,4- and 1,6-cyclisation.[122]

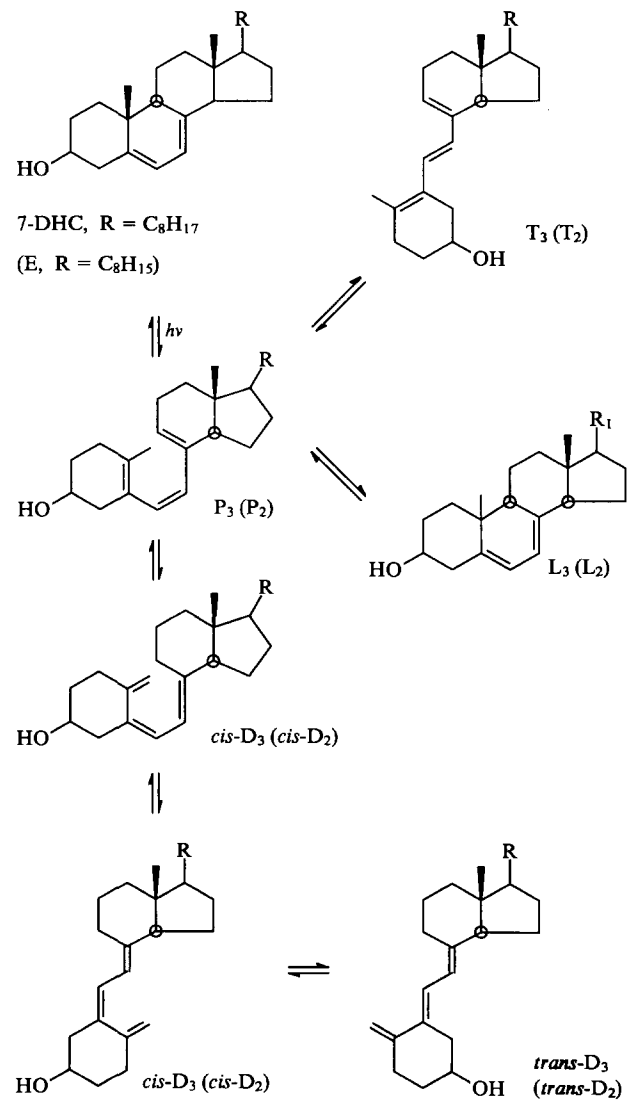
Thus irradiation of 2-phenyl-1,2-dihydronaphthalene **76** with UV light at a wavelength of 300 nm leads to three primary photoproducts: *endo*- and *exo*-6-phenylbenzobicyclo[3.1.0]hex-2-enes **77** and **78** and 7,12-dihydrodibenzo[*a*,*b*]cyclooctatetraene **79**.[44]



76 **77** **78** **79**

It has been shown[44] by means of experiments with 3,4-d_2-labelled specimens of compound **76** that the two isomers (compounds **77** and **78**) are formed via two paths — via the mechanism of the di-π-methane rearrangement and as a result of the electrocyclic ring opening with subsequent photocyclisation.

The complex photochemistry of 7-dihydrocholesterol (7-DHC) and ergosterol (E) became understood as a consequence of the studies of Havinga and coworkers.[119,120] Together with the electrocyclic ring opening and the formation of the (*Z*)-trienes P_2 and P_3, *Z*–*E* isomerisation, 1,4-ER, dimerisation, and sigmatropic transformations take place. The ratios of the products formed depend on the temperature, the diene concentration, and the wavelength of the irradiating light. The following scheme gives an idea about the photochemistry of the process (at a temperature below 0 °C):



It was shown that the singlet and triplet transformations of 7-DHC lead to different products.[119] Photolysis in the range 271–310 nm gives relatively high yields of P_3 (provitamin D); irradiation at shorter wavelengths leads to the predominance of tachysterone (T_3), while irradiation at longer wavelengths gives rise to compound L_3.[145,147]

In the synthesis of vitamin D, the photochemical reaction is usually arrested at 50% conversion of 7-DHC and provitamin D (P_3) is isolated by fractional crystallisation. The provitamin is then converted into the target product as a result of a 1,7-sigmatropic shift.

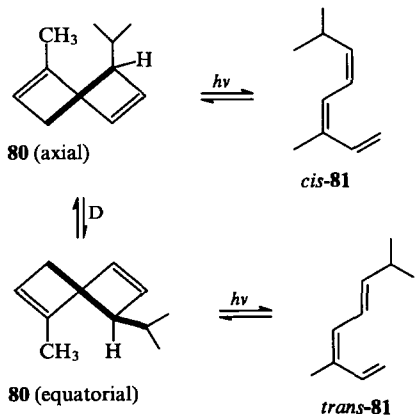
It has been noted[145,148] that, when the technique involving laser photolysis with subsequent irradiation by light at wavelengths of 248 and 473 nm, 248 and 353 nm, and 254 (300) and more than 330 nm is used, predominantly P_3 (P_2) is formed.

The photochemistry of vitamin D stimulated studies on the photochemical reactions of simple hexa-1,3,5-trienes and related systems. The principle of Non-Equilibriation of Excited-state Rotamers (NEER) was developed as a result of these investigations.[119,149,150] According to this principle, the lifetime of the singlet state is not long enough for the isomerisation of different conformers, so that conformers of each type give rise to their own assortment of products.

Thus the ratios and compositions of the substances formed on photolysis of hexatrienes are determined by the isomeric compositions of the conformers of the initial compound in the ground state.[119]

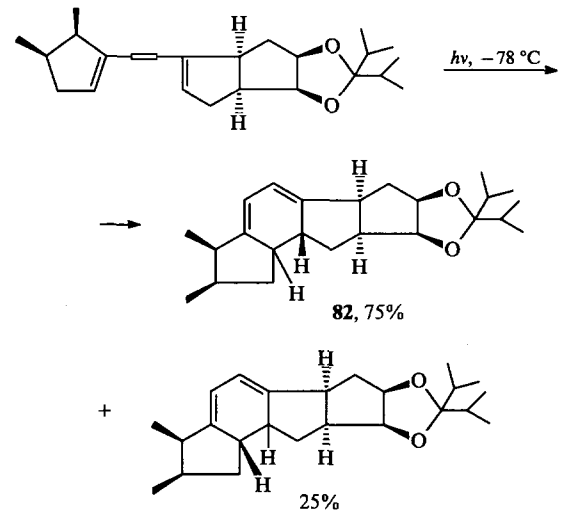
Later the NEER principle was extended to simple hexatrienes. It was shown that an increase in the bulk of the substituents in the 2- and 5-positions in the triene system increases the fraction of the *cis*-(*Z*)-*cis*-isomer and therefore promotes cyclisation.[151]

In their study of the influence of the conformational control on the ratio of the products formed on photolysis of α-phellandrene **80**, Baldwin and Krueger[152] demonstrated the applicability of the NEER principle to retro-ER.[152] They showed that the fraction of the isomer with the axial isopropyl group increases with decrease in reaction temperature and there is a consequent increase in the fraction of the *cis*-isomer of compound **81**.

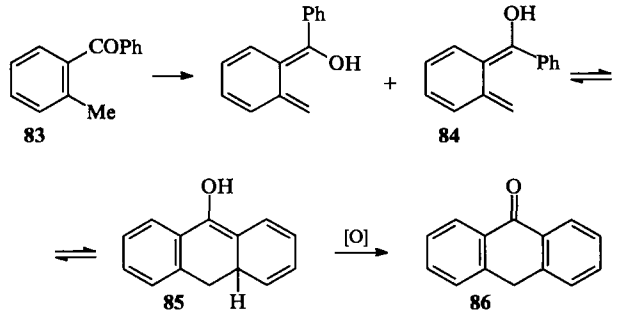


It is essential to note that, in conformity with the orbital symmetry conservation rules, the formation of both *cis*- and *trans*-**81** from the axial isomer of compound **80** is allowed. The preferential formation of *cis*-**81** from the axial isomer of compound **80** and of *trans*-**81** from the equatorial isomer served as a basis for the principle, formulated by Baldwin,[152] which states that the mode of the reaction corresponds to the conformation of the diene in the ground state. When a triene is formed via the 'corresponding' path (the formation of *cis*-**81** from the axial **80**), the *p*-orbitals generated began to overlap with the existing π-system in the early stages of the reaction, whereas in the operation of the 'noncorresponding' path (the formation of *trans*-**81** from the axial **80**), they should pass through the node in the plane of the π-system. The concepts introduced by Baldwin are very closely related to the term 'torquoselectivity' introduced by Houk in a study of the thermal opening of the ring in cyclobutenes.[7–9]

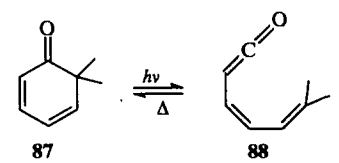
By using the correspondence principle, Whitesell et al.[150] achieved the stereoselective synthesis of the principal fragment in ikarugamycin **82**.



Hexatrienes containing a hydroxy-group in the 5-position are unstable owing to their conversion into the keto-form. However, by irradiating 2-methylbenzophenone **83**, Wilson et al.[153] were able to generate compound **84**, which cyclises, following the absorption of a second photon, to compound **85**, which is oxidised to anthrone **86**.[153]



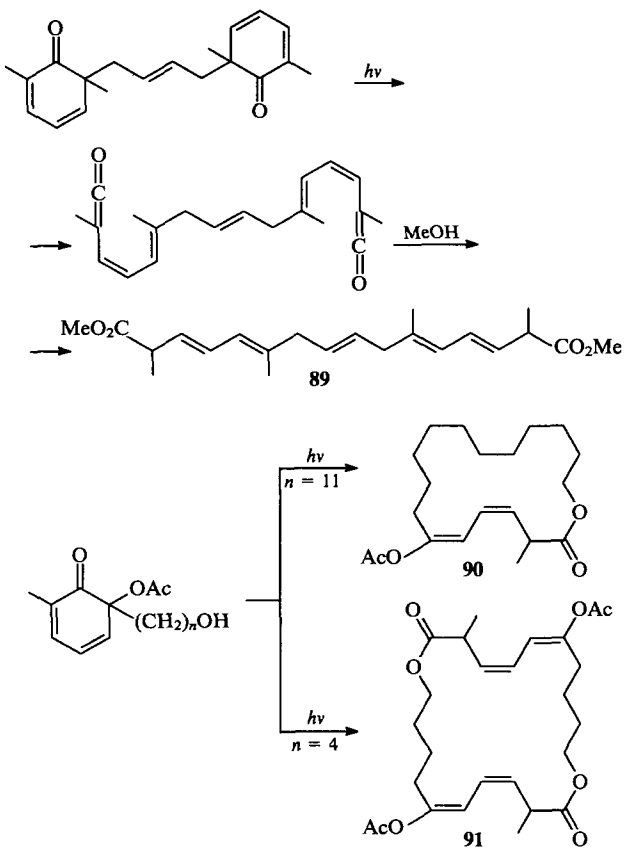
The photochemical opening of the ring in cyclohexa-2,4-dienone **87** results in the formation of the triene **88** containing the ketene group.[154,155]



The reaction proceeds via a n,π^* excited singlet state. The ketene **88** is thermally unstable and is reconverted into the initial compound,[156] but it may be 'trapped' by different nucleophiles.

Since the initial cyclohexadienones **87** are readily available, this reaction constitutes a valuable synthetic method for the preparation of diverse organic compounds with unusual structures.[157]

The most striking examples illustrating the effectiveness of this method are the syntheses of dimethylcrocetin **89**, the pigment saffron,[158] and the macrocyclic lactones **90** and **91**.[159]



VII. 1,6-Electrocyclic reactions in heteroatomic systems

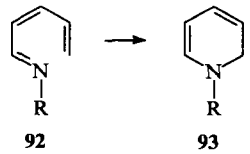
The introduction of heteroatoms into a conjugated π-system hardly alters the symmetry and mechanism of the cyclisation. The substitution of the terminal methylene group by a heteroatom diminishes the exothermicity of the reaction and lowers the barrier to the cyclisation process.[4,16] It has been noted that the introduction of heteroatoms into the terminal positions in the triene system diminishes the difference between the activation energies for the processes proceeding via allowed and forbidden paths.[16] When two heteroatoms are introduced into the terminal positions, the cyclic form is strongly destabilised and the open-chain structure becomes more stable.[4,16] Analysis of the correlation diagrams for the electronic states of the cyclic and open-chain forms leads to the conclusion that the cyclisation of 1,6-dioxatrienes is prohibited in the ground state in both ways — disrotatory and conrotatory.[160] The data on the 1,6-ER of heteroatomic systems are divided arbitrarily into subsections depending on the type (nitrogen, oxygen, sulfur) and number of heteroatoms.

1. Reactions of nitrogen-containing compounds

A nitrogen atom may be introduced into any position in hexa-1,3,5-triene without a significant alteration of the π-system. ER have been described in the literature for all the isomeric mono-azatrienes.[4]

In the general case, the 1-azahexatrienes **92** are less stable than their cyclic isomers — 2-dihydropyridines **93** (Scheme 3).[4]

Scheme 3

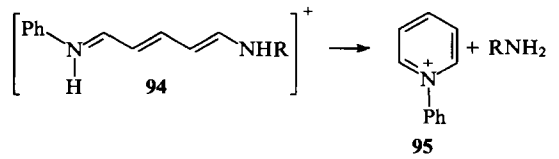


R = H, Alk, Ar.

Reactions involving the opening of the rings in pyridinium salts by nucleophiles,[4] the cyclisation of Konig's salts,[161] rearrangements of the Dimroth[162] and Kost–Sagitullin[163] types, the transformation of oxazines into pyridines,[164] and nucleophilic substitution in heteroaromatic compounds via the ANRORC mechanism[165] have been thoroughly investigated. All these reactions include at least one 1,6-ER of 1-azahexatrienes.

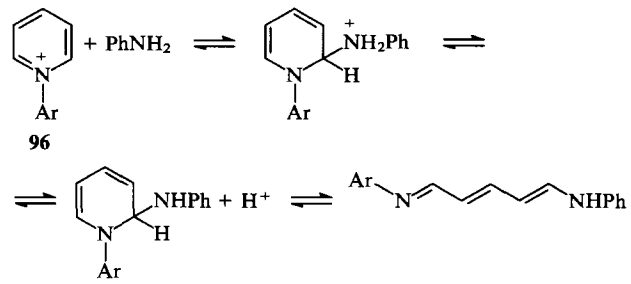
It has been shown that the cyclisation of Konig's salts **94** to the pyridinium salts **95** is catalysed by both bases and acids.[4]

The *cis–trans* isomerisation of compound **94** takes place very readily; E_a is only 6 kcal mol^{-1}.[4] Unfortunately all the atoms in compounds **94** and **95** are located in one plane and their structure does not therefore yield information about the stereochemistry of the process.



Numerous studies, surveyed in Marvell's book,[4] have been devoted to the reactions involving the opening of pyridinium rings by nucleophiles.

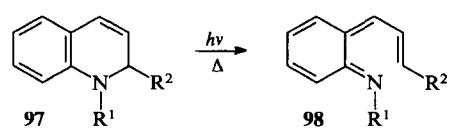
Kinetic investigations indicate the acceleration of the reaction after the introduction of electron-accepting substituents into the *para*-position in the phenyl group. Thus the opening of the ring in dinitrophenylpyridinium **96** by sodium hydroxide is 10^6 times faster than in the unsubstituted phenylpyridinium.[4] It has been noted[166] that the reaction mechanism may change when the pH of the medium is altered. The ring opening reaction is apparently fast and is not the rate-limiting stage in the overall process.



Ar = 2,4-$(NO_2)_2C_6H_3$.

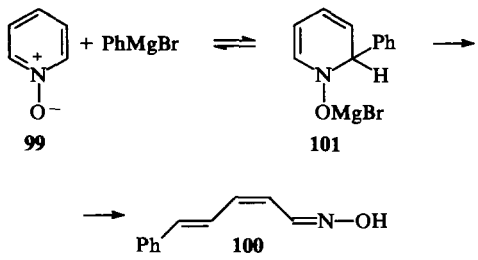
It has been observed that the Schiff bases of retinal analogues cyclise extremely readily to dihydropyridine analogues.[167] It has been shown[167] that the rate of the process is influenced by steric and conformational factors. Data concerning the use of retinal azomethines as models simulating the spectroscopic and chemical properties of certain pigments of halobacteria, particularly bacteriorhodopsin, were analysed in the same communication.[167]

When the dihydroquinolines **97** are irradiated with UV light at 196 °C, the monocyclic compounds **98** are formed. These cyclise slowly to the initial compounds at room temperature.[4]



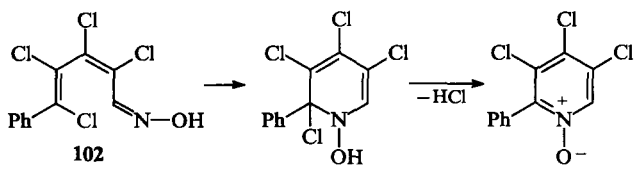
R1 = COOEt, CN; R2 = CN, OH.

On interaction with a Grignard reagent, pyridine *N*-oxide **99** affords the dienyloxime **100**.[4] The last stage of this process is the electrocyclic opening of the ring in the intermediate dihydropyridine **101**.

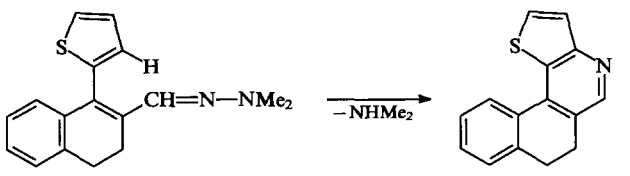


99 **101** **100**

Like the hydrazones **103** having double bonds in the *cis*-positions, the dienyloximes **102** are capable of being converted into dihydropyridines. The latter may be stabilised by the abstraction of a water or hydrogen chloride molecule[4] and, in the case of the hydrazone **103**, by the abstraction of dimethylamine.[168,169]



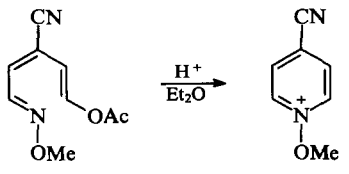
102



103

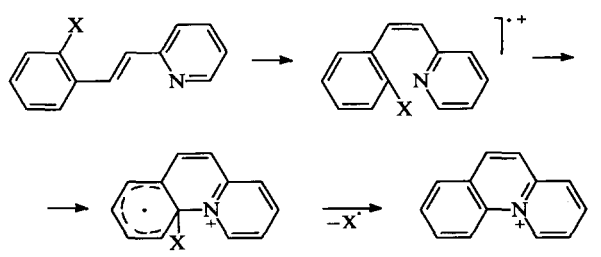
The cyclisation reactions of the trienes **102** and **103** apparently take place with a low activation energy E_a and the rate of the overall process is limited by other stages.

The formation of the pyridinium salts **104**, additionally stabilised as a consequence of their aromatic properties, is the driving force in the cyclisation of compounds **105** in acid media.[170]



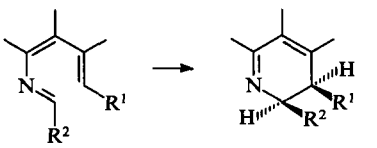
105 **104**

A single study[171] of 1,6-ER with participation of radical species containing the 1-azahexatriene system has been published.



X = H, Me, F, Cl.

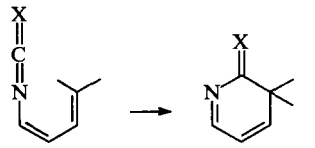
The introduction of a nitrogen atom in the 2- and 3-positions in the hexatriene system 'perturbs' the orbitals only slightly and should not alter the cyclisation mechanism. The results of calculations and experiments[4] confirm this conclusion and indicate a disrotatory mechanism for the cyclisation of 2-aza-hexa-1,3,5-trienes **106**.



106

R^1, R^2 = Alk.

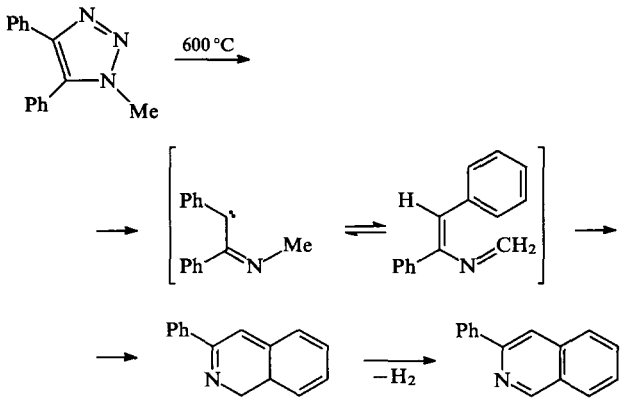
The cyclisation of the dienyl isocyanate **107**[172] and of the carbodiimide **108**[173,174] can take place without rotation relative to the N=C bond by analogy with the 1,4-ER of iminoketenes.[5]



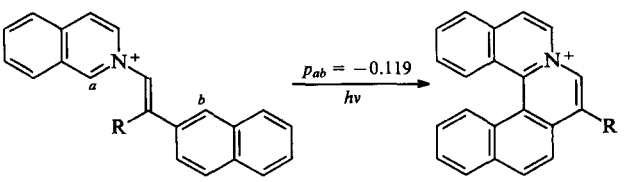
107, X = O.

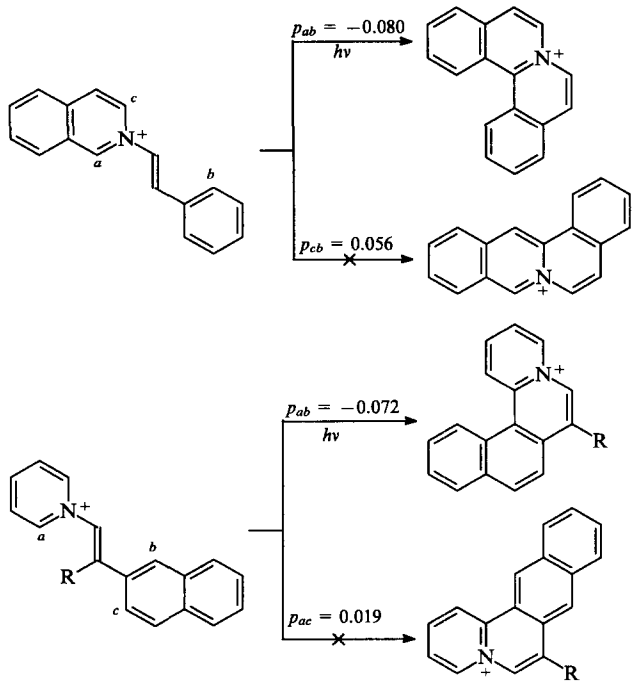
108, X = NPh.

The thermal transformation of 1-methyl-4,5-diphenyl-1,2,3-triazoles into 3-phenylisoquinolines can apparently also include the 1,6-electrocyclic closure of the 2-azatrienyl system.[175,176]

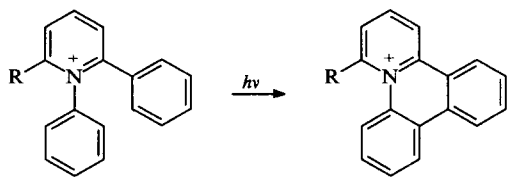


There are examples of the cyclisation of 2-azatrienes containing a quaternary nitrogen atom in the molecule.[4,177,178] It has been shown[177,178] that the order of the bond (p) between the atoms being linked (C_a, C_b, and C_c) must be negative for cyclisation to occur.





The photocyclisation of compounds **109**, containing the azoniahexa-1,3,5-triene system, has been studied in detail by Dorofeenko and coworkers[179] and their successors[180] and constitutes yet another example of 1,6-ER.

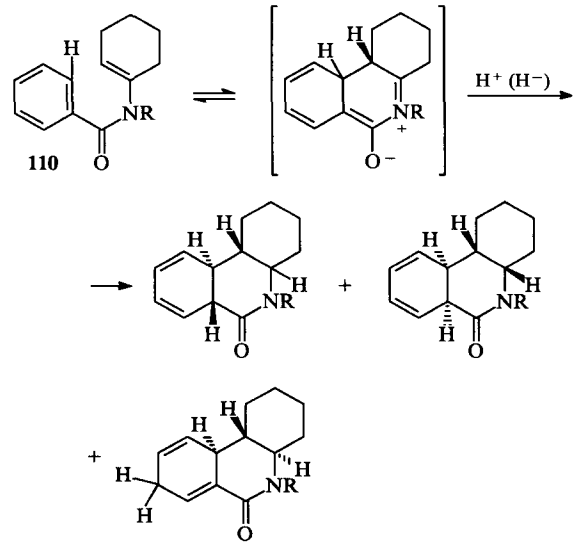


109

R = Me, COOH, Ph.

There exists a single study[181] on the basis of which one may reach a conclusion concerning the mechanism of the cyclisation of 3-azahexatrienes. The authors[181] showed that reductive photocyclisation of the enamides **110** takes place in a conrotatory manner in conformity with the orbital symmetry conservation rules (Scheme 4).[1-3]

Scheme 4



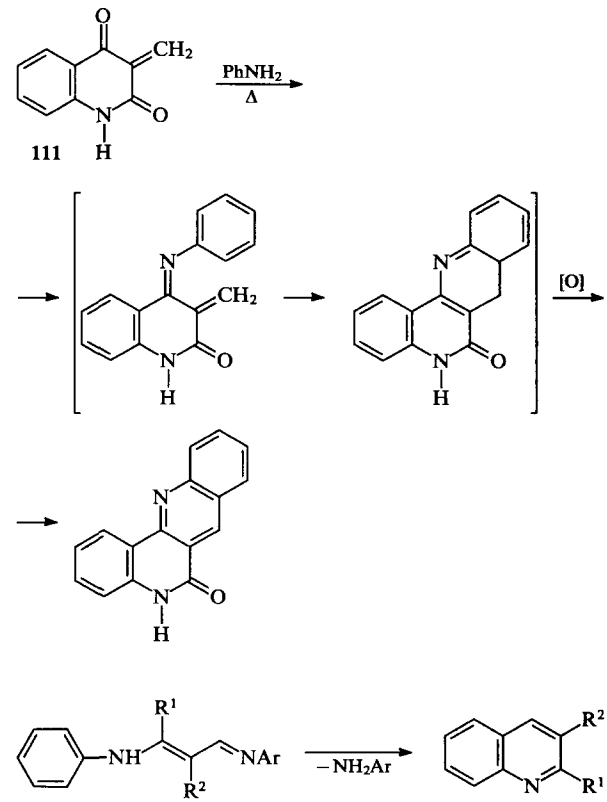
110

R = Alk, Ar.

The photocyclisation of enamides[182] has been used by the same workers to synthesise the alkaloid naucleficine.

The dihydropyridines **111**, formed on thermal cyclisation of 3-azahexatrienes, are converted into aromatic compounds as a result of the oxidation or elimination of low-molecular-mass products, which hinders the study of the stereochemistry of this reaction (Scheme 5).[4,183]

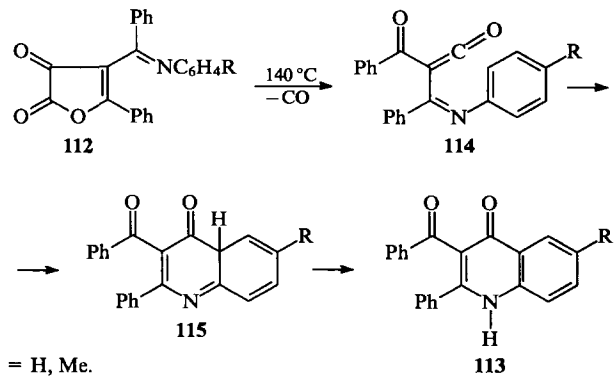
Scheme 5



111

R¹, R² = H, Me.

The transformation of the furandione **112** into the quinolinone **113** apparently involves the cyclisation of the iminoketenes **114** to the hydropyridine **115**. The latter is stabilised as a result of the 1,3-sigmatropic shift of a hydrogen atom.[184]



112 **114**

115

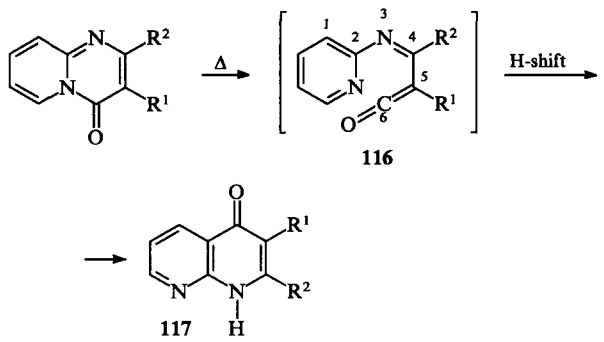
R = H, Me.

113

The formation and 1,6-ER of the iminoketenes **116** constitute the basis of the rearrangement of pyrido[1,2-*b*]pyrimidines to pyridopyridones **117**.[185]

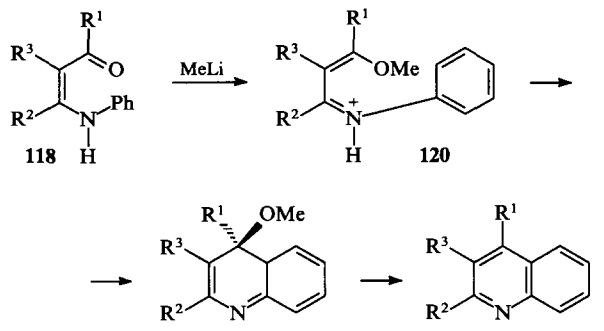
It has been shown[186] that the methylation of the ketoenamines **118** by dimethyl sulfate leads to the quinolines **119**.

It has been suggested[186] that the reaction proceeds via the intermediate cation **120**. Taking this into account, one may conclude that the cyclisation of 3-azoniahexatrienes may be achieved not only photochemically but also thermally.



116

117

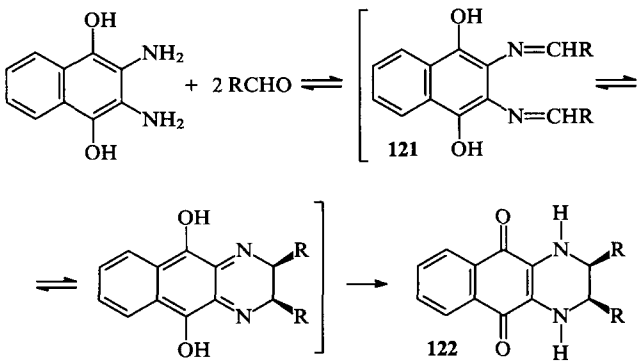


118 120 119

R^1, R^2, R^3 = H, Me, Bu^t.

It has been demonstrated with the aid of quantum-chemical calculations that the substitution of two CH groups in the 2- and 4-positions and also in the 2- and 5-positions in the hexatriene system should not alter the mechanism of the cyclisation reaction.[171] Experimental data fully support these conclusions (Scheme 6).[4]

Scheme 6

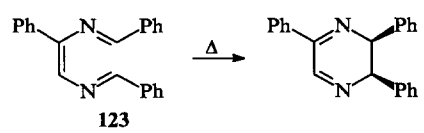


121 122

R = 2-HOC$_6$H$_4$, 2-OH-3-MeOC$_6$H$_3$,
2-OH-4-MeOC$_6$H$_3$, 2-OH-5-MeOC$_6$H$_3$,
4-MeC$_6$H$_4$, 4-NH$_2$C$_6$H$_4$.

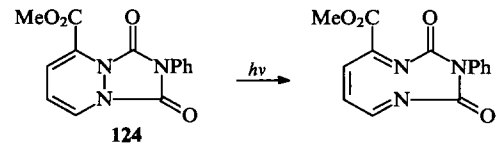
It has been shown[187] that the azomethine imines **121** cyclise via a disrotatory process with the ultimate formation of the quinones **122**. Freeman and Kim demonstrated the possibility of the occurrence of this reaction for the acyclic 2,5-diaza-1,3,5-trienes.[188]

A more rigorous demonstration of the disrotatory cyclisation mechanism has been achieved by Padwa et al.[189] in a study of the cyclisation of the triene **123**.



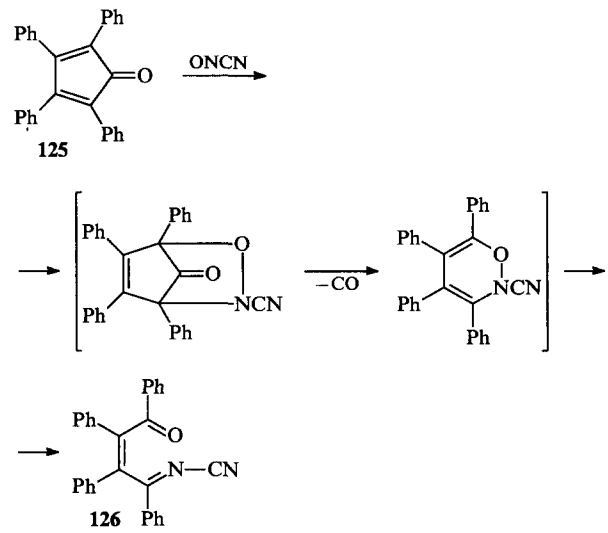
123

The photochemical opening of the ring in the dihydropyridazine **124** is an example of a reaction involving the 1,6-diazahexatriene system.[190]



124

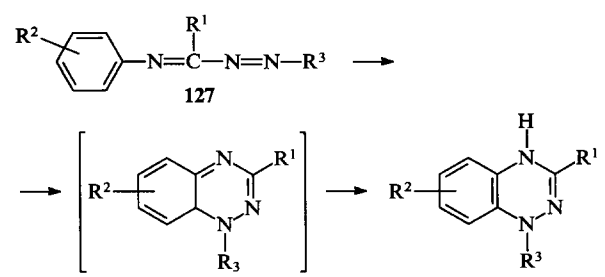
1,6-Diazahexa-1,3,5-trienes are more stable than their cyclic isomers. This apparently applies also to systems having other heteroatoms with lone pairs in the terminal positions. Thus the reaction of the cyclopentadienone **125** with nitrosocyanogen leads to the formation of 1-oxa-6-azahexa-1,3,5-triene **126** in a pure form and in a high yield.[191]



125 126

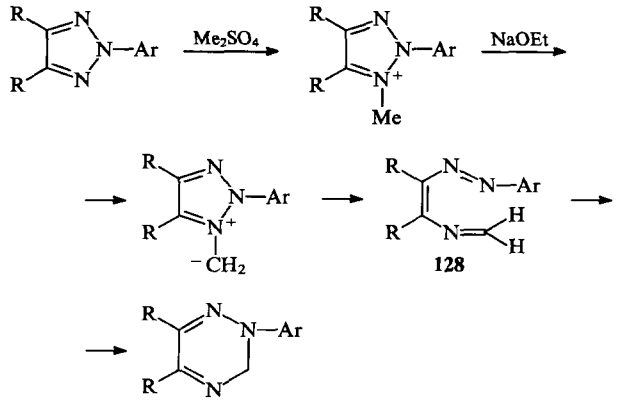
Nucleophilic substitution in pyramidines, which proceeds via the ANRORC mechanism and has been discovered and studied in detail by van der Plas and coworkers,[165,192] includes the 1,6-ER of 1,5-diazahexatrienes as one of the stages.

The cyclisations of 1,4-diaryl-1,2,4-triaza-1,3-dienes **127**,[193] 1-aryl-1,2,5-triazadienes **128**,[175,176] as well as aromatic and heteroaromatic diazonium salts belong to the class of 1,6-ER of triene systems with three nitrogen atoms. They will be examined in the next section.

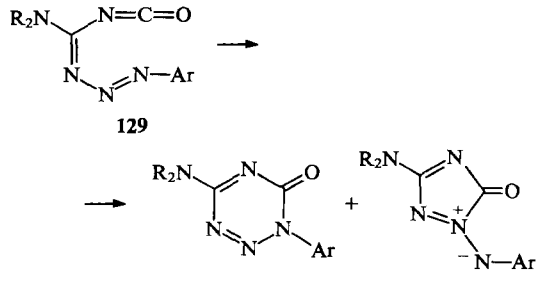


127

R^1, R^2, R^3 = H, Me, Ar, COMe, COPh, CO_2Alk.



The cyclisation of the isocyanates **129** is an example of the ER of trienes with four nitrogen atoms.[194]



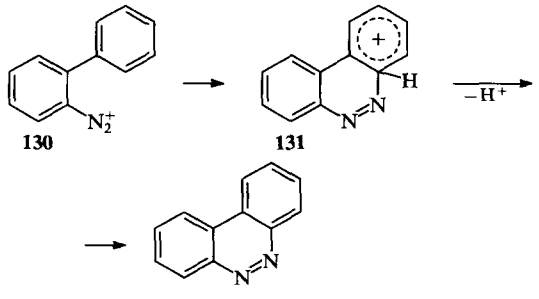
2. Cyclisation of heterocyclic diazo-compounds and diazonium salts

One of the possible mechanisms of the cyclisation of aromatic diazonium salts and heterocyclic diazo-compounds, in the *ortho*-positions of which there are groups containing multiple bonds, involves a monorotatory 1,6-electrocyclic reaction. This reaction is used widely in the synthesis of a wide variety of six-membered heterocyclic compounds such as pyrazines, v-triazines, and thiadiazines.

Since these processes have many features in common, they are described in a separate subsection.

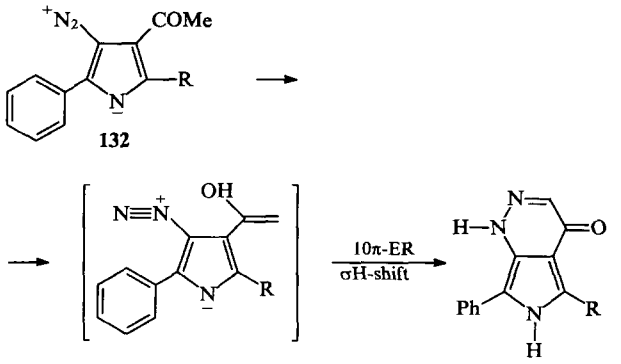
a. The formation of the N–C bond

The cyclisation of diazonium salts and heterocyclic diazo-compounds containing a vinyl group in the β-position (the Widman–Stoermer reaction) is treated as an intramolecular azo-coupling for the aryl derivatives **130**.[195–198]



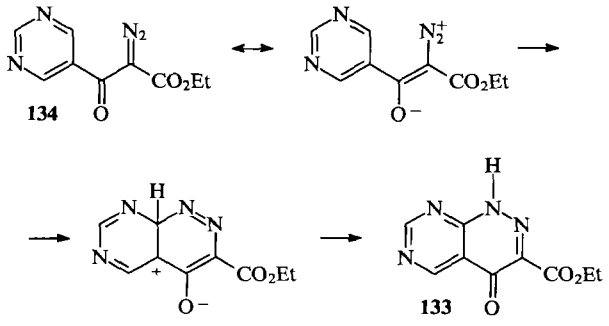
Unfortunately, experimental and theoretical studies on the mechanisms of this reaction are not described in the literature; the intermediate complexes **131** have not been characterised, the influence of the π-system on the energy relations of the cyclisation reaction has not been elucidated, and kinetic studies have not been carried out.

Presumably, the diazoketones **132** cyclise via a similar mechanism. It is of interest to note that the methylketo-group, tentatively in the enolic form, and not the aromatic ring, participates in the reaction.[199]



R = H, Me.

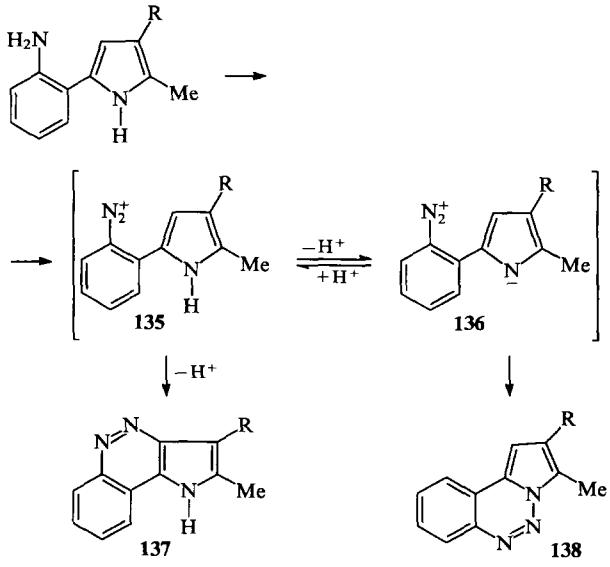
The occurrence of this reaction requires the presence of sulfuric acid. Thus, on heating in DMF, the initial compound **132** remains unaltered.[199]



The condensed pyridazines **133** are also formed on cyclisation of pyrimidinyl diazoketones **134**.[200,201]

If the molecule of the diazo-compound contains a pyrrole ring in the *ortho*-position relative to the diazonium group, the reaction can proceed via two paths, depending on the pH of the medium, with formation of a C–N or N–N bond.[202,203]

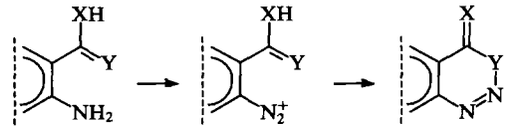
These results have been explained[203] by the existence of an acid–base equilibrium between the diazo-compounds **135** and **136**, each of which gives rise to its own cyclisation product — compounds **137** and **138** respectively.



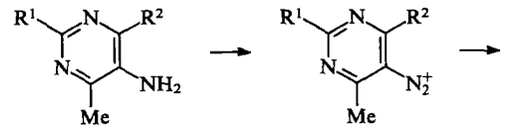
R = COMe, CO_2Et, H.

b. The formation of N–N and N–S bonds

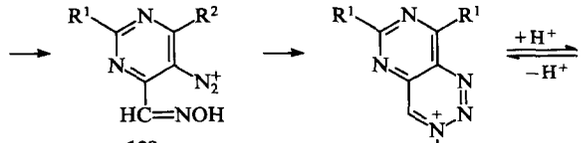
The diazotisation of heterocyclic and aromatic amines containing amide, amidine, and thioamide groups in the *ortho*-positions takes place via intermediate diazo-compounds with formation of condensed 1,2,3-triazines and thiadiazines.



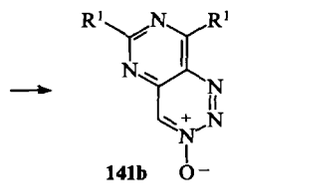
X, Y = O, S, NR.



140



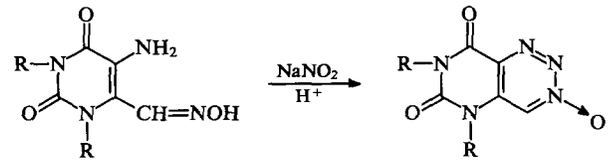
139 **141a**



141b

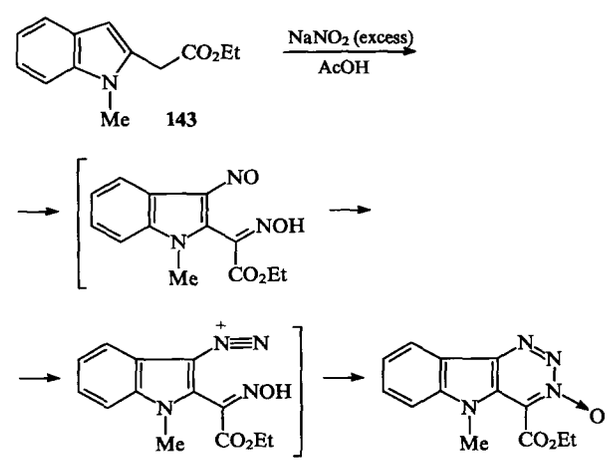
Thus the diazooximes **139**, formed from the amines **140** as a result of diazotisation and nitrosation reactions, cyclise to pyrimido[4,5-*d*]-1,2,3-triazines **141**.[196,204]

The interaction of the amines **142**[196] and indoles **143**[205] with nitrous acid affords analogous results.



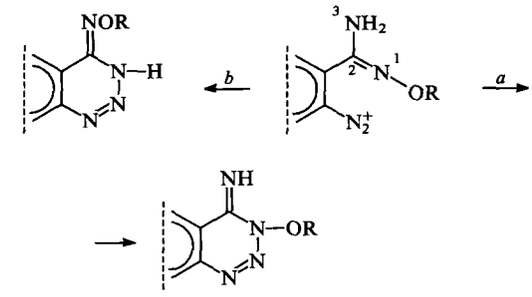
142

R = H, Alk.



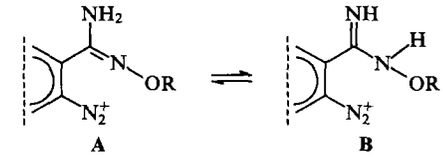
Diazo-compounds containing an amidinoxime group can cyclise, in principle via two paths — with participation of the N(1) and N(3) atoms.

However, it has been shown[196,206] that this reaction involves the formation of a N–N bond with the N(1) atom linked to the oxygen atom (route *a*).



R = H, Alk.

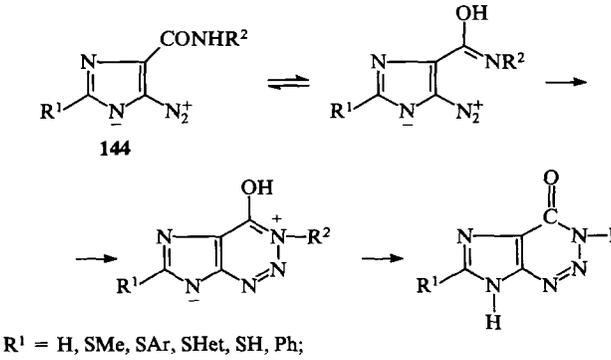
The higher reactivity of the nitrogen atom linked to the oxygen atom can be accounted for either by the α-effect of the lone pair of the oxygen atom or by the existence of amidinoximes fully in the tautomeric form **A** and by the high energy barrier to the conversion of form **A** into form **B**.



A **B**

R = H, Alk.

Data indicating a higher reactivity of the amide nitrogen atom linked to the heteroatom with a lone pair are confirmed by the series of studies of Mokyushin and coworkers[192–195] on the cyclisation of heterocyclic diazo-compounds containing an amide¶, hydroxyamide, and hydrazide group in the *ortho*-positions.[207–210] The authors showed that, despite their tendency to cyclise, the diazo-compounds **144** (R^2 = H, Alk, Ar) may be isolated and characterised spectroscopically. However, this does not apply to compounds **144** with R^2 = OH, NH_2, or N=CHAr.



144

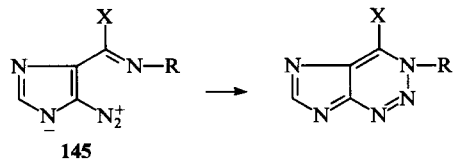
R^1 = H, SMe, SAr, SHet, SH, Ph;

R^2 = H, Alk, Ph, OH, NH_2, NCH_2Ar.

They cyclise already during their synthesis, which indicates their higher reactivity compared with other representatives of this series.

¶ The cyclisation of diazo-compounds with the *o*-amide group as a method of synthesis of condensed triazinones has been described in numerous publications.[207–215]

The heterocyclic diazo-compounds **145**, containing the amidine and imidate groups, also cyclise to triazines under the conditions of the synthesis.[196]

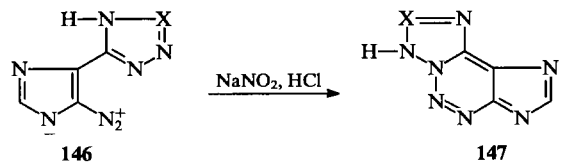


145

X = OAlk, NH_2, SMe.

Nevertheless, Mokrushin and coworkers[216] were able to isolate and characterise spectroscopically the diazo-compounds **145** (X = SMe).

The cyclisation of the diazo-compounds **146**, in which the amidine group is represented by a triazole or tetrazole ring, leads to the formation of the tricyclic compounds **147**.[217-219]

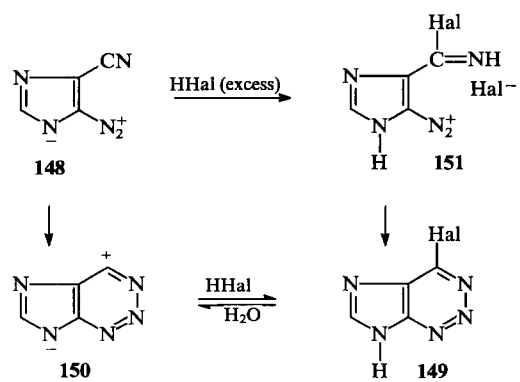


146 **147**

X = CH, N.

The diazo-compounds **148**, containing a cyano-group in the *ortho*-position, are converted into the imidazotriazines **149** on treatment with hydrogen chloride or bromide.[220,221] In aqueous media, the reaction proceeds in the opposite direction.

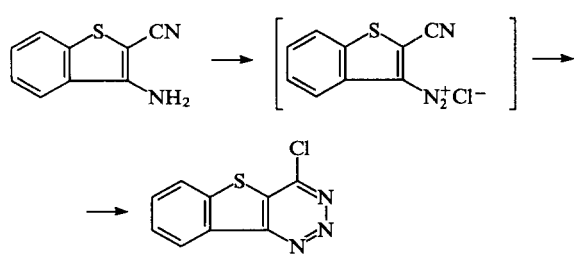
The authors[220,221] suggested that this reaction is achieved via the intermediate compound **150**. However, in our view, the mechanism involving the diazoimine **151** as an intermediate is more probable.



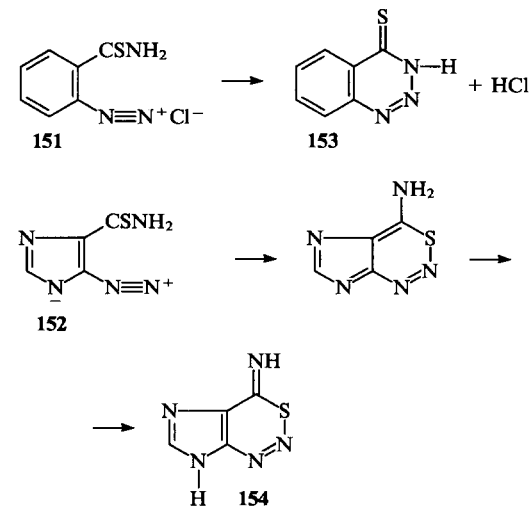
148 **151** **150** **149**

Hal = Cl, Br.

Beck and Yahner observed a similar reaction but in other systems.[222]



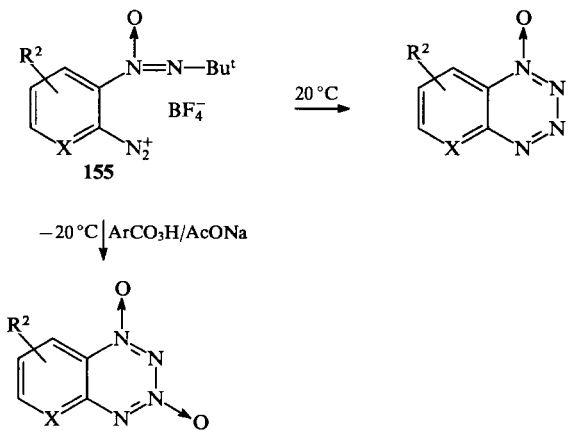
It is of interest to note that the cyclisation of the aromatic diazonium salts **151** and of the heterocyclic diazo-compounds **152**, containing a thiocarbamoyl group in the molecule, takes place via different paths with formation of 1,2,3-triazinethiones **153**[223,224] and thiadiazines **154**.[225,226]



151 **153** **152** **154**

It is not understood whether this is associated with the different reactivities of the diazo- and diazonium groups or with the different thermodynamic stabilities of the imidazo- and benzo-thiadiazines.

The cyclisation of the diazonium salts **155**, containing an azoxy-group in the *ortho*-position, leads to the *N*-oxides of heterocycles with four nitrogen atoms — tetrazines.[227,228]



155

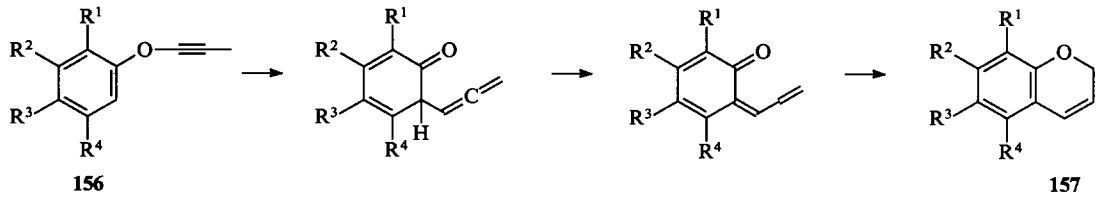
3. Reactions of oxygen-containing compounds

a. Compounds with one oxygen atom

The 1,6-ER of dienones to pyrans, which is extremely interesting from the standpoint of theoretical studies and practical use, belongs to processes of this type. It constitutes the basis of the manifestation of the photochromic and thermochromic properties by spiropyrans,[229] chromenes,[230,231] and spirooxazines[232] and is one of the stages in a wide variety of chemical transformations of, for example, the propargyl ethers **156** into the benzopyrans **157**,[4] of the pyrylium salts **158** into the pyridinium salts **159**[233,234] (on treatment with aliphatic and aromatic amines), of compounds **160** into the benzene derivatives **161** (on treatment with phosphoranes[235] and enamines[236]), and also of the isoxazolium salts **162** into the 1,3-oxazines **163**[237] (Scheme 7).

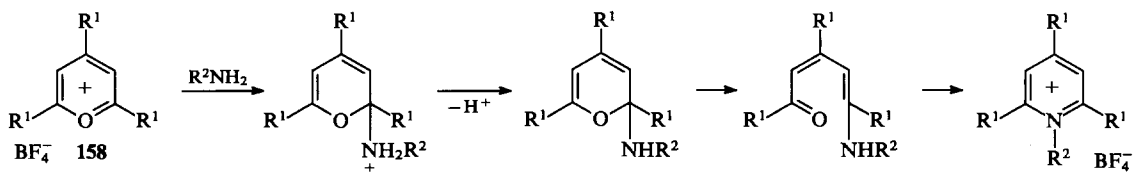
It has been shown that, on heating with diethyl ethynedicarboxylate, the dithioacetal **164** gives rise to the thiapyranone **165**. This illustrates a series of consecutive pericyclic reactions: cycloaddition (CP), 1,4- and 1,6-ER and sigmatropic rearrangements (Scheme 8).[238]

Scheme 7



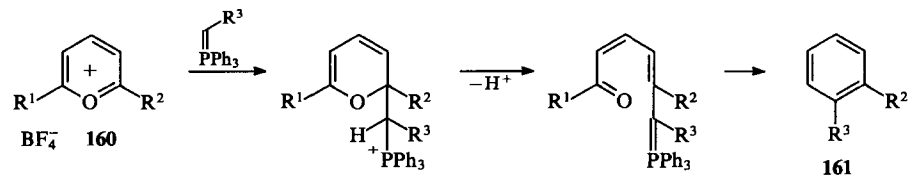
156 157

R^1, R^2, R^3, R^4 = H, Me, Cl, OMe.



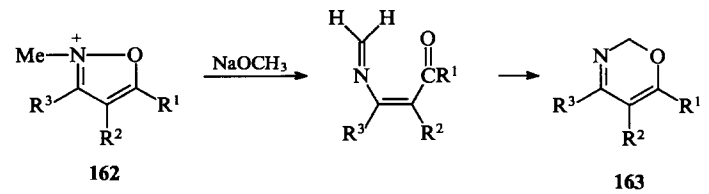
158 159

R^1 = Ph, 4-FC_6H_4; R^2 = Bu, Bz, C_6H_{11}, Ph.



160 161

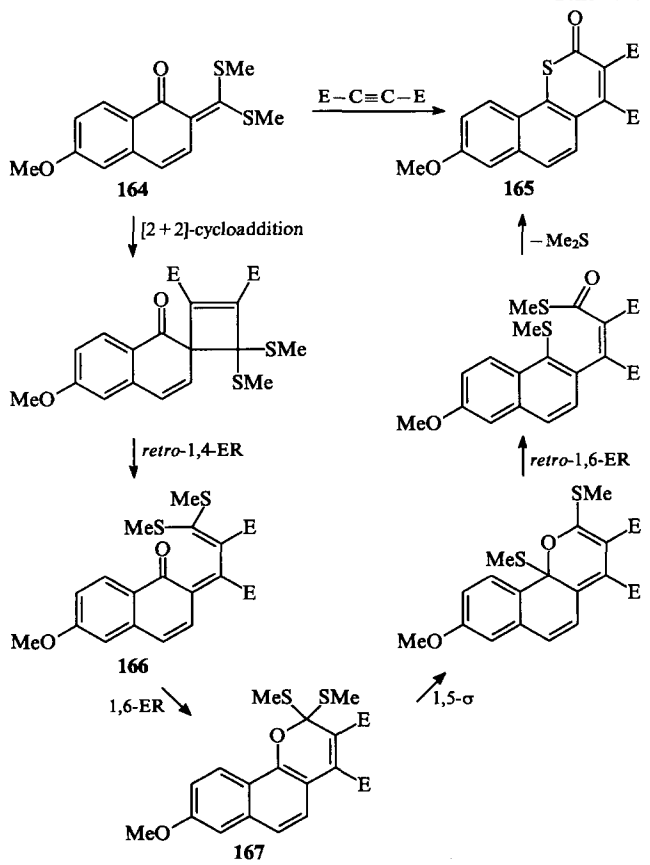
R^1, R^2 = Me, OMe; R^3 = CO_2Et.



162 163

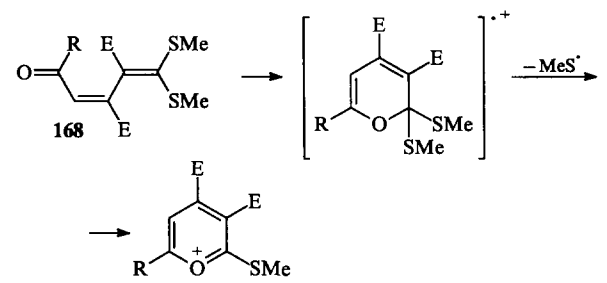
R^1, R^2, R^3 = H, Ph.

Scheme 8



E = CO_2Et.

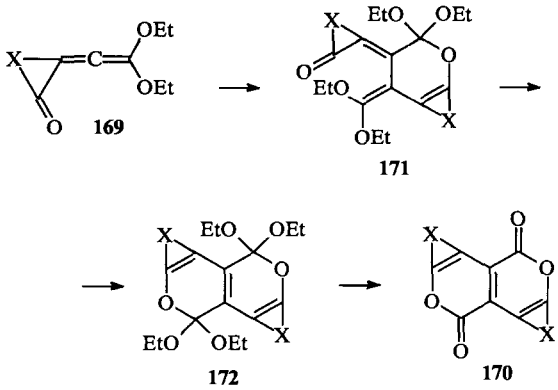
It has been shown[238] that the 1,6-ER of compound **166** to compound **167** is analogous to the mass-spectrometric decomposition of compound **168**.



E = CO_2Et.

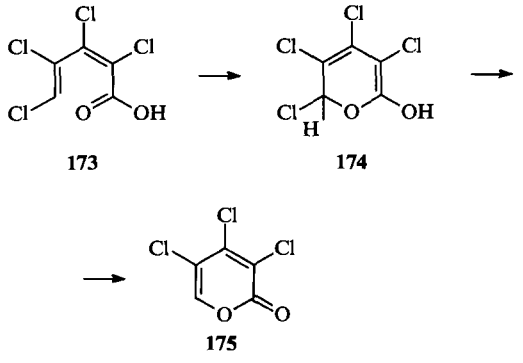
Saalfrank et al.[239] showed that compound **169**, which is stable at moderate temperatures, gives rise to the pyranone **170** on thermolysis, probably as a result of the consecutive [4 + 2]-cycloaddition and 1,6-ER reactions of the intermediate dienone **171** and the hydrolysis of the diacetal **172**.

The cyclisation of the polyhalodienone **173** does not stop at the ER stage. The 2*H*-pyran **174** formed is stabilised as a result of the elimination of a hydrogen halide molecule and is converted into the pyran-2-one **175**.[240,241]



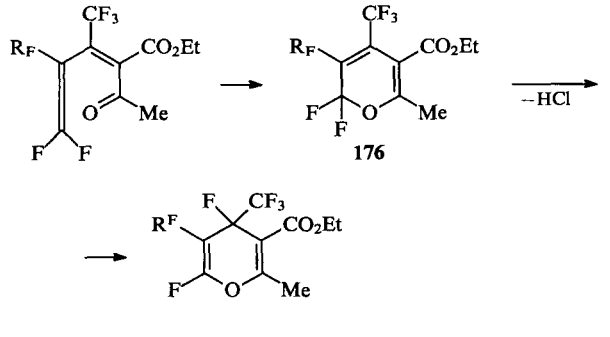
169 171 172 170

X = $(CH{=}CH)_2$.



173 174 175

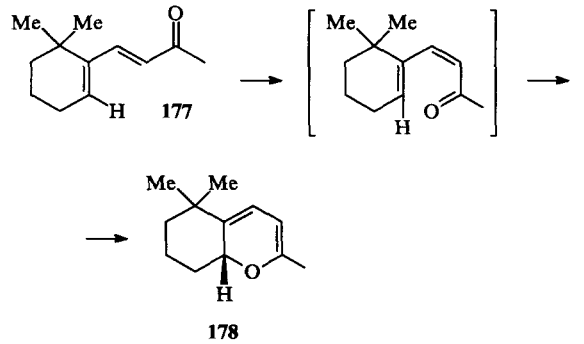
The polyfluorinated pyrans **176** are stabilised by the 1,3-sigmatropic shift of a fluorine atom.[242]



176

R_F = $(C_2F_5)_2CCF_3$, $C(CF_3)_3$, C_2F_5, F.

A study of the products of the irradiation of the *trans*-dienone **177** (to which the structure of the pyran **178** had been initially attributed) by ^{1}H NMR spectroscopy showed that at 55 °C the products consist of 18.8% of the dienone **177** and of 82.2% of the 2*H*-pyran **178**.[4]

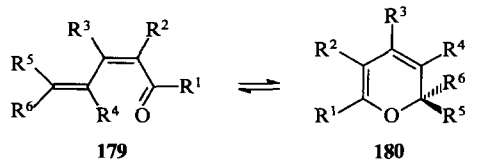


177 178

It has been shown that the ring closure in *cis*-β-ionone is a rapid unimolecular reaction which is relatively insensitive to the solvent.[4] The enthalpy and entropy of activation for this process are 20 kcal mol^{-1} and −5 entropy units, whereas the corresponding quantities for the cyclisation of *cis,cis*-1-cyclohexenylpenta-1,3-diene are 34 kcal mol^{-1} and −5 entropy units respectively. Thus the substitution of the terminal methylene group by an oxygen atom lowers the activation energy by 14 kcal mol^{-1}. Several causes accounting for this phenomenon have been put forward in Marvell's book.[4]

The available literature data did not permit conclusions concerning the influence of the electron-donating and electron-accepting properties of the substituents on the rate of this 1,6-ER.

According to Benson's data,[4] the difference between the enthalpies of formation of *cis*-pentadienes and α-pyrans is −0.1 kcal mol^{-1}. In the absence of other strong interactions, the equilibrium between the dienones and pyrans is therefore determined by entropy factors.



179 180

R^1–R^6 = H, Alk, OAlk, NHAlk, COOAlk, COAlk, CN, Ar.

A systematic and detailed study of the influence of the structure on the equilibrium between dienones and the isomeric 2*H*-pyrans has been carried out by Krasnaya and co-workers.[243–248] They showed that the intensification of the steric interactions between the substituents in the α- and γ-positions as well as the introduction of a dimethylamino-group in the β-position displace the equilibrium towards the pyran form, whereas an increase in the capacity of the solvent for specific solvation entails an increase in the fraction of the diene form. Among compounds **179** (R^4 = Br, OEt), containing bromine or the ethoxy-group, solvatochromism is most pronounced. In hexane or tetrachloroethene, they exist in the form of 2*H*-pyrans, whilst in water or in a water–methanol mixture they are present as the dienones.

It is of interest to note that the content of valence isomers may depend on the state of aggregation of the given substance. Thus compound **179** [R^1, R^2 = $-(CH_2)_4-$, R^4 = OEt] exists in the crystalline state as the dienone **179**, whilst in solution or in the melt it is present as two isomers — the dienone **179** and the pyran **180**.

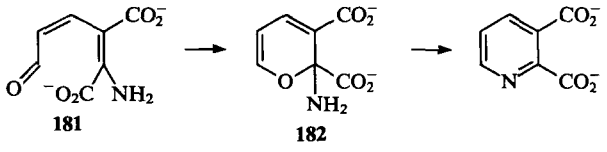
The authors[242–249] explain their findings by the fact that, with increase in the steric hindrance between the substituents R^5 and R^3 and also between R^4 and CO, the equilibrium shifts towards *cis*-form of the dienone, which is favourable for cyclisation. Their explanations are similar to those used by Duperrier and Dreux,[250] who showed that the steric interaction between R^3 and R^5 and also between R^4 and CO can be important for the cyclisation reactions, while the groups R^4 and R^6, conjugated with the π-system, displace the equilibrium towards the dienone.

In connection with the manifestation of photochromic properties by chromenes and spiropyrans, a series of theoretical and experimental studies have been carried out on the photochemical reactions of these compounds.[251–260] It has been shown[258] that $^1(\pi\pi^*)$ singlet state of the spiropyran is decisive in this process but that in the photochemical reaction a crossing of the type $^1(\pi\pi^*)-{}^3(n\pi^*)$ or $^1(n\pi^*)-{}^3(\pi\pi^*)$ takes place.

However, Khlomanskii and Dyumaev[259] believe that these processes do not fully account for the nature of the primary photochemical step in spiropyrans.

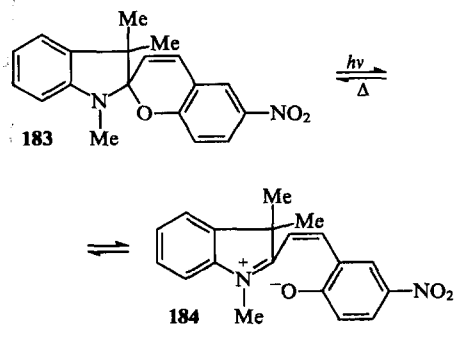
The rapid reactions of dienones and 2*H*-pyrans are the cause of the ready isomerisation of retinal relative to the double bonds.[261,262] It has been shown that pyrans are reduced via the dienones initially formed.[263,264]

In connection with the high sensitivity of the equilibrium between dienones and 2*H*-pyrans to the influence of the pH of the medium, temperature, and irradiation by light, it has been suggested[18] that this ER plays an important role in biochemical processes in living organisms. The study by Keys and Hamilton[265] constitutes a confirmation of this hypothesis. It was shown in the latter that one of the key stages in the biosynthesis of pyridine-2,3-dicarboxylate in animals is the cyclisation of 2-amino-β-carboxymuconate ε-semialdehyde **181** to the pyran **182**.



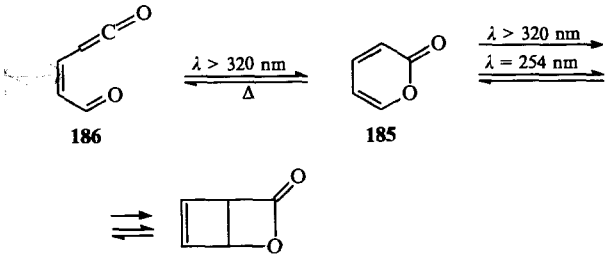
181 **182**

In this connection, one should also note that the system **183**↔**184** functions as an agent transferring aminoacids through liposomes.[266]



183 **184**

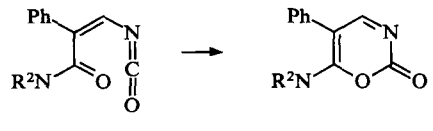
The replacement of the terminal double bond by the ketene group in the dienone leads to the displacement of the equilibrium towards the cyclic form.[4] The low-temperature photolysis of the pyranone **185** makes it possible to identify the ketene **186**, which is converted irreversibly into the initial compound after the cessation of UV irradiation.[267–269]



186 **185**

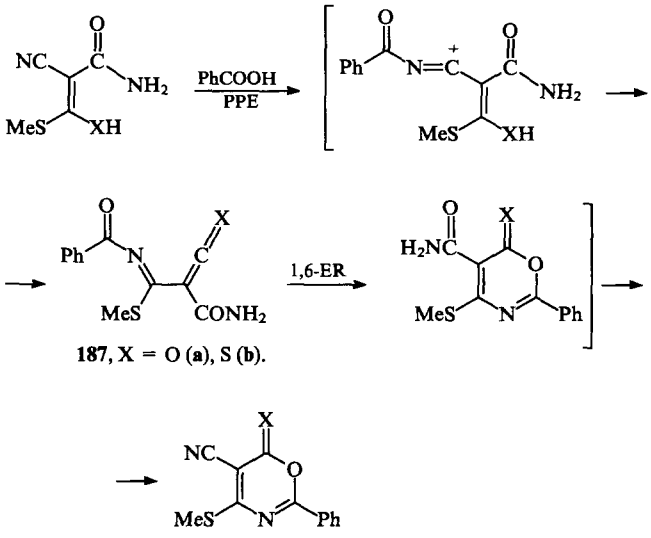
This fact made it possible to carry out a kinetic study of the cyclisation of the ketene **186**. The activation energy for the ketene is 9.4 kcal mol^{-1} and its lifetime at 26.5 °C is only 2.4 μs.

Isocyanates containing the 2-azadienone system also readily cyclise to oxazinones.[270–272]



R = Alk, R_2N —  .

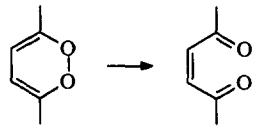
It has been shown that the 1,6-ER of the aza-analogues of compound **186** — the ketenes **187a** and the thioketenes **187b** — is one of the stages in the double O,N- and N,N-rearrangements.[273,274]



187, X = O (**a**), S (**b**).

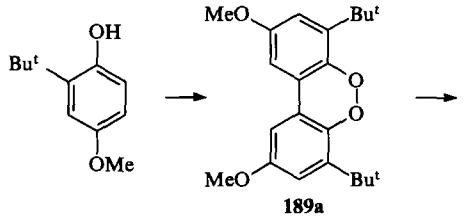
b. Compounds with two oxygen atoms

The reaction involving the opening of the ring in the potential 1,2-dioxine **188** should have a low activation energy and should be largely exothermic according to Marvell.[4]

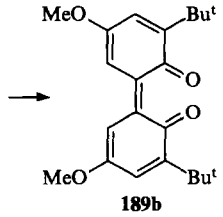


188

Nevertheless, Baltes and Volbert[275] were able to obtain its derivative — the dioxine **189a** — by oxidising 2-*tert*-butyl-4-methoxyphenol. The colourless compound **189a** acquires a deep blue colour on dissolution in nonpolar solvents, apparently as a result of its conversion into the diketone **189b**.



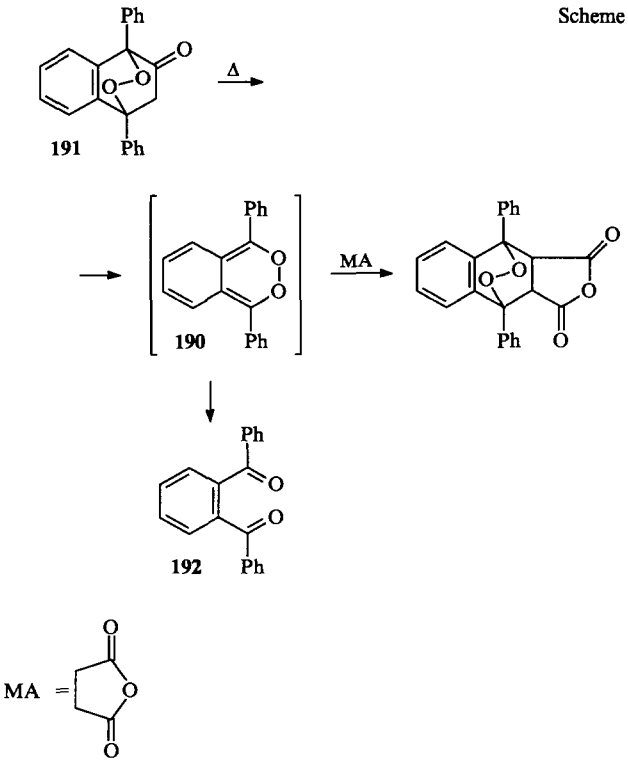
189a



189b

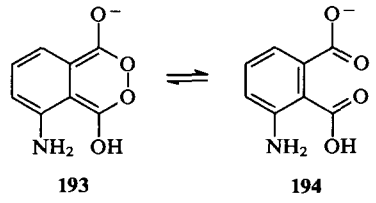
Proof of the existence of *o*-xylylene peroxide **190** as an intermediate in the decomposition of compound **191** was obtained chemically in its reaction with maleic anhydride (MA). In the absence of MA, electrocyclic opening of the dioxine ring and the formation of *o*-dibenzoylbenzene **192** take place (Scheme 9).[276]

Scheme 9



Chemiluminescence is observed during the formation of compound **192**, which indicates its existence in an excited state.

In a discussion of the chemiluminescence, Michl[277] suggested that the endoperoxide **193** is a direct precursor of the luminescent phthalate ion **194** and put forward qualitative arguments explaining why the dissociation of the O–O bond leads to chemical excitation.



Michl's model is most clearly illustrated by a qualitative correlation MO diagram (Fig. 2).

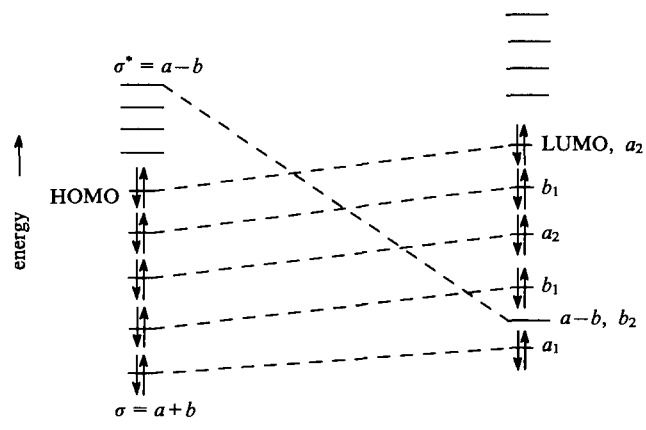
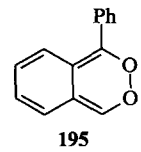


Figure 2. Qualitative correlation diagram for the MO of compounds **193** and **194**.

In the endoperoxide **193**, $a + b$ is a bonding orbital and $a - b$ is an antibonding orbital. With increase in the O–O distance, the energies of the two orbitals approach one another. In a rapid nonadiabatic reaction, the electrons do not have sufficient time to pass to an orbital with a different symmetry. This entails the failure to fill the $a - b$ orbital, whereas the LUMO becomes doubly occupied, i.e. we arrive at a doubly excited state, the transition from which to the ground state is accompanied by chemiluminescence.

Michl's qualitative model has been developed and refined by means of quantum-chemical calculations in terms of the HAM (Hydrogen Atom in Molecule) approximation.[160]

The authors[160] showed that two intersections on the correlation MO diagrams are important for the manifestation of the phenomenon of chemiluminescence. The activation energy for the opening of the endoperoxide ring in compound **193** is only 6 kcal mol^{-1}. Schuster and coworkers[278] demonstrated the unexpected stability of the *o*-xylylene peroxide **195**.

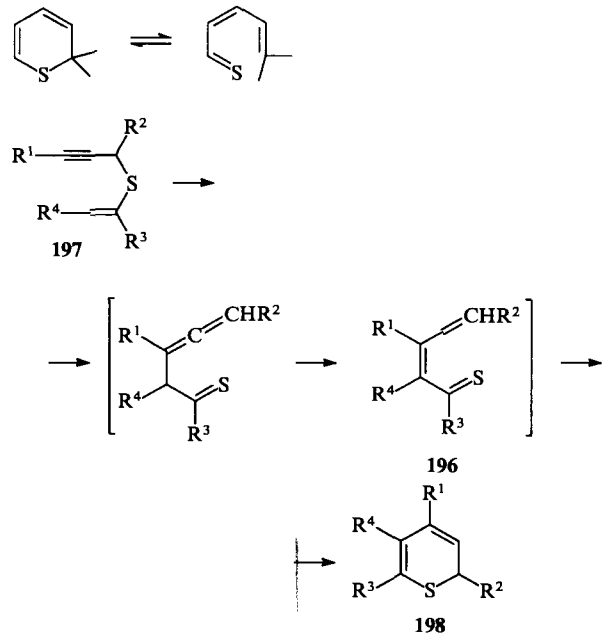


Calculations in terms of the HAM approximation explain such behaviour in the following way: the replacement of the phenyl group by an OH group increases the energy of the HOMO and lowers that of the LUMO, which diminishes the energy gap and promotes the nonadiabatic transition, lowering thereby the activation energy for the ring opening process.[160]

On the basis of calculations for the conversion of butene-1,4-dione into 1,2-dioxacyclohexadiene in terms of the MINDO/3 approximation, Pichko[138] concluded that cyclisation of this compound has a 'disrotatory' mechanism.

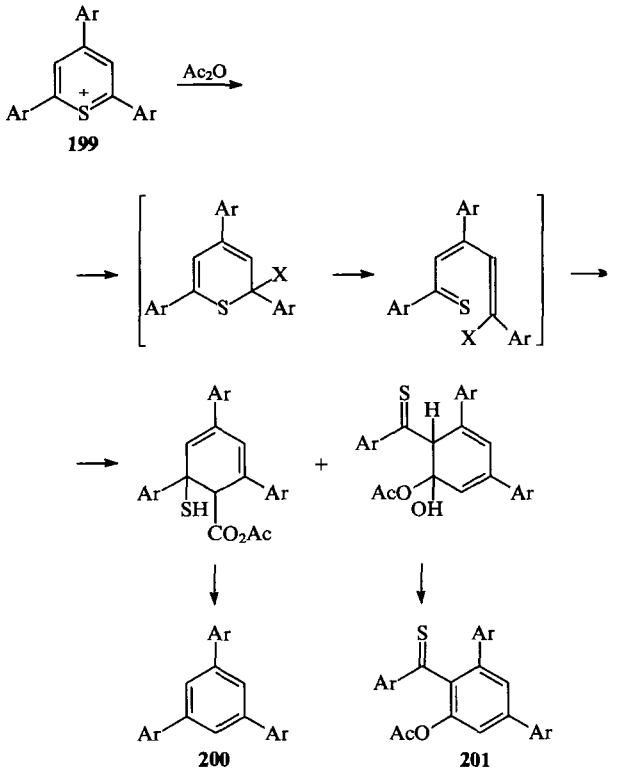
4. Reactions of sulfur-containing compounds

It has been shown by MINDO/3 calculations that thiopyrans are much more stable than their open-chain isomers.[254] Experimental data are fully consistent with the calculated results. Thus, the 1-thiahexatriene **196**, formed from the sulfide **197**, cyclises to the thiopyran **198** under the conditions of its synthesis.[4]



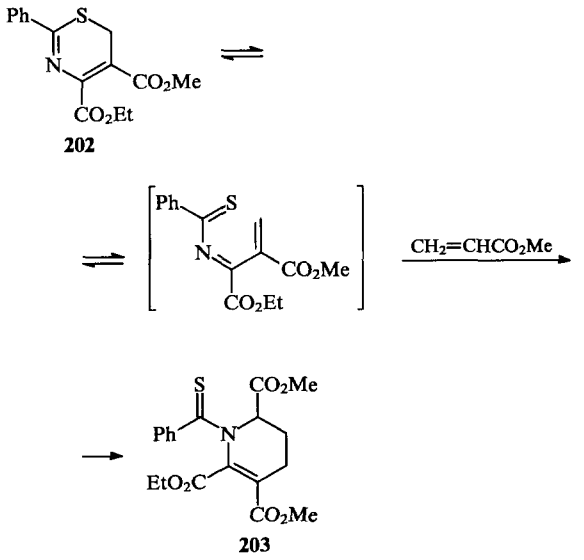
R^1, R^2, R^3, R^4 = Me, Et.

Nevertheless, the transformations of the thiopyrylium salts **199** into compounds **200** and **201** on treatment with acetic anhydride, described by Zimmermann and Fischer,[279] and of the thiazine **202** into the pyridine **203** in the presence of a dienophile[280] confirmed the possibility of the electrocyclic opening of the thiopyran ring.

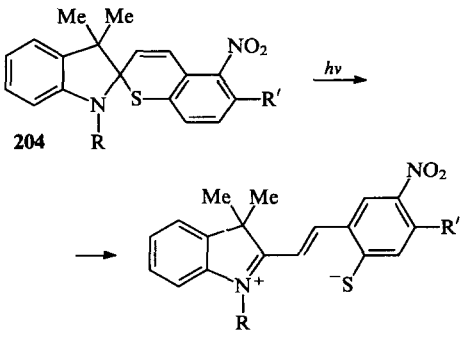


X = CH_2COOAc.

Ar = RC_6H_4, R = Ph, 4-Me, 4-MeO, 4-Cl, 4-Br.



Data concerning the manifestation of photochromic properties by the spirothiopyrans **204** — structural analogues of the spiropyrans **183** — have been published.[281] The authors[281] suggest that the photochromism of these compounds is associated with the electrocyclic opening of the thiopyran ring.

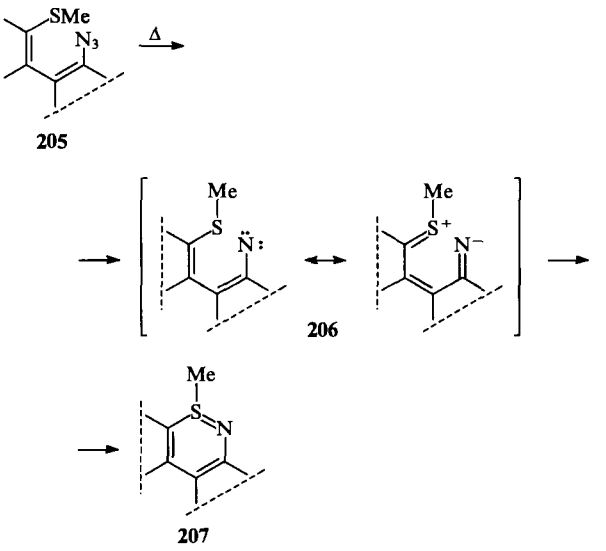


R = Me, Pr^i, $C_{18}H_{37}$,

R′ = $CH_2O_2CCMe{=}CH_2$, $CH_2OC(CH_2)_{20}Me$.

Theoretical and experimental studies[282] have demonstrated that, like thiopyrans, 1,2-dithiines are more stable than the isomeric 1,6-dithiahexatrienes.

The thermolysis of aryl, heteroaryl, and vinyl azides **205**, containing the thioether group, entails the initial formation of the nitrenes **206**, which then cyclise to the thiazines **207**.[283]



Compounds **206** may cyclise via the electrocyclic mechanism or as a result of the interaction of the lone pair of the nitrogen atom and the unoccupied orbital localised on the nitrogen atom, i.e. the heteroelectrocyclic mechanism.[5] Unfortunately, there have been no theoretical studies on this reaction.

* * *

Together with the striking advances in the application of 1,6-electrocyclic reactions in the synthesis of a whole series of different substances of practical importance and its application to achieve an understanding of the processes occurring in living nature, there have been only a few publications dealing with the study of the details of the mechanism of the 1,6-ER by computational methods.

So far it is not clear what causes the low activation energy in the reactions of hexa-1,3,5-trienes the double bond of which forms part of allene and heteroallene groups and the anomalous stability of the heteroanalogues of norcaradiene. The role of the π-system in the cyclisation of aromatic diazonium salts containing vinyl and azomethine groups in the *ortho*-position has not been discovered.

There is no doubt that the solution of these problems will lead to a fuller understanding of the characteristics of electrocyclic reactions.

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Modern problems in the high-temperature electrochemical synthesis of the compounds of Group IV – VI transition metals

V I Shapoval, V V Malyshev, I A Novoselova, Kh B Kushkhov

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Abstract. The present state of research in the field of high-temperature electrochemical synthesis of the carbides, borides, and silicides of Group IV–VI metals in ionic melts is reviewed. Modern problems in electrochemical synthesis and possible future developments are discussed. The results of recent studies of high-temperature electrochemical synthesis are reported. The bibliography includes 103 references.

I. Introduction

An increasing interest in the development of new and effective methods of preparing high-melting compounds (the carbides, boride, and silicides of Group IV–VI metals) has been stimulated by the ever increasing number of applications of these compounds in modern technology. A comparative analysis of currently available methods of synthesis of quasimetallic high-melting compounds (QHC) showed that the high-temperature electrochemical synthesis (HES) in ionic melts,[1] though inadequately investigated to date, is one of the most promising methods.

The HES of quasimetallic high-melting compounds is based on multielectron processes leading to the electrodeposition of metals and nonmetals from ionic melts.[2–4] Lack of information on the theoretical basis and on the controlling principles of both the multielectron processes and the HES had initially prevented the practical application of electrosynthesis methods. This explains the original lack of interest in these methods. However, the systematic data on the multielectron processes leading to the deposition of high-melting metals and nonmetals obtained during the last two decades have provided a scientific basis and understanding which have stimulated an increasing interest in the problems of HES.[2,5–21]

V I Shapoval, V V Malyshev, I A Novoselova Institute of General and Inorganic Chemistry of the Ukrainian National Academy of Sciences, prosp. Palladina 32/34, 252680 Kiev, Ukraine. Fax (7-044) 444 30 70
Kh B Kushkhov Department of Physical Chemistry, Kabardino–Balkarsk State University, ul. Lenina 34, 260017 Nal'chik. Fax (7-866) 222 15 85

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II. Methods of high-temperature electrochemical synthesis

1. Variants of the method of high-temperature electrochemical synthesis

The high-temperature electrochemical synthesis of QHC is based on the simultaneous or the sequential generation of multielectron electrochemical reactions resulting in the formation and deposition of the required product (carbide, boride, silicide) on the cathode. It should be noted that the presence of electronic conduction in the deposited compound is a necessary condition for the realisation of electrochemical synthesis.

There are two methods of achieving HES.[1] In the first variant the molten electrolyte contains one of the components in a molecular or an ionic form which is discharged on the electrode (consisting of the other component). The species to be discharged is either a compound of carbon, silicon, or boron which can be reduced to the elemental state on a high-melting metal cathode (electrochemical carbidisation,[22,23] silicidation,[24,25] boridation[26–28]) or an oxyanion of a high-melting metal which is reduced to the metal on a graphite cathode.[29,30] All these processes are slow even at relatively high temperatures, and they yield only compounds of variable composition in the form of coatings.

In the second variant the electrolyte contains both components, which are discharged simultaneously or sequentially on an indifferent electrode: the discharge products can then react chemically. Both theoretically and practically this variant seems more promising than the first, because it allows QHC of the required composition to be produced, either as coatings or as finely divided powders, simply by varying the electrolysis conditions (composition and temperature of the electrolyte, and current density).

2. Synthesis of the carbides of high-melting metals

The electrochemical synthesis of molybdenum and tungsten carbides was first reported by Andrieux and Weiss,[31] who obtained powders of the carbides by electrolysing a melt of composition $LiF-NaBO_2-Na_2CO_3-MO_3$ (where M = Mo, W). The stoichiometric composition of the deposited powders depended on the $[CO_3^{2-}]:[MO_3]$ concentration ratio.

The further development of the HES of carbides involved the choice of new electrolyte compositions. The conditions used in the synthesis of high-melting metal carbides are shown in Table 1. It is noteworthy that in every case the molten mixtures invariably contained fluoride, borate, or carbonate components. The high-melting metal was introduced as an oxide or as an alkali metal oxy-salt.

Table 1. Electrochemical systems and conditions for the HES of the carbides of high-melting metals.

Electrolyte	Component with high-melting metal	Component with carbon	Electrolysis parameters		T/K	Cathodic product	Ref.
			U/V	$10^{-2}i_k$/A m^{-2}			
$LiF-NaBO_2$	WO_3, MoO_3	Na_2CO_3	3		1050–1100	WC, W_2C (Mo_2C)	31
$NaF-KF-Na_2B_4O_7$	Na_2MoO_4	Na_2CO_3		86	1300	Mo_2C	32
$NaCl-NaF-NaOH-B_2O_3$, ($NaBO_2$, $Na_2B_4O_7$)	Na_2WO_4	Graphite anode		10–150	1300	WC	33
$NaF-KF-Na_2B_4O_7$	Ta_2O_5, Nb_2O_5	Na_2CO_3	0.3–0.8		1100	TaC, NbC	34
$LiF-NaF-KF$	K_2TaF_7	K_2CO_3	0.4–0.9		1023–1073	Ta_2C	34
$NaF-KF$ $LiF-NaF$ $LiF-KF$ $LiF-NaF-KF$	K_2TiF_6, R_2HfF_6, K_2ZrF_6, K_2NbF_7, K_2TaF_7, K_2CrF_6 K_3MoCl_6	K_2CO_3	1.5		973–1023	Cr, Mo, W, Nb, Ta, Ti, Zr, Hf carbides	35–41
$LiF-NaF-KF$	Na_2WO_4 or tungsten anode	K_2CO_3	1.0–1.5	2–7	973–1023	W_2C	39, 40, 45
$LiF-KF$	K_2SiF_6	Li_2CO_3		3–5		SiC	45
$LiF-NaBO_2$	K_2SiF_6	Na_2CO_3		3–5		SiC	45

An interesting method of preparing metal carbides was disclosed in an American patent.[33] Its most important feature is the omission of carbonate ions from the melt, using a dissolvable graphite anode as the source of carbon. However, the potential use of this method is limited by anodic effects on the carbon electrode and by the corrosiveness of the molten medium.

In an attempt to extend the method[33] to other carbides it was noted[36] that if the fluorides were thoroughly dried the graphite anodes did not lose mass, and no carbides were formed. This was attributed[36] to the fact that carbon can react electrochemically with the melt only in the presence of water, and therefore a variant of the HES of carbides based on the Mellors–Senderoff method was proposed.[41–49] The following are its most characteristic features: the electrolyte contains only fluoride anions; the proportion of alkali metal cations varies from 15% to 75% of the total number of cations; the melt does not contain complex formers.

These requirements are satisfied by the ternary LiF–NaF–KF eutectic. By adding potassium carbonate and oxides or halides of the high-melting metal to it, Stern and coworkers[35–40] obtained coatings of the carbides of Group IV–VI metals. However, it is doubtful whether the carbonate ion and the fluoride complexes K_2TaF_7, K_2NbF_7, K_2CrF_6, K_2TiF_6, K_2ZrF_6, and especially K_3MoCl_6 are compatible and can coexist with a LiF–NaF–KF melt. Indeed, in a later paper[44] Stern describes only the preparation of tungsten carbide using Na_2WO_4.

It has been reported[45] that silicon carbide (SiC) can be deposited electrolytically from a $NaF-KF-K_2SiF_6-Li_2CO_3$ melt in the form of powders, coatings, or dendrites.

Only one attempt to develop theoretical foundations for the electrochemical synthesis of carbides has been reported.[36] However, the mechanism of these processes was not discussed in sufficient depth.

3. Synthesis of the silicides of high-melting metals

The HES of silicides was first achieved by Dodero,[46] who synthesised the silicides of titanium, zirconium, and chromium by the electrolysis of molten mixtures of Na_2SiF_6 and K_2SiF_6 with the oxides and fluorides of titanium, zirconium, and chromium.

$TiSi_2$ was synthesised by the electrolysis of an $NaCl-KCl-K_2SiF_6-K_2TiF_6$ melt.[47] These workers[47] studied the cathodic processes involved in the deposition of $TiSi_2$ from chloride–fluoride melts.

The electrodeposition of Group IV–VI silicides from a melt containing a eutectic mixture of alkali metal fluorides, silicon (in the form of potassium silicofluoride), and the high-melting metal (in the form of its fluoride) has been described in a patent.[48] A more detailed description of the electrodeposition of tantalum silicide coatings has also been published.[49]

The conditions used in the preparation of the silicides of high-melting metals are summarised in Table 2.

4. Synthesis of the borides of high-melting metals

In 1929 Andrieux[50] described the preparation of borides by the electrolysis of molten fluorides and oxides of alkali and alkaline earth metals containing the oxides of boron and of a high-melting metal. He synthesised 17 borides, including TiB_2, ZrB_2, TaB_2, NbB_2, VB_2, and CrB_2. According to Andrieux and Barletty[51] the oxides of the high-melting metal and boron are reduced by the lithium, magnesium, or calcium initially deposited at the cathode.

More recently Andrieux and Weiss[52] reported the preparation of MoB and WB by the electrolysis of mixtures of the fluorides, oxides, and borates of alkali and alkaline earth metals containing the oxide of the transition metal.

Table 2. Electrochemical systems and conditions for the HES of the silicides of high-melting metals.

Electrolyte	Component with high-melting metal	Component with silicon	U/V	T/K	Cathodic product	Ref.
Na_2SiF_6 (K_2SiF_6)	TiO_2, ZrO_2, Cr_2O_3, fluorides Ti, Zr, Cr	Na_2SiF_6 (K_2SiF_6)	1.9–2.1	1273	$TiSi_2$, $ZrSi_2$ $CrSi_2$	46
$NaCl-KCl$	K_2TiF_6	K_2SiF_6	1.3–1.5	973	$TiSi_2$	47
$LiF-KF$	K_2TaF_7	K_2SiF_6	1.2	1023	$TaSi_2$, $TiSi_2$, $ZrSi_2$	48, 49
$NaF-KF$	K_2TiF_6					
$LiF-NaF-KF$	K_2ZrF_6					

Table 3. Electrochemical systems and conditions for the HES of the borides of high-melting metals.

Electrolyte	Component with high-melting metal	Component with boron	Electrolysis parameters		T/K	Cathodic product	Ref.
			U/V	$10^{-2}i_k$/A m^{-2}			
$M_xO_y-M_xF_y$ (M is an alkali or alkaline earth metal)	M_zO_y (M′ is a metal of Groups IV–VI)	B_2O_3	3–10	30–100	1223–1273	TiB_2, ZrB_2, NbB_2, TaB_2, Mo_2B_5, Cr_xB_y, WB	50, 51
$M_xO_y-M_xF_y$	M'_zO_y	MBO_2			1223–1323	MoB, WB	52
$CaB_4O_7-CaF_2$	Cr_2O_3	B_2O_3			1273–1372	Cr_3B_4, CrB Cr_5B_3, Cr_2B	53
$LiBO_2-NaBO_2$	TiO_2 $(Li,Na)_2TiO_3$	$LiBO_2$ $NaBO_2$		4–40	1123–1223	TiB_2	54–57
$Na_2B_4O_7$	M_2O_5 ($NaMO_3$, Na_2MO_6) M = V, Nb, Ta	$Na_2B_4O_7$ (B_2O_3)		0.2–20	1073–1273	M_3B_2, MB, (M = V, Nb, Ta)	58
NaCl–KCl	K_2TiF_6 (K_2ZrF_6)	KBF_4		10–20	973–1023	TiB_2 (ZrB_2)	59
MF	Ti (anode)	BF_3 (gas) B (anode)		1–50	810–1033	TiB_2	60
LiF–KF	K_2TiF_6 TiF_3	KBF_4		1–20	943–1073	TiB_2	62
MBO_2–MF	TiO_2	B_2O_3			1073–1173	TiB_2	63
NaCl–Na_3AlF_6–Na_2CO_3	TiO_2	$Na_2B_4O_7$		1.5×10^4	1273	TiB_2	64, 65
NaCl–Na_3AlF_6–NaOH–NaF	$ZrSiO_4$ (ZrO_2)	$Na_2B_4O_7$		120–240	1025	ZrB_2	63, 64
Na_3AlF_6–NaOH	HfO_2	$Na_2B_4O_7$		150	1323	HfB_2	65
LiF–NaF–KF	K_2ZrF_6 (ZrF_4)	B_2O_3		0.5–10	1023	ZrB_2	66
$K_2ZrF_6-KBF_4$	ZrO_2	B_2O_3		10–20	873	ZrB_2	67
KF	WO_3 (MoO_3)	KBF_4			1173–1273	W_2B_5, WB (Mo_2B_5, MoB)	68

The synthesis of a series of chromium borides of different composition has also been reported.[53] These compounds were obtained by gradual changes in the Cr_2O_3 content of the fluoride–borate melts.

The HES of borides was subsequently developed in three directions: electrolysis from purely oxide melts, from purely halide melts, and from mixed oxide–halide melts. The conditions used in the preparation of the borides of high-melting metals are summarised in Table 3.

Pure oxide melts were studied by Schlain and coworkers[54–57] in the preparation of coatings of titanium boride. They used melts of alkali and alkaline earth metal borides with added titanium oxide. Titanium or sintered TiB_2 were used as anodes. The TiB_2 anode offered more stable electrolysis conditions. The rate of deposition of the coatings was between 20 and 220 μm h^{-1}.

A method of preparing coatings of vanadium, niobium, and tantalum borides has been disclosed.[58] The authors suggest the use of a purely oxide melt based on borates: the bath was made of graphite or heat-resistant steel, the anode was the body of the bath or an electrode made of graphite, heat-resistant steel, or an alloy of vanadium, niobium, or tantalum.

Another patent[59] claims the electrodeposition of titanium and zirconium diborides (though the method is equally applicable to other borides) from the fluoride–chloride melt NaCl–KCl–K_2TiF_6(K_2ZrF_6)–KBF_4. A method of preparing coatings of TiB_2 by the electrolysis of molten salts using a soluble anode or an anode of pure boron in the presence of BF_4^- ions (introduced as gaseous BF_3 has also been disclosed.[60] The composition of the bath must include an alkali metal fluoride. A method of depositing TiB_2 coatings on various items by the electrolysis of LiF–KF–K_2TiF_6–TiF_3–KBF_4 melts has been developed.[61]

The electrosynthesis of tantalum boride from the chloride–fluoride melt KCl–K_2TaF_7–KBF_4 has been achieved,[62] and an attempt has been made to identify the mechanism of the process. A mixture of tantalum mono- and diboride or only one of these borides could be obtained by varying the composition of the electrolyte, the anodic current, and the cell voltage.

An analysis[63] of the current–voltage curves for the electrolytic dissociation of TiO_2 and B_2O_3 showed that the direct deposition of the boride TiB_2 from a fused borate–fluoride bath is the primary process. Substantial depolarisation of the cathodic process through the formation of TiB_2 is possible.

Another patent[64] proposes a method of synthesising the borides ZrB_2 and TiB_2 from melts of sodium chloride, fluoride, borate, and carbonate. A detailed description of the electrolytic preparation of metal diborides from their oxides and ore concentrates has also been given.[65]

A method of preparing zirconium diboride from a fluoride–oxide melt has been patented.[66] ZrF_4 can replace K_2ZrF_6 as the source of zirconium. Zirconium diboride has been prepared also from a fluoride–oxide melt containing only zirconium and boron components.[67] In this case the process is controlled by the concentration of B_2O_3 in the melt, and at high current densities metallic zirconium is deposited as well as the diboride.

Aleonard[68] extended Marion's method (described by Hagenmüller[53]) to the preparation of molybdenum and tungsten borides. He also used fluoride–oxide melts.

III. Modern problems in high-temperature electrochemical synthesis

An analysis of the state of problems in the HES of quasimetallic high-melting compounds has shown that (as a rule) electrosynthesis is carried out by a purely empirical choice of melt composition and of experimental conditions. The very small number of publications (approximately thirty) devoted to this problem is noteworthy.

Most of these publications dealt with the HES of titanium and zirconium borides, titanium silicides, and molybdenum and tungsten carbides. There are also a few unrelated papers on the preparation of tungsten and molybdenum borides, and of compounds of Group V metals. No information at all is available on the electrosynthesis of molybdenum and tungsten silicides, and of three-component high-melting compounds. However, in the whole of this work no reference can be found to the mechanism and to the controlling principles of the HES processes, without which the practical exploitation of the method is severely limited.

Because of these limitations studies in depth have been pursued in our laboratories during the past 15 years: their aim has been to create theoretical foundations for the HES and for the principles underlying the realisation and control of multielectron reactions, and to explain their mechanism. The following problems were formulated in order to achieve these objectives:

(1) to develop a thermodynamic basis for the high-temperature electrosynthesis of QHC, and to use it to identify possible variants and regimes of the electrosynthesis and to choose the components for the synthesis;

(2) to establish the mechanism of the electrolytic reduction of large complex anions of high-melting metals and nonmetals, and to develop the principles underlying the realisation and control of multielectron processes;

(3) to develop methods of approximating and identifying the conditions for reconciling the potentials of different processes for the deposition of the components;

(4) to define methods for controlling the form (powders, or coatings) of the cathodic deposits.

Table 4. Electrochemical systems and conditions for the HES of multicomponent high-melting compounds.

Electrolyte	Component with high-melting metal	Component with nonmetal	Electrolysis parameters		T/K	Cathode product	Ref.
			U/V	$10^{-2}i_k$/A m^{-2}			
KCl–NaCl–Na_3PO_4	Na_2WO_4 (Na_2MoO_4)	CO_2	2.5	5–20	1023	WC (Mo_2C)	79
KCl–NaCl–NaF	WO_3 ($Na_3WO_3F_3$)	CO_2	1.9	5–20	1023	WC (W_2C)	79
Na_2WO_4	Li_2WO_4	Li_2CO_3	1.8	100–170	1073–1173	WC	81
	Li_2MoO_4	Li_2CO_3	1.7	100–170	1073–1173	Mo_2C	81, 82
NaCl–LiF	Na_2MoO_4 (Na_2WO_4)	Na_2CO_3		100–1000	1073	Mo_2C (W_2C)	83, 84
KCl–KF	K_2CrO_4	K_2SiF_6 (SiO_2)	3–4		1173	Cr_3Si, $CrSi_2$	85, 89
NaCl–Na_3AlF_6	Na_2MO_4 (M = Mo, W)	SiO_2	3–4	1000	1173	M_3Si_5, MSi_2 (M = Mo, W)	86, 87
	K_2CrO_4	B_2O_3	3–4	100–300	1173	Cr_2B, CrB, CrB_4	89
	Na_2MO_4 (MO_3) (M = Mo, W)	$Na_2B_4O_7$ (B_2O_3)	3.5–4	100–300	1173	MoB_4, WB_4	90
NaCl–KCl–NaF	$TiCl_3$	KBF_4		50–150	963–1123	TiB_2	91, 92
	K_2ZrF_6	KBF_4		30–120	963–1123	ZrB_2	91
NaCl–KCl	K_2TaF_7	KBF_4		5–20	973–1023	TaB_2	95
NaCl–KCl–NaF	K_2TaF_7	K_2SiF_6		200–400	1073–1173	Ta_2Si_5	96
$Na_2B_4F_7$	Fe–M anode (M = V, Nb, Ta)	$Na_2B_4O_7$		2	1173	VB, NbB_2, TaB_2	97
NaCl–Na_3AlF_6	Na_2MO_4 (M = Mo,W)	SiO_2		130–250	1173	$M(Al,Si)_2$	98
KCl–NaCl–$MgCl_2$	Na_2MoO_4	$CoCl_2$	1.0–1.1		1023	Co_3Mo	101
KCl–NaCl–$NaPO_3$	Na_2MoO_4	$CoCl_2$ ($NiCl_2$)	1.1		1023	Co_3Mo (Ni_3Mo)	101
KCl–NaCl	Na_2MoO_4 $Na_2Mo_2O_7$	$CoCl_2$ ($NiCl_2$)	1.1		1023	Co_3Mo (Ni_3Mo)	101
	Na_2WO_4 $Na_2W_2O_7$	$CoCl_2$ ($NiCl_2$)	1.1–1.2		1023	Co_3W (NiW)	102
KCl–NaCl–NaF	$Na_3WO_3F_3$	$CoCl_2$	1.2		1023	Co_3W	102
KCl–NaCl–$MgCl_2$	Na_2MoO_4	CO_2 $CoCl_2$	1.3		1023	Co_6Mo_6C, Mo_2C	101
KCl–NaCl–$NaPO_3$	Na_2MoO_4	CO_2, $CoCl_2$	1.2		1023	Co_6Mo_6C, Mo_2C	101
KCl–NaCl	Na_2WO_4 $Na_2W_2O_7$	CO_2, $CoCl_2$	1.3		1023	W_2C, WC Co_3W_3C	102
	Na_2WO_4 $Na_2W_2O_7$	PO_2 $NiCl_2$	1.2		1023	W_2C, WC Ni_6W_6C	102
KCl–NaCl–NaF	WO_3	CO_2, $CoCl_2$	1.1		1023	Co_3W_3C	102
	WO_3	CO_2, $NiCl_2$	1.1		1023	WC, W_2C, Ni_6W_6C	102

The high-temperature electrochemical synthesis of QHC can take place in two regimes: the thermodynamic (or quasi-equilibrium) or the kinetic regime. According to a theoretical analysis of the electrochemical preparation of alloys[5] the thermodynamic regime is established when the deposition potential of the components are similar ($\Delta U \leqslant 0.2$ V). Under these conditions the composition of the alloy is independent of the current density over a wide range. In the opposite case ($\Delta U > 0.2$ V) we meet the kinetic regime, and the composition of the alloy is independent of the potential difference. In order to deposit carbides, borides, and silicides with a greater interaction energy the range of values of the potential for the thermodynamic regime is increased by G_f/zF, where G_f is the Gibbs free energy of formation of the QHC from the elements in their standard state; z is the total number of electrons contributing to the electrosynthesis of the QHC (for Mo_2C this number is $z = 16$).

The thermodynamic foundations of the HES of quasimetallic high-melting compounds and of the choice of systems for the synthesis were established by an analysis of the equilibrium potentials (voltages) for the decomposition of various compounds of high-melting metals of Groups IV–VI and of nonmetals (C, B, Si) at high temperatures (900–1200 K), using thermodynamic data obtained for these compounds.[69,70] Bartlett and Johnston[71,72] carried out a similar analysis of electrochemical processes involving the carbonate ion and carbon dioxide.

A comparison of the temperature dependences of the deposition potentials of the Group IV–VI metals and of carbon, boron, and silicon shows that those of the high-melting metals of Group IV are similar to those of boron and silicon, with a corresponding similarity between the deposition potentials of the high-melting metals of Group VI and carbon. Under these conditions the electrolysis can be carried out in the thermodynamic regime. The electrochemical synthesis of the carbides of Group VI metals and of the borides and silicides of Group VI metals is possible only in the kinetic regime, because in these systems the deposition potentials are markedly different.

A comparative study of the results obtained in studies of the elecrochemical reduction of the oxy-anions of high-melting metals and nonmetals in chloride, chloride, fluoride, and oxide melts having different acid–base properties has revealed three mechanisms for the formation of electrochemically active species:[2,3,73] the cationisation of an anion with formation of cationised species, the breakdown of an oxy-anion with formation of oxide–halide complexes, and the formation of dimeric complexes.

By constructing electrochemically active species of different structure and composition we can generate conditions enabling multielectron electrochemical processes to be realised. This approach allows us to control the rate of formation of these species in multielectron systems and the potential of the charge transfer reaction, to reconcile the potentials of different processes, and to achieve the HES of quasimetallic high-melting compounds.

Problems arising in the electrochemical synthesis of quasimetallic high-melting compounds are currently being studied by workers from various countries.[4,34,39,44,94]

The results of those workers, and those obtained by the present writers, on the electrochemical synthesis of quasimetallic high-melting compounds from various salt systems are discussed below. The compositions of the systems examined, the experimental conditions, and the compositions of the products in the HES of carbides, silicides, and borides, and also of double carbides, are shown in Table 4.

IV. High-temperature electrochemical synthesis of multicomponent high-melting compounds

1. Synthesis of molybdenum and tungsten carbide powders under an excess pressure of carbon dioxide

The potential application of the HES method can be extended by using carbon dioxide (whose concentration in the melt can be controlled by an excess pressure) as a source of carbon for the synthesis. This allows us to produce a buffer molten electrolyte based on low-melting alkali metal chlorides and having prescribed acid–base properties [cationised[74] $\{M_x^{2+}[M'O_4^{2-}]\}^{2x-2}$, dimeric[75,76] $M'_2O_7^{2-}$, fluoride oxide[77] $M'O_2F_4^{2-}$ (where M′ = Mo; W, M = Li^+, Ca^{2+}, Mg^{2+}, Al^{3+})], and to obtain a direct electrochemical synthesis of carbides in the presence of an excess pressure of carbon dioxide. The effects of the electrolyte composition, of the CO_2 pressure over the melt, of the temperature, of the cathodic current density, and of the design and materials of the electrodes on the phase composition and on the properties of the carbide powders thus obtained have now been established.[74,76] The reactions which provide the foundations of the HES and the special technological features of the process have been described.[74,78] We have developed a new design of electrolysis cell which can be used at 973–1073 K and under an excess pressure of CO_2 of up to 2×10^6 Pa. The specific surface of the powders was 6–10 $m^2\ g^{-1}$. The rate of deposition of WC in an NaCl–KCl–Na_3PO_4 electrolyte was 0.2–0.4 g $A^{-1}\ h^{-1}$ with a current yield of up to 56%; in a KCl–NaCl–NaF electrolyte the corresponding parameters were 0.35–0.52 g $A^{-1}\ h^{-1}$ and up to 75% respectively (see Table 4).[79]

2. Synthesis of highly dispersed powders of molybdenum and tungsten carbides from oxide melts

The low solubility of CO_2 in halide oxide melts allows us to work at low current densities (i_k) and to produce particles with diameters of 2–5 μm. Smaller particles (<2 μm) can be obtained in tungstate–molybdate–carbonate oxide melts by increasing i_k. The electrolytic reduction of the CO_3^{2-}, MoO_4^{2-}, and WO_4^{2-} ions in a melt of Na_2WO_4 takes place at low potentials.[75,79] This allows their simultaneous reduction, and therefore also the HES of the carbides. The specific surface of the powders is 10–20 $m^2\ g^{-1}$, the yield of product is 0.71 g $A^{-1}\ h^{-1}$, and the current yield is 93%–97%.

Graphite or vitreous carbon are used most effectively as anode material; nickel as cathode material. Highly dispersed powders often contain up to 5–7 mass% of free carbon and sorbed oxygen. Annealing the synthesised molybdenum and tungsten carbide powders in activated hydrogen almost completely eliminates the free carbon (from 7 to 0.1 mass%) and lowers the oxygen content by an order of magnitude (from 5 to 0.2–0.3 mass%).[80] The crystal lattice parameters of the monocarbide WC prepared in this way ($a = 2.906 \pm 0.003$; $c = 2.837 \pm 0.006$ Å) coincide with the accepted values.

3. Electrodeposition of molybdenum and tungsten carbide coatings from oxide and halide oxide melts

One advantage of HES over other methods of synthesis is its suitability for the production of coatings. The electrodeposition of Mo_2C coatings was achieved[75,79] from the purely oxide melt Na_2WO_4–Li_2MoO_4–Li_2CO_3. In this system the MoO_4^{2-} and CO_3^{2-} ions can be reduced simultaneously by electrolytic reduction. The experimental melts are stable, nontoxic, and nonhygroscopic, and do not require a protective atmosphere. Continuous oxides were obtained at 1073–1223 K and current densities between 10^2 and 10^3 A m^{-2}. The rate of deposition of the coating was 5–20 μm h^{-1}, the current yield of the product was up to 60%, its thickness was up to 50 μm (see Ref. 81).

The main shortcoming of oxide melts is the high concentration of tungsten and molybdenum. A eutectic NaCl–LiF melt was used in order to lower the concentration, and the deposition potentials of molybdenum, tungsten, and carbon were

determined for this medium.[82,83] The deposition potential of molybdenum from MoO_4^{2-} was 200 mV higher than the deposition of tungsten from WO_4^{2-}, and almost equal to the deposition potential of carbon from CO_3^{2-}. This accounts for the possibility of depositing coatings of Mo_2C and W_2C. The crystallisation of WC as a continuous coating could not be achieved. The rate of deposition of W_2C and Mo_2C was up to 10 μm h^{-1}, the current yield as a coating was up to 40%, the thickness up to 20 μm. The microhardness of Mo_2C was 1800–1900, that of W_2C ws 2900–3100 kg mm^{-2}.

An interesting study[84] of the effect of silver ions on the electrodeposition is relevant to the control of the structure of tungsten carbide coatings prepared from halide–oxide melts. It was established that the addition of 10^{-3} mol% of AgCl to a melt of the LiCl–KCl eutectic containing K_2CO_3 and K_2WO_4 produces [at $i_k = (2-50) \times 10^2$ A m^{-2}] hexagonal crystals of the carbides W_2C and WC instead of the needles and dendrites obtained in the absence of AgCl.

4. Synthesis of chromium, molybdenum, and tungsten silicides from halide–oxide melts

A thermodynamic analysis combined with voltammetric measurements showed that the HES of the silicides of Group VI metals can be achieved only in the kinetic regime, in which the more electropositive component (Cr_2O_3, Mo, W) is deposited first, and the other component (Si) is next deposited on its surface.[85–88] The diffuse reaction path leads to the formation of silicides of various compositions, up to the highest (MSi_2).

The $KCl-KF-K_2SiF_6-K_2CrO_4$ system has been used for the high-temperature electrochemical synthesis of chromium silicides. Depending on the composition and on the electrolysis parameters both individual phases (Cr_3Si and $CrSi_2$) and mixtures of these phases (with a small amount of free silicon) could be obtained.[85,89]

The electrochemical synthesis of molybdenum and tungsten silicides has been achieved in a molten chloride–cryolite mixture containing molybdate (or tungstate) and silica.[86,87] The HES is strongly influenced by the temperature and by the current density. Below 1123 K the reaction of the molybdenum (or tungsten) with the silicon does not go to completion, and at higher temperatures (>1223 K) the stability of the metallic salt deposit decreases. When $i_k < 5.6 \times 10^3$ A m^{-2} the product is contaminated by free metal, and when $i_k > 1.2 \times 10^3$ A m^{-2} a phase of the double silicide $(Al,Si)_2M$ appears (where M = Mo, W). The specific surface of the powders is 5–15 m^2 g^{-1}, the particle size is 0.5–2.0 μm, the rate of deposition of $MoSi_2$ is 0.2–0.3, that of WSi_2 is 0.3–0.45 g A^{-1} h^{-1}.

5. Synthesis of chromium, molybdenum, and tungsten borides from halide–oxide melts

The large difference between the electrodeposition potentials of chromium,[85] molybdenum,[86] and tungsten[87] from a chloride–cryolite melt containing sodium chromate (molybdate, tungstate) and the deposition potentials of the oxide fluoride complexes of boron[89] from the same systems, which can be as high as 0.7–0.8 V, suggests that the HES of the chromium, molybdenum, and tungsten borides can be carried out only in the kinetic regime. The electrochemical synthesis of chromium borides was achieved from a chloride–cryolite melt containing chromate and boron oxide.[89] Depending on the composition of the melt and on the electrolysis parameters both the individual phases (Cr_2B, CrB, CrB_4) and their mixtures could be obtained. The yield of the single-phase product CrB_4 was 0.14–0.21 g A^{-1} h^{-1}, the specific surface was 8–17 m^2 g^{-1}.

The electrochemical synthesis of molybdenum and tungsten borides was achieved from a molten chloride–cryolite mixture containing molybdenum (or tungstate) or molybdenum (or tungsten) oxide, and borax (or boric oxide).[90] The synthesis process was optimised by establishing the regimes leading to the production of the single-phase higher boride MB_4, which offers the most valuable physical and mechanical properties. At concentrations of B_2O_3 and $Na_2B_4O_7$ between 10 and 20 mass% complete boridation of the high-melting metal is observed, with formation of the MoB_4 and WB_4 phases. The yield of these products is 0.2–0.3 and 0.3–0.45 g A^{-1} h^{-1} respectively, and the specific surface of both powders is 5–15 m^2 g^{-1}.

6. Synthesis of titanium, zirconium, and hafnium borides from halide melts

The possible use of chloride and chloride–fluoride melts (containing not more than 10 mass% of fluoride) for the HES of titanium and zirconium borides has been studied.[91] It was found that the formation of MB_2 on the cathode (where M = Ti, Zr) is accompanied by a substantial energy effect [?overpotential. (Ed. of Translation)] of 0.32 for TiB_2 and 0.38 V for ZrB_2 (at 973 K). The potentials at which the synthesis takes place depend on the difference between the reduction potentials of the components, i.e. on the form of the electrically active species. In the BCl_3-TiCl_4, MBF_4-MTiF_6, $MBF_4-M_2TiF_6$, BCl_3-ZrCl_4, MBF_4-ZrCl_4, and $MBF_4-M_2ZrF_6$ systems (in a melt of KCl–NaCl) the difference between the deposition potentials of the high-melting metal and of boron is not more than 0.2 V. The HES conditions are chosen by varying the cation/anion composition of the electrolyte. By changing the electrolysis parameters we can obtain titanium and zirconium diboride powders having surface areas between 1×10^3 and 5×10^4 m^2 kg^{-1}, or continuous coatings up to 20 μm thick (see Table 4). The quality of the coatings is improved by carrying out the process in the refining regime with a MB_2 anode. The mechanism of the cathodic processes taking place during the HES of titanium diboride has been examined in detail.[92]

It was found[93] that the HES of hafnium diboride is possible only in the thermodynamic regime. In addition to the waves produced by the electrolytic reduction of the complexes of tervalent boron with quadrivalent hafnium, a wave at potentials more positive than the discharges of BF_4^- and HfF_6^{2-} by 0.1 and 0.35–0.4 V respectively was observed in a voltammetric study of the $NaCl-KCl-KBF_4-K_2HfF_6$ system. It was tentatively attributed to complex species: heteronuclear complexes produced by the interaction of the complexes of hafnium(IV) and boron(III). Coatings of hafnium diboride having a microhardness of 3200 ± 250 kg mm^{-2} were produced in this study.

7. Synthesis of the borides and silicides of vanadium, niobium, and tantalum from halide melts

It has been shown[94] that the borides of Group V metals can be prepared by HES from chloride–fluoride melts. Thermodynamic calculations led to the conclusion that the borides of the vanadium subgroup are characterised by a kinetic synthesis regime from chloride and fluoride melts. The conditions and regime for the synthesis of TaB_2 from chloride–fluoride melts and the potential regions for the deposition of tantalum, boron, and tantalum diboride have been determined[95] as a function of the activity of the fluoride ion in the melt. It was concluded from voltammetric measurements that conditions consistent with the thermodynamic synthesis regime can be achieved by varying the anion composition of the electrolyte (see Table 4).

The conditions and the regime of the synthesis of powdered Ta_5Si_3 from chloride–fluoride melts and the deposition potentials of Ta, Si, and Ta_5Si_3 have been determined[96] as a function of changes in the acid–base properties of the melt. It was concluded from voltammetric measurements that the thermodynamic synthesis regime applies in this case.

The electrodeposition of the borides of elements in the VA subgroup is described in a patent.[97] The method combines the following procedures: preparation of the borate melt, saturation of the melt with compounds of the elements from the VA subgroup by anodic dissolution of Fe–M alloy anodes (where M = V, Nb, Ta), and cathodic treatment of the articles to be coated. VB, NbB_2, and TaB_2 coatings were produced.

8. Electrochemical synthesis of the double silicides of molybdenum (or tungsten) and aluminium

When chloride–cryolite melts are electrolysed to deposit the disilicides of molybdenum and tungsten increasing the current density produces deposits of the double disilicides $M(Al, Si)_2$, where M = Mo, W.[98] If the chloride–cryolite melt contains more than 1.5 mass% of Na_2MO_4 the product contains molybdenum (or tungsten) disilicide and metallic molybdenum (or tungsten). If the concentration of Na_2MO_4 is less than 0.5 mass% some free silicon appears in the product, and in the concentration range $0.5 < [Na_2MO_4] < 1.5$ mass% silicon–aluminium alloys are formed. Depending on the current density the specific surface of the disilicide powders lies in the range 11.3–15.2 $m^2\ g^{-1}$ (see Table 4).

9. Synthesis of two-component intermetallic compounds based on molybdenum(tungsten) and cobalt(nickel)

Construction materials and coatings based on the high-coercivity wear and corrosion resistant W–Co, W–Ni, Mo–Co, and Mo–Ni alloys have recently stimulated wide interest. They are usually prepared by electrodeposition from aqueous solutions.[99] However, this method has several shortcomings: the concentration of nonmetals (O_2, N_2, H_2) in the final product is high, the rate of deposition is low ($i_k \leqslant 1 \times 10^3$ A m^{-2}), and alloys of constant composition cannot be obtained. The use of melts avoids these shortcomings.

Nickel and cobalt are much more noble (electropositive) than molybdenum and tungsten. Furthermore, to achieve the HES of intermetallic compounds based on molybdenum(tungsten) and cobalt we must find a method of bringing their deposition potentials closer together, and conditions compatible with their simultaneous discharge. This can be done by controlling the electrolytic reduction potential of the $[MO_4^{2-}]$ anions through acid–base interactions. We used the cationisation of the oxide complexes $\{M'_x[MoO_4^{2-}]\}^{2x-2}$ (where $M' = Ba^{2+}$, Ca^{2+}, Mg^{2+}), which are decomposed with formation of dimeric[75,76] and halide oxide complexes.[100] In the case of the Mg^{2+} cation it is possible to superpose the electrolytic reduction waves of Co^{2+} and $\{Mg_x[MoO_4^{2-}]\}^{2x-2}$ and to bring the deposition potentials of cobalt and tungsten to within 300 mV of each other (see Refs 100 and 102). Better results were obtained for the decomposition of $[MO_4^{2-}]$, in which the corresponding processes can be exactly superposed.[101,102]

These studies led to the choice of three systems for the synthesis of binary alloys based on molybdenum and two systems for tungsten alloys (see Table 4).

10. Synthesis of three-component hard alloy compositions

In powder metallurgy cobalt and nickel powders, which act as a binder component, are added to the charge when articles of molybdenum or tungsten carbide are made by hot pressing. This fact, and other unique properties of the ternary alloys, stimulated the search in the $WO_3–CO_2–CoCl_2$ system[102] for conditions which allow the simultaneous electrodeposition of carbon, tungsten(molybdenum), and cobalt(nickel), aimed at the HES of binary carbides. From the results of a study[103] of the electrolytic reduction of CO_2 dissolved in halide melts under an excess pressure systems for testing the possibility of bringing together the deposition waves of carbon from CO_2, of cobalt(nickel) from the $[MCl_4]^{2-}$ complex, and of molybdenum(tungsten) from various complex ionic forms were chosen. The simultaneous deposition of three components [carbon, molybdenum(tungsten), and cobalt(nickel)] was realised in systems with differences in discharge potential not greater than 200 mV. In the latter case the CO_2 acts not only as a source of carbon but also as an acidic additive which shifts the molybdenum(tungsten) deposition potential towards more positive values.

The compositions of the liquid electrolytes and the conditions for the synthesis are summarised in Table 4. In all the systems potentiostatic electrolysis is applied, at the potentials corresponding to the simultaneous deposition of the three components. A pure binary carbide was obtained only in one system. The yield of the single-phase product Co_3W_3C is 0.4–0.6 g $A^{-1}\ h^{-1}$, the particle size is 0.3–1.0 μm. Evidently the composition of the three-component alloy and its purity are determined by several factors: the ratio of the partial currents of the reacting components, the energetics of their interaction, and the possibility of parallel reactions between two components. The latter reactions are responsible for the presence of impurities of high-melting metal carbides.

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The Smiles rearrangement of *o*-aminophenyl phenyl ethers

T N Gerasimova, E F Kolchina

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Abstract. A systematic account is given of the literature data on the Smiles rearrangement of *o*-aminophenyl phenyl ethers including data obtained by means of model studies on polyfluoro-derivatives. Attention is concentrated on the influence of the structure of *o*-aminophenyl phenyl ethers on their reactivity. The bibliography includes 51 references.

I. Introduction

The Smiles rearrangement plays an important role in the synthesis of condensed heterocyclic systems comprising activated aromatic halo-compounds and asymmetric bifunctional nucleophiles. In a general form, it can be represented by Scheme 1, which includes the inversion of the side chain in a type **1** structure.[1–3] An activated aromatic or heteroaromatic ring is the migrating residue, while the side chain may be part of the aromatic system.

Scheme 1

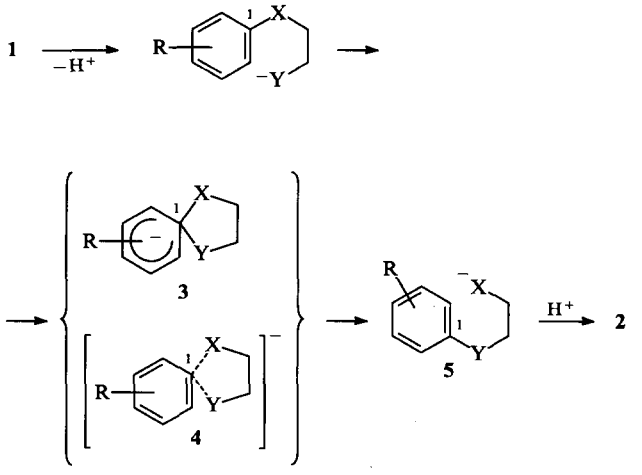


1 **2**

Transformations of this kind were first investigated by Smiles and co-workers in 1931 in relation to *o*-hydroxy-derivatives of diaryl sulfones and sulfides.[4] Later the Smiles rearrangement was extended to a large number of aromatic derivatives with different combinations of groups X and YH and the most important factors affecting its rate were determined: activation of the migrating aromatic ring, mobility of the substituting group, nucleophilicity of the attacking centre, and acidity of the functional group YH.[1,2]

The Smiles rearrangement is usually carried out in a basic medium. The proposed reaction mechanism includes the YH ionisation stage and nucleophilic attack by the anion Y^- on the 1-position in the aromatic ring accompanied by the formation of an intermediate Meisenheimer spiro-complex **3** or the transition state **4** (Scheme 2).[1,2]

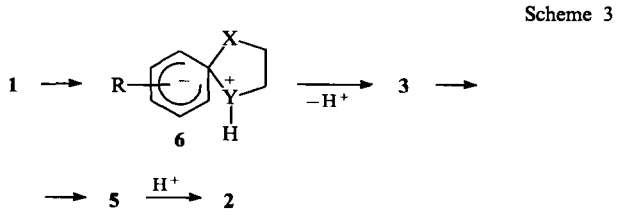
Scheme 2



The type **3** intermediates, including those with the functional groups X and Y linked by the *o*-phenylene fragment, were isolated or detected in solution by spectroscopic methods.[5–8] The Smiles rearrangement can occur as a reversible process,[1,2] which presupposes the irreversibility of the formation stages and of further reactions of the intermediate **3** and is most probable when the nucleophilicities of the centres X and Y are similar.[6]

Examples of the Smiles rearrangement which do not require the presence of bases and which occur without preliminary ionisation of the group YH are known. In such cases, the nucleophilic attack by the latter on the 1-position leads to the formation of a type **6** zwitterionic spiro-complex which is then converted into the intermediate **3** via deprotonation (Scheme 3).

Scheme 3



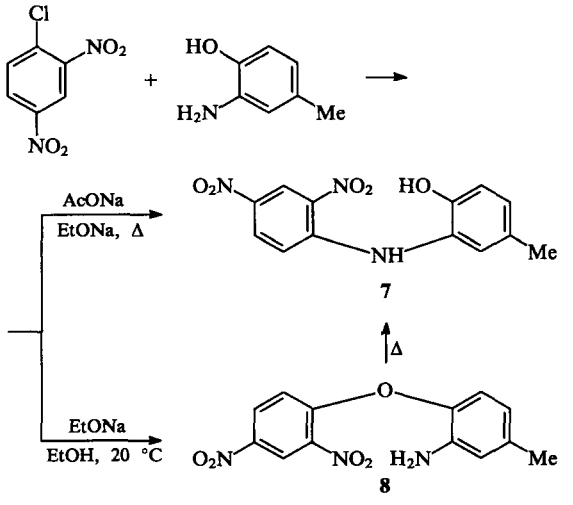
T N Gerasimova, E F Kolchina Laboratory of Organic Photosensitive Materials. Novosibirsk Institute of Organic Chemistry, Siberian Division of the Russian Academy of Sciences, prosp. akad. Lavrent'eva 9, 630090 Novosibirsk, Russian Federation. Fax (7-383) 235 47 52. Tel. (7-383) 235 79 96 (T N Gerasimova)

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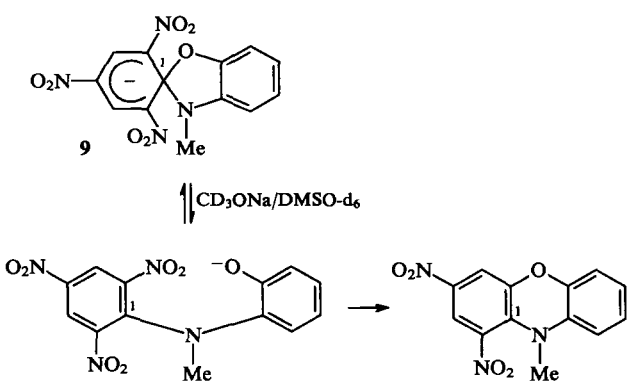
The rearrangement of *o*-aminophenyl phenyl ether to aryl(*o*-hydoxyaryl)amines, discovered and first investigated by Roberts and de Worms,[9] belongs to transformations of this kind. It has been demonstrated on numerous examples that this rearrangement plays a significant role in the synthesis of phenoxazines from aromatic polynitrohalo-compounds and *o*-aminophenols, preceding the final intramolecular cyclisation stage and determining the structure of the reaction products.[2,10,11] In the 1960s, a series of unexpected aspects of this reaction were discovered.[12,13] However, in a review[2] devoted to the Smiles rearrangement the data concerning the transformations of *o*-aminophenyl phenyl ethers were treated systematically to an inadequate extent. This factor as well as the results of our investigations in recent years, obtained by extending the Smiles rearrangements to aromatic polyfluoro-compounds,[14] led us to write the present review.

II. Rearrangement of *o*-aminophenyl phenyl ethers

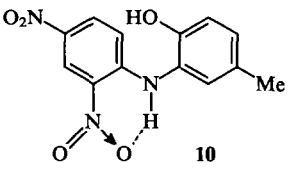
It was shown in 1934[9] that the interaction of 1-chloro-2,4-dinitrobenzene with 2-amino-*p*-cresol affords either the diphenylamine **7** or the diphenyl ether **8**, depending on the reaction conditions. On heating, compound **8** rearranges to the amine **7**. The reaction takes place in basic and hydroxyl-containing solvents (pyridine, aniline, alcohols, etc.) and is retarded in an alkaline [sic] medium. According to the authors,[9] the rearrangement of the ether **8** takes place without the preliminary ionisation of the amino-group, i.e. proceeds via Scheme 3.



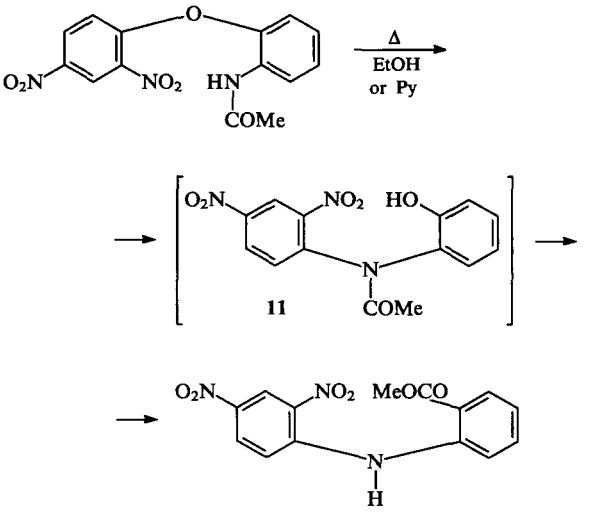
It is assumed that aryl(*o*-hydroxyaryl)amines do not undergo the Smiles rearrangement.[1,2,15-19] The reversible formation of the spirocyclic complex **9** from *N*-methyl-*N*-picryl-2-aminophenol has been established by spectroscopic methods.[5,20] Presumably the absence of the Smiles rearrangement in the given instance is due to the relative ease of the dissociation of the C(1)–O bond with formation of a stable phenoxide anion.



The rearrangement of the ether **8** to the amine **7** is not accompanied by cyclisation and the formation of a phenoxazine. This feature, which has been explained by the formation of an intramolecular hydrogen bond stabilising the unreactive structure **10**,[18,21,22] made it possible to observe the Smiles rearrangement 'in a pure form' and helped to discover the influence of the nature of the substituents at the nitrogen atom and in the aromatic rings on the rate of the transformation.

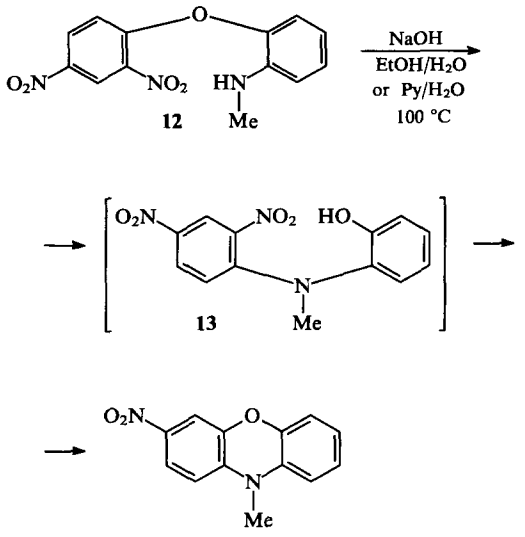


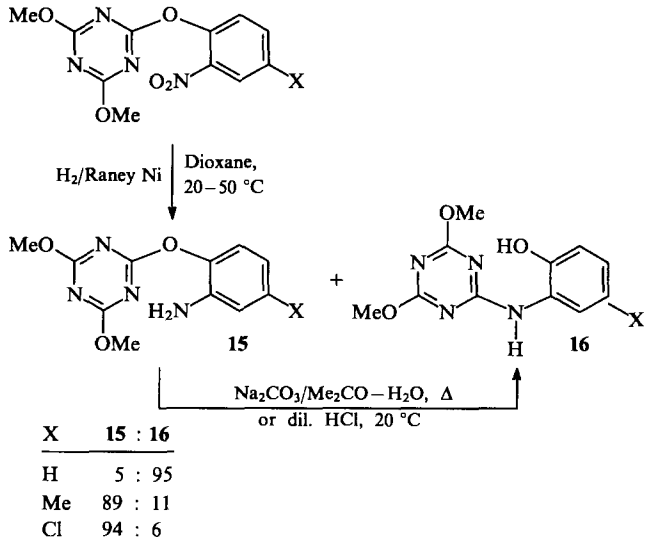
It has been shown that the higher the electron-accepting capacity of the acyl residue the greater the lowering of the rate of rearrangement caused by the *N*-acylation of *o*-aminophenyl ethers. Since the rearrangement of *o*-*N*-acyl-substituted diphenyl ethers takes place in a neutral medium, one may suggest that it takes place via Scheme 3.[9,23] The Smiles rearrangement is accompanied in this case by the migration of the acyl residue from the nitrogen atom to the oxygen atom, tentatively in accordance with a stepwise mechanism via the intermediate *o*-hydroxyamine **11**.[24]



The introduction of the electron-donating *N*-methyl group into the molecule of 2-aminophenyl 2,4-dinitrophenyl ether also lowers its capacity for the rearrangement. Thus compound **12** is stable under the conditions of the transformation of the NH_2 analogue and leads slowly to *N*-methyl-3-nitrophenoxazine only on heating in an alkaline solution.[25] The *para*-location of the nitro-group and of the heterocyclic nitrogen atom in the molecule of the phenoxazine formed indicate that the cyclisation stage is preceded by the rearrangement to the diphenylamine **13**. The latter is unstable under the reaction conditions because an intramolecular hydrogen bond, of the kind stabilising the NH_2 analogue, cannot be formed.[21,25]

Although the rearrangement of the *N*-methyl-substituted ether **12** requires an alkaline medium, its occurrence via Scheme 3 is most likely. The activating effect of alkali is apparently manifested in the stage involving the conversion of the zwitterionic type **6** spiro-complex into the intermediate **3**. The reaction mechanism involving the deprotonation of the spirocyclic complex as the rate-limiting stage had been established earlier as a result of a kinetic study of the rearrangement of 2-aminophenyl 2,4-dinitrophenyl sulfide[26] and of a series of similar processes.[8,27,28]



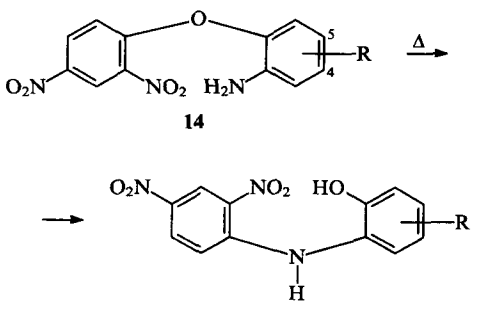


X	15 : 16
H	5 : 95
Me	89 : 11
Cl	94 : 6

The influence of substituents in the ring carrying the amino-group on the rearrangement of *o*-aminophenyl phenyl ethers is fairly complex and not unambiguous. When Scheme 3 operates, the rearrangement should be facilitated by substituents increasing the basicity of the attacking amino-group or stabilising the phenoxide anion formed. The study of the rearrangement of type **14** ethers showed that the highest rate of transformation is attained for R = H; the introduction of a substituent of any kind into the *para*- or *meta*-position relative to the amino-group slows down the reaction, the greatest effect being manifested in the case of 5-methyl-substituted compounds (Table 1).[29,30]

Table 1. The durations of the rearrangement of the diphenyl ethers **14** in the 4:1 acetic acid–pyridine mixture at 50 °C.

R	*t*/min	R	*t*/min	R	*t*/min
4-H	5	4-Cl	60	5-H	5
4-Me	7	4-Br	30	5-Me	90
4-OMe	13	4-I	15	5-I	7
4-NH_2	50				

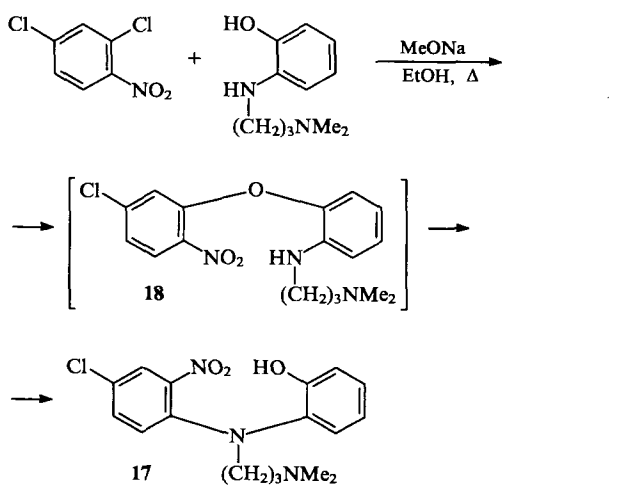


The direct dependence of the rate of rearrangement on the sum of the Hammett constants $(-\sigma_m + \sigma_p)$ of the substituent X has been discovered similarly for *o*-aminophenoxytriazines **15**, which are partly converted into the amines **16** during their synthesis by the reduction of the corresponding nitro-compounds: H(0) > Me (−0.101) > Cl (−0.146).[31]

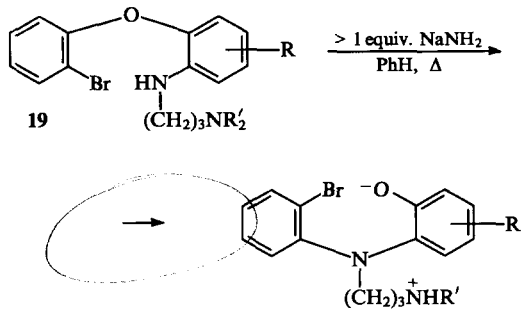
On this basis, the activation of the migrating aryl residue was recognised as the most important factor determining the possibility of the occurrence of the Smiles rearrangement.[1,2] The rearrangements of *o*-aminophenyl phenyl ethers were investigated mainly in relation to 2,4-dinitro-derivatives.[9,23,25] We are not aware of any attempts to achieve them for mononitro-analogues.

Data on the synthesis and reactions of the picryl ether of 2-amino-*p*-cresol, presented by Roberts and de Worms,[9] have been quite justifiably questioned by Drozd and coworkers.[20] As already mentioned above, the possibility of the occurrence of the Smiles rearrangement as a result of migration of an activated heterocyclic residue has been demonstrated in a number of studies.[31–33] Thus prolonged maintenance of the ether **15** (X = H) in acetone in the presence of sodium carbonate leads to its complete transformation into the amine **16**. A characteristic feature of the rearrangement in this case is the fact that it is catalysed not only by a base but also by an acid.[31] The catalytic effect of the acid is apparently associated with the enhancement of the electron-accepting capacity of the migrating ring by the protonation of the heterocyclic nitrogen atom.[34] The replacement of the methoxy-groups in compound **15** by the more electron-donating diethyl amino-groups suppresses the rearrangement.[31] However, the need for a high degree of activation of the migrating ring for the occurrence of the Smiles rearrangement of *o*-aminophenyl phenyl ethers was soon questioned.

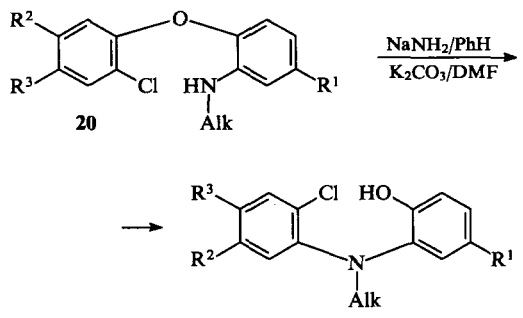
In 1961, Bonvicino et al.[22] suggested that the reaction involving the formation of aryl(*o*-hydroxyaryl)amino **17** from *o*-*N*-(3-dimethylaminopropyl)phenol and 2,4-dichloro-1-nitrobenzene involves the rearrangement of the intermediate ether **18**.



In conformity with this hypothesis, they carried out the rearrangement of the ether **19** by refluxing it in benzene in the presence of an excess of sodium amide.[12]



This is the first example of the Smiles rearrangement with a halogen atom as the activating group. According to the authors,[12] it is determined by the higher nucleophilicity of the N-anion formed from the *N*-alkylamino-group under the reaction conditions. Indeed, 2-amino-5-chlorophenyl 2-bromophenyl ether, which gives rise to a somewhat less nucleophilic N-anion, does not change on prolonged refluxing with sodium amide in xylene.[22] However, it was shown later that type **20** ethers, which also do not contain strong electron-accepting groups in the molecule, do undergo the rearrangement on refluxing in dimethylformamide (DMF) in the presence of potassium carbonate, i.e. under conditions which in all probability do not ensure the formation of N-anions.[13,35] Examples of the nonactivated Smiles rearrangement in the presence of a base have been described also for other classes of compounds, but have not so far been explained convincingly.[2,13,36,37]



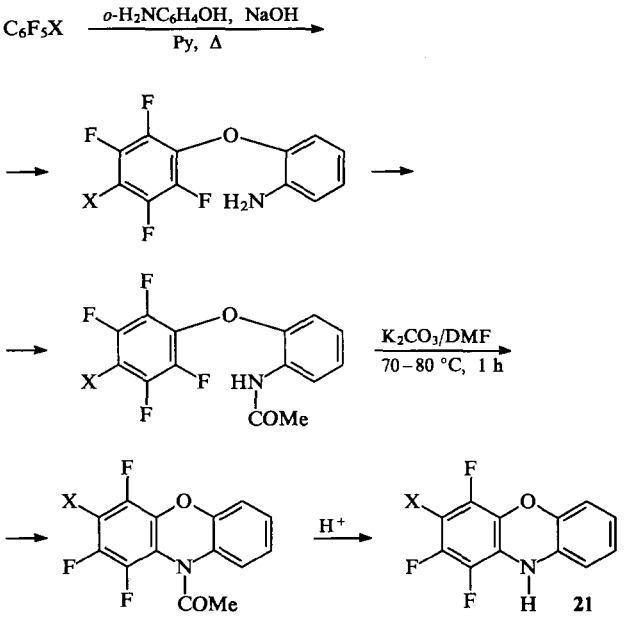
R^1, R^2, R^3 = H or Cl

Alk = CH_2Ph, $(CH_2)_3NMe_2$

On the whole, systematic studies by Roberts and also subsequent investigations quoted in the present review make it possible to outline the limits of the applicability of the Smiles rearrangement among *o*-aminophenyl phenyl ethers and to establish certain characteristics of the influence of structural factors on this process. However, the mechanism and elementary stages of the rearrangement remain unelucidated. There have also been no kinetic studies. This is partly due to the fact that in most cases the rearrangement of *o*-aminophenyl phenyl ethers is accompanied by side reactions, in the first place intramolecular nucleophilic cyclisation to phenoxazine derivatives.[2,10] There are not many examples of its observation 'in a pure form'. In our view, the problem of the synthesis of systems with a specified structure and the difficulty of analysing the reaction mixtures and of the determination of the structures of the product formed are also complicating factors. Polyfluoro-substituted *o*-aminophenyl phenyl ethers of the type 4-$XC_6F_4OC_6H_4NHY$-2', which can be readily synthesised from the simplest polyfluorobenzenes and *o*-aminophenol, are convenient objects from this point of view.[38-40] These ethers contain a fluorinated aromatic ring, the electron-accepting properties of which can be readily varied by altering the substituent X. The possibility of employing ^{19}F NMR spectroscopy for the analysis of the reaction mixtures and the identification of the products is a great advantage of the fluoro-compounds.

III. The Smiles rearrangement of aromatic polyfluoro-compounds

The Smiles rearrangement of aromatic polyfluoro-compounds was first observed by the present authors in the synthesis of polyfluorinated derivatives of phenoxazine from the compounds C_6F_5X and *o*-aminophenol.[41] It was shown with the aid of ^{19}F NMR spectroscopy that the molecule of the phenoxazine **21** (X = H or Cl) contains the OAr group and the substituent X in the *meta*-positions relative to one another. The change in the relative positions in the intramolecular cyclisation stage suggested that the formation of the phenoxazine system is preceded by the Smiles rearrangement.



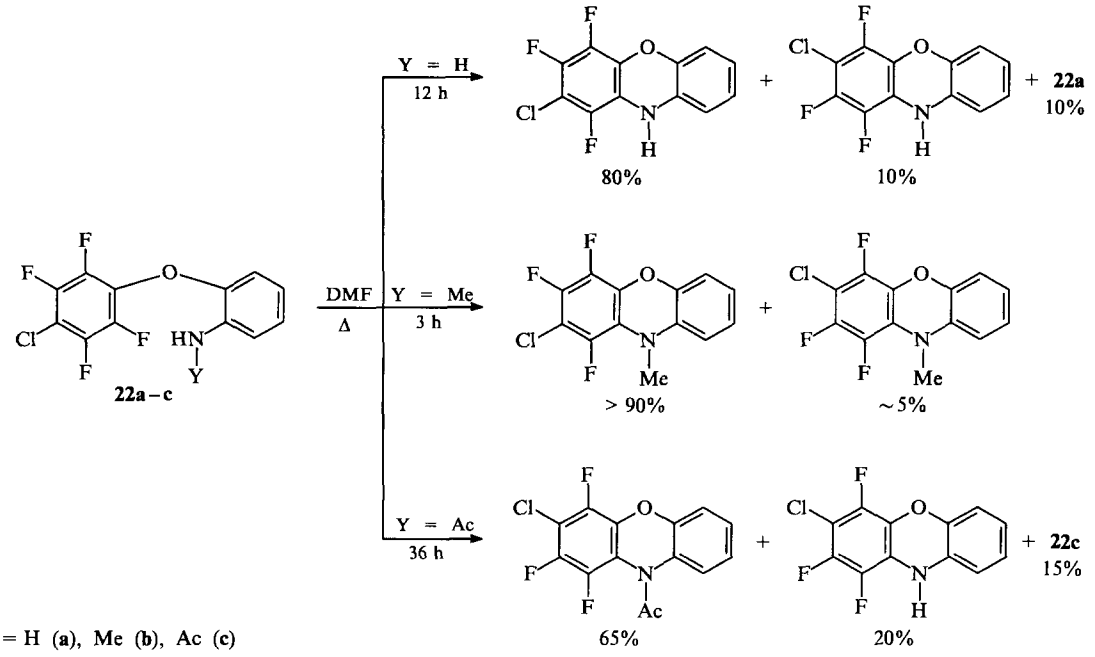
X = F, H, Cl

The transformations of polyfluorinated *o*-aminophenyl phenyl ethers have been investigated in detail in relation to compounds **22a-c** containing a chlorine atom in the fluorinated part of the molecule and the NHY group (Y = H, Me, Ac) in the nonfluorinated part.[14,42] It was shown that their refluxing in DMF leads to cyclisation to phenoxazines as a result of intramolecular nucleophilic substitution of the *ortho*-fluorine atom. The *N*-alkyl-substituted ether **22b** reacts faster, while the *N*-acetyl derivative **22c** reacts significantly more slowly than compound **22a**, which contains the NH_2 group (Scheme 4).

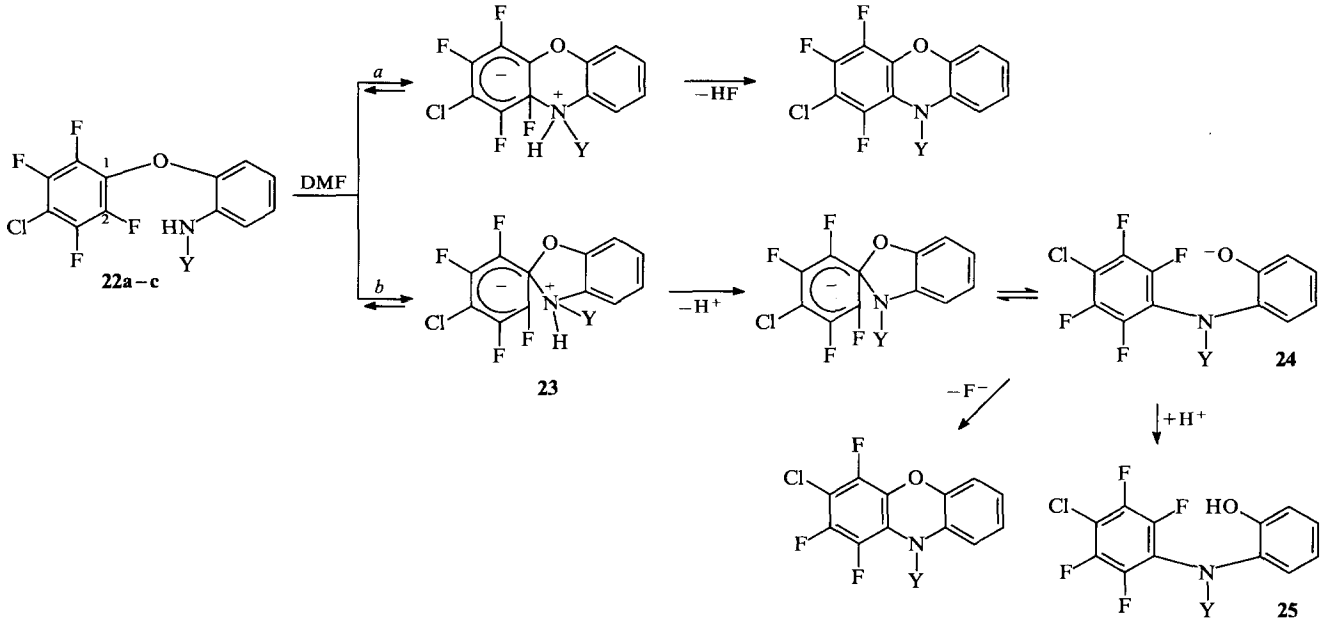
The structure of the phenoxazines formed indicates two reaction paths (Scheme 5): nucleophilic cyclisation as a result of the attack by the nitrogen atom on the 2-position with subsequent elimination of the fluoride ion (path *a*) and cyclisation with preceding Smiles rearrangement (path *b*). The second path is preferred because it involves the attack by the nucleophile on the most electrophilic C(1) carbon atom in the *para*-position relative to the chlorine atom, which agrees with the rules governing the directing effect in aromatic polyfluoro-compounds.[43,44]

The reaction path is determined by the nature of the group NHY. In the case of the ether **22c**, the molecule of which contains the comparatively weakly nucleophilic acetamido-group, the reaction proceeds wholly via path *b*. The diphenyl ethers **22a, b** are cyclised predominantly as a result of the

Scheme 4

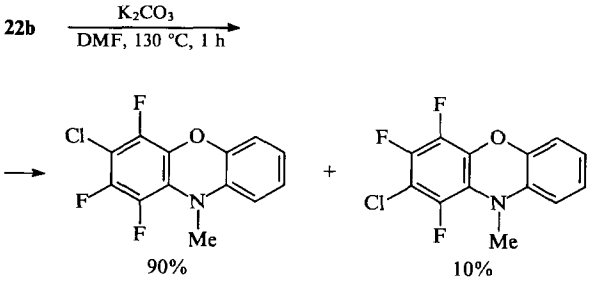


Scheme 5

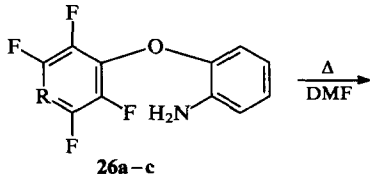


substitution of the fluorine atom in the 2-position in the fluorinated ring without the Smiles rearrangement. Such a change in the reaction path in the case of compounds containing more nucleophilic reaction centres (NH_2 and MeNH groups) is caused, in our view, by the greater difficulty in the second stage of process *b*, namely the deprotonation of the spiro-complex **23**. An essential condition for the occurrence of path *a* is the reversibility of the stage involving the formation of this complex.

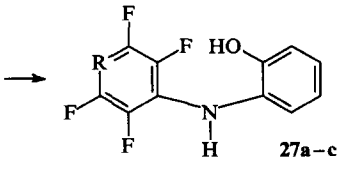
As already mentioned in the preceding section, examples of the Smiles rearrangement with deprotonation of the spiro-complex as the rate-limiting stage have been described in the literature. It has been shown that such processes are susceptible to general base catalysis.[26–28] Accordingly, the introduction of potassium carbonate into the reaction of the ether **22b** drives the process predominantly via path *b*.



The only argument in support of the occurrence of the Smiles rearrangement in the case of the ethers **22a–c** is the structure of the phenoxazine derivatives formed from them. The corresponding aryl(*o*-hydroxyaryl)amines **25**—the rearrangement products—were not detected in the reaction mixtures. Presumably the introduction into the *para*-position of the fluorinated aromatic ring of the diphenyl ether molecule of an additional electron-accepting group, increasing the electrophilicity of the reaction centre 1 compared with the centre 2, makes it possible to reduce the reaction temperature and to stop the process at the rearrangement stage. Indeed, heating in DMF of type **26** ethers, containing a powerful electron acceptor in the *para*-position relative to the oxygen atom, led to the formation of the isomeric aryl(*o*-hydroxyaryl)amine **27**. Analysis of the ^{19}F NMR spectra of the reaction mixtures showed that the rearrangement is the only type of reaction.[45,46]



26a–c



27a–c

R = C—NO_2, C—CF_3, N

This made it possible to measure the rate of reaction of the ethers **26** when they are kept in DMF in the temperature range 60–120 °C and to estimate in this way their relative capacities for the Smiles rearrangement. The reaction rate constants were calculated from the first-order equation

$$k = \frac{1}{t}\ln\left(\frac{c_0}{c}\right) = \frac{1}{t}\ln\left(1 + \frac{H_a}{H_e}\right),$$

where t is the time, H_a is the integral intensity at the signals due to the F(3) and F(5) atoms [or F(2) and F(6)] in the ^{19}F NMR spectrum of the amine **27**, and H_e is the integral intensity of the signal due to the F(6) and F(5) atoms [or F(2) and F(6)] in the ^{19}F NMR spectrum of the ether **26** (Table 2).

Table 2. The rate constants for the rearrangement of the *o*-aminoaryl aryl ethers 4-$RC_6F_4OC_6H_4NH_2$-2′ **26a–c** in DMF.

Compound **26** (R)	Temperature/°C	Reaction rate constant $10^4 k/s^{-1}$
26a (C–NO_2)	60	2.17
	70	3.93
	80	7.59
	90	12.20
26b (C–CF_3)	90	0.12
	100	0.21
	110	0.53
	120	1.03
26c (N)	70	0.82
	80	1.66
	90	3.34
	100	7.21

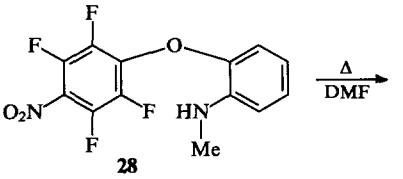
The activating effect of the group R in the rearrangement of the ether **26** increases in the sequence (the relative rate constants at 90 °C are indicated in brackets) C–CF_3(1) < N(27) < C–NO_2(100) and corresponds to the influence of these groups on the rate of the nucleophilic substitution of the fluorine atom by an amino-group in aromatic polyfluoro-compounds.[47,48]

Roberts and coworkers[9,29] noted the activating effect of water on the rearrangement of *o*-aminophenyl phenyl ethers in aprotic solvents. At the same time, it is known that the addition of water to polar aprotic solvents can reduce the rate of the Smiles rearrangement.[28] Kinetic measurements on the rearrangement of the ethers **26** in DMF containing 20% of water showed that its influence on the rate of reaction is determined by the nature of the substituent R (Table 3). A catalytic effect has been observed for compounds **26a, c**. As in the case of 2-amino-4-methylphenyl 2,4-dinitrophenyl ether,[9] it may be due to the formation of hydrogen bonds with a substituent and the consequent enhancement of its electron-accepting properties. In conformity with this hypothesis, the rate of rearrangement of the ether **26b**, containing the CF_3 group in the molecule, is somewhat lower in aqueous DMF than in dry DMF.[46]

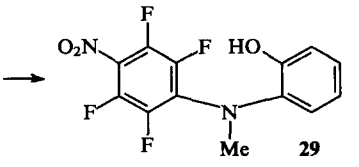
Table 3. The rate constants for the rearrangement of the *o*-aminoaryl aryl ethers 4-$RC_6F_4OC_6H_4NH_2$-2′ **26a–c** in the 80:20 DMF–H_2O mixture.

Compound **26** (R)	Temperature/°C	$10^4 k/s^{-1}$	$\frac{k_{DMF\cdot H_2O}}{k_{DMF}}$
26a (C–NO_2)	60	11.8	5.4
26b (C–CF_3)	100	0.15	0.7
26c (N)	70	1.01	1.2

The influence of *N*-substituents on the rearrangement of polyfluoro-substituted *o*-aminophenyl phenyl ethers has been investigated in relation to the derivatives of the ether **26a**.[14,42,48] The rate of rearrangement of the *N*-methyl-substituted ether **28**, which is unambiguously transformed into the isomeric amine **29** on heating in DMF, was measured by a procedure similar to that described for compound **26**.



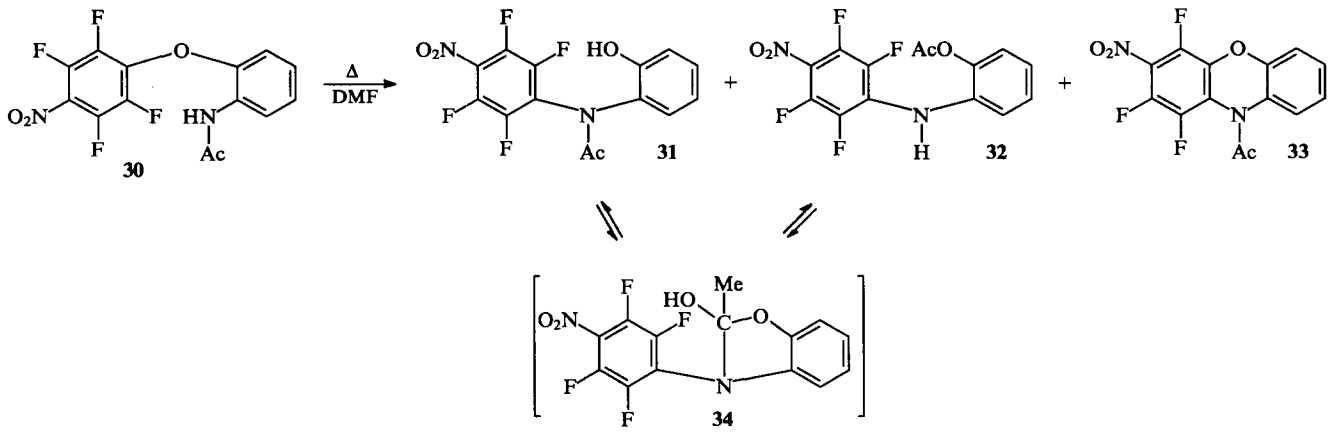
28



29

A mixture of three compounds (compounds **31–33**) has been obtained from the acetamido-substituted diphenyl ether **30**. The formation of the amine **31** indicates the occurrence of the Smiles rearrangement. The presence of compound **32** in the reaction mixture is evidence that the rearrangement is accompanied by the migration of the acetyl group from the nitrogen atom to the oxygen atom.[49,50] A similar rearrangement had been observed earlier for nonfluorinated compounds,[9,24,25] but, in contrast to its dinitro-analogue **11**, the amine **31** was not only detected in the reaction mixture but was also isolated in a pure form. The dissolution of any of the isomeric compounds **31** and **32** in DMF leads to the rapid (during the dissolution and measurement of the ^{19}F NMR spectra) formation of a **31**:**32** = 3:1 equilibrium

Scheme 6



mixture. The data of Pavlova and Rachinskii[51] suggest that the migration of the acetyl group from the N atom to the O atom, observed under these conditions, takes place via the cyclic structure **34** (Scheme 6).

The fact that heating of the diarylamine **31** in DMF under the conditions of the transformation of the ether **30** does not lead to the phenoxazine **33** is very interesting. The presence of the latter in the reaction mixture obtained from the ether **30** is in all probability caused by the cyclisation of the intermediate type **24** phenoxide anion (see Scheme 5).

The Smiles rearrangement precedes the formation of compounds **32** and **33**. This makes it possible to estimate its rate by studying the kinetics of the consumption of the initial ether **30**. The rate of its transformation was determined from the time variation of the integral intensities of the signals due to the fluorine atoms in the ^{19}F NMR spectrum. The rate constant was calculated from the first-order equation

$$k = \frac{1}{t}\ln\left(\frac{c_0}{c}\right) = \frac{1}{t}\ln\left(\frac{H_0}{H}\right),$$

where t is the time, H_0 the initial integral intensity of the signals due to the F(3) and F(5) atoms [or F(2) and F(6)] in the ^{19}F NMR spectrum of the initial ether **30**, and H is the integral intensity of the signals due to the same atoms in the ^{19}F NMR spectrum at time t. The rate constants found for the rearrangement of compounds **28** and **30** and the ether **26a** at 90 °C are presented in Table 4.[14]

Table 4. The rate constants for the rearrangement of the diaryl ethers 4-$NO_2C_6F_4OC_6H_4NHY$-2′ in DMF at 90 °C.[14]

Compound	NHY group	Reaction rate constant, $10^4 k/s^{-1}$
26a	NH_2	12.2
28	NHMe	7.40
30	NHAc	1.32

Thus both the *N*-methyl-substituted ether **28** and the *N*-acetyl derivative **30** rearrange in DMF more slowly than compound **26a** containing a free amino-group in the molecule. The observed effect of *N*-substitution may be interpreted within the framework of the mechanism based on Scheme 4 and agrees with the hypothesis, put forward above, that variation of the substituent alters the rate-limiting stage in the Smiles rearrangement. Whereas the rate-limiting stage for the acetamido-compound **30** in a neutral medium involves in all probability the formation of a type **23** zwitterionic complex, the rate of the process for compound **28**, containing the more nucleophilic *N*-methylamino-group, may be determined by deprotonation[28] and in both cases the introduction of a base into the reaction sphere should have an activating effect. Indeed the transformation of the ethers **28** and **30** in the presence of potassium carbonate takes place below room temperature. The rearrangement of the ether **26a** is apparently of an intermediate type.

Thus the use of model aromatic polyfluoro-systems combined with ^{19}F NMR spectroscopy made it possible to expand greatly the possibilities for the study of the Smiles rearrangement of *o*-aminophenyl phenyl ethers and to obtain primary kinetic data concerning the influence of the nature of the reactants on the rate of reaction. Further development of studies on these lines may not only make a significant contribution to investigations of the Smiles rearrangement, but will undoubtedly promote the practical employment of the reactions of aromatic polyfluoro-compounds with bifunctional nucleophiles in the synthesis of a wide variety of fluoro-substituted heteroaromatic systems.

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S-Cationoid reagents in organic synthesis

I V Koval'

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Abstract. The review is devoted to the methods of preparation, properties, and applications in organic synthesis of compounds of divalent, tetravalent, and hexavalent sulfur which may bear a positive charge on the sulfur atom, such as sulfenium, sulfonium, and sulfoxonium (oxosulfonium) reagents. The bibliography includes 178 references.

I. Introduction

During the last 10 – 15 years, the development of the chemistry of organic compounds of sulfur has been characterised by the extensive application of S-cationoid reagents, which play the extremely important role of active intermediates in many synthetic reactions, such as, for example, the selective oxidation of alcohols, the transfer of various functional groups, the introduction of a carbon – carbon double bond, the generation of radical-cations, ylides, etc. Such intermediates play an extremely important role in biological methylation processes occurring in living organisms[1,2] and also in processes involving the cleavage of peptides at the methionine units.

The majority of the S-cationoid reagents are unstable under the usual conditions, so that they are generated and employed as a rule in situ during the chemical reaction. Of the S-cationoid intermediates known at the present time, sulfonium salts have been the most thoroughly investigated. Convenient preparative methods of synthesis of the latter have been developed, their physicochemical properties have been investigated comprehensively, and their synthetic applications have been discovered. Some of the sulfonium salts, for example dimethylbromosulfonium bromide, dimethylchlorosulfonium chloride, dimethyl(*N*-succinyl)sulfonium chloride, etc., have entered the reference literature on preparative organic chemistry as important reagents for organic synthesis.

The interest manifested in sulfonium salts induced at the relevant time the appearance of a series of review publications,[1-3] which fully reflected the state of the chemistry of sulfonium salts during that period, but by now many new S-cationoid reagents have appeared and will be considered in the present review (the literature up to 1993 inclusive is considered).

I V Koval' Department of Chemical Technology of Macromolecular Compounds, Ukrainian Chemico-Technological University, prosp. Gagarina 8, 320005 Dnepropetrovsk, Ukraine.
Fax (7-056) 247 33 16. Tel (7-056) 247 24 91

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II. Cationoid sulfenium reagents

The cationoid sulfenium reagents include complexes having the general formula RS^+Y^-, in which the sulfenium cation RS^+ (R = Alk, Ar) is stabilised by an anionoid species Y^- of the type BF_4^-,[4-9] $SbCl_6^-$,[10] ClO_4^-,[11-13] etc.

$$RSX + MY \longrightarrow RS^+Y^- + MX$$

R = Me, Ph; X = Cl, Br; M = Ag, Li;

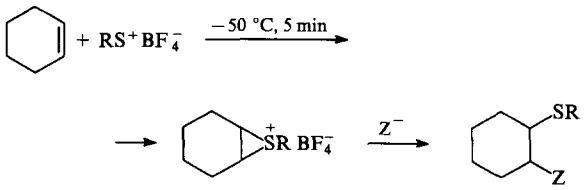
Y = BF_4, ClO_4, $SbCl_6$.

According to Cappozzi et al.,[14] the problem of the structure of these complexes still remains unsolved. In connection with the relatively low stability of cationoid sulfenium reagents, they are generated in situ in inert organic solvents (methylene chloride, nitromethane, dichloroethane) at low temperatures (−50 to −20 °C). Their synthesis is based on an exchange reaction.

The resulting solutions of cationoid sulfenium reagents are relatively stable in the temperature range indicated and are used in the synthesis of polyfunctional sulfides. These syntheses are based on the electrophilic addition of cationoid sulfenium reagents to alkenes and the subsequent interaction of the intermediate episulfonium cations with nucleophiles introduced into the reaction medium in the last stage.[4,5]

The use of cationoid sulfenium reagents in reactions with alkenes makes it possible to carry out the electrophilic addition in two stages, the stages involving the addition of the electrophile RS^+ and the nucleophile Z^- being separated in time and independent of one another (Scheme 1).

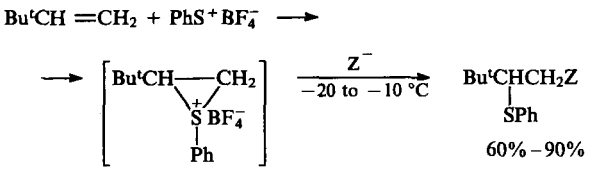
Scheme 1



R = Me, Ph; Z = OH, MeO, Cl, Br, OAc, $(EtCO_2)_2CH$, AcNH.

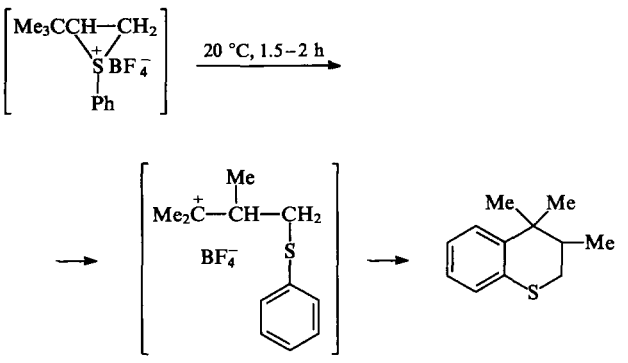
It is noteworthy that, in the addition of cationoid sulfenium reagents to alkenes with a branched structure, it is possible to direct the addition reaction towards the formation of products with a rearranged skeleton. For example, the episulfonium ion formed in the reaction of *tert*-butylethene with the complex

$PhS^+BF_4^-$ reacts at −20 to −10 °C with nucleophiles, affording polyfunctional sulfides in 60%–90% yields.[4]

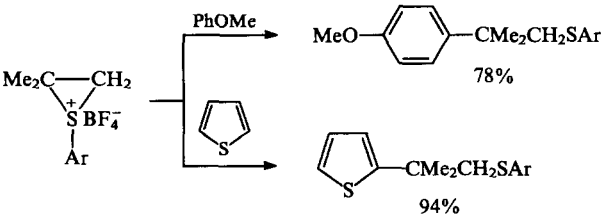


Z = OH, OMe, $MeCO_2$, H, $(EtCO_2)_2CH$, NEt_2.

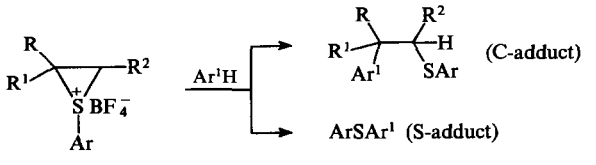
However, if the solution of the episulfonium complex obtained at −20 °C is maintained at 20 °C for 1.5–2 h, the main reaction product is 3,4,4-trimethylthiochroman regardless of the nature of the nucleophile Z,[4] which is due to the rearrangement of the episulfonium complex at the higher temperature to an intermediate carbonium ion, which in fact participates in the alkylation reaction.



It has been shown[9,15] that the stable *S*-arylepisulfonium complexes are capable of reacting not only with active nucleophiles but also with aromatic π-donors, which greatly expanded the limits of the applicability of the cationoid sulfenyl reagents in the synthesis of polyfunctional sulfides. For example, the interaction of episulfonium complexes with certain aromatic and heterocyclic compounds takes place in the absence of catalysts under mild conditions (−20 to 0 °C) in accordance with the general mechanism of the Friedel–Crafts reaction and leads to the formation of aryl(heteroaryl)-substituted sulfides.[15]

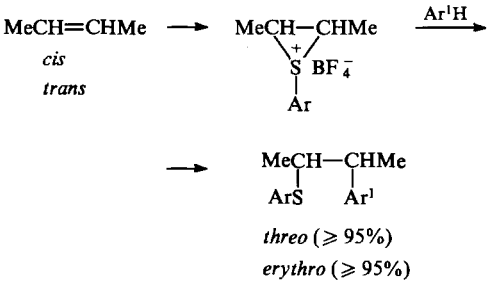


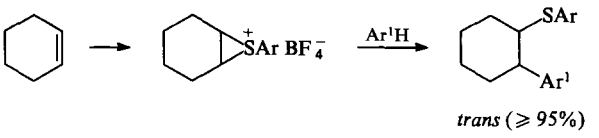
However, one should note that the reactions of the episulfonium complexes with aromatic compounds do not take place unambiguously, especially in the case of nonactivated aromatic compounds. This is due to the ambident nature of the episulfonium cation, which may react with the aromatic π-donor with participation of both a carbon atom (to form C-adducts) and the sulfur atom (to form S-adducts).[15]



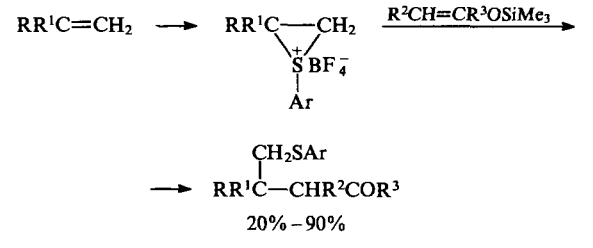
R, R^1, R^2 = H, Alk.

This disadvantage may be eliminated to some extent by varying the nature of the substituent at the sulfur atom. Thus in the reaction of the *S*-mesitylepisulfonium complex with aromatic compounds, the yield of the S-adduct does not exceed 5%–10%.[9] In the interaction of asymmetric episulfonium complexes with aromatic compounds, adducts of the Markovnikov type are formed exclusively, while in the case of the episulfonium complexes obtained from *cis*- or *trans*-but-2-ene and cyclohexene the stereochemistry of the products corresponds to the stereospecific anti-opening of the episulfonium ring by the aromatic π-donor, which indicates, according to Ibragimov and coworkers,[15,16] that the reaction proceeds via the intermediate formation of a bridged carbenium ion and not an open-chain β-arylthiocarbenium ion.

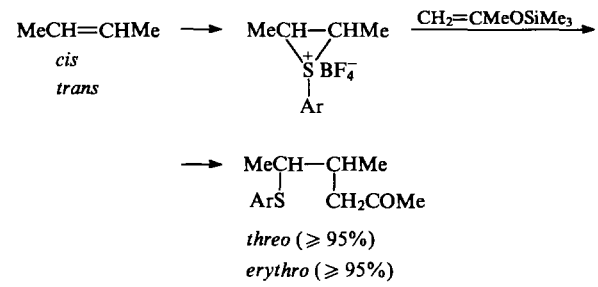




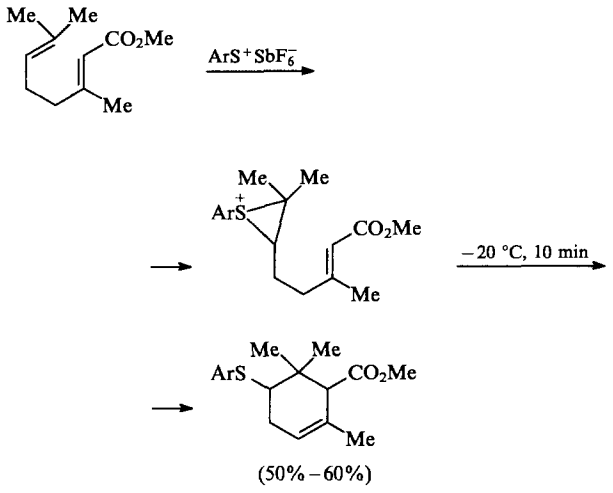
The trimethylsilyl ethers of enols proved to be active π-donors in reactions with episulfonium complexes. It has been shown[9,16] that the episulfonium complexes interact with such ethers even at −30 °C (1–2 h), affording γ-carbonyl-substituted sulfides, the structure of which corresponds to the Markovnikov and *trans*-stereospecific opening of the episulfonium ring by the nucleophile.

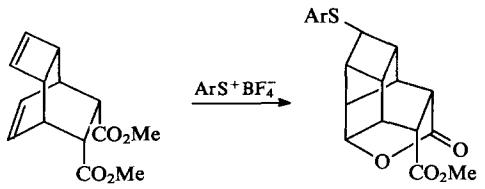


R = Me, Ph, H; R^1 = H, Me; R^2 = H; R^3 = Ph; R^2+R^3 = $-(CH_2)_4-$.

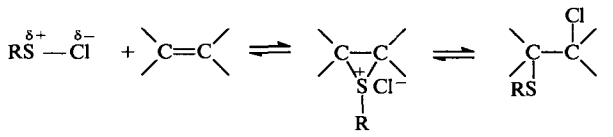


In the interaction of cationoid sulfenium reagents with dienes, the intermediate episulfonium cation may react with the π-electron system of the second double bond, giving rise to cyclic products.[9]

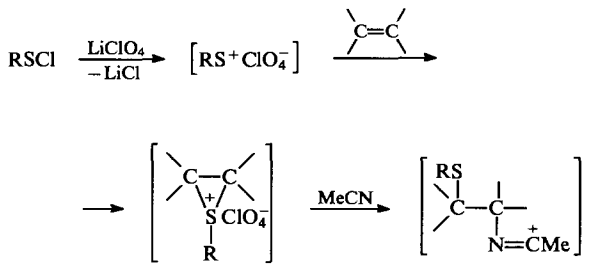




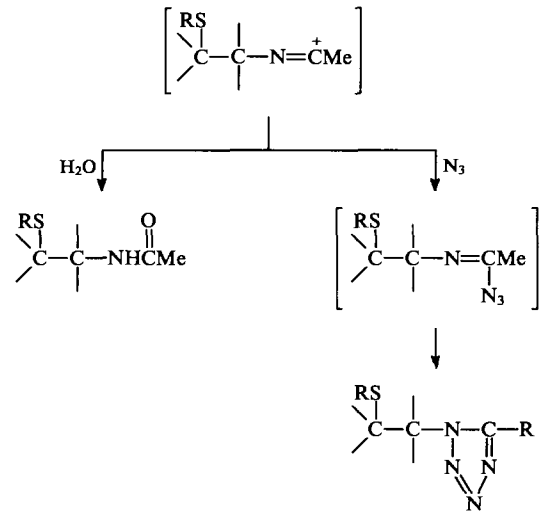
It is known[1] that the addition of sulfenyl chlorides to alkenes proceeds in accordance with the Ad_E2 mechanism, in which the cationic intermediate is the episulfonium cation—a weak electrophile which does not react with weak nucleophiles.



The method of the coupled addition of sulfenyl chloride to alkenes in the presence of a strong electrophile, for example lithium perchlorate, developed by Zefirov and coworkers,[11–13] is therefore of special interest. In this case, the sulfenyl chloride reacts even with acetonitrile, which is a weak nucleophile.



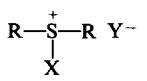
The immonium ion formed under these conditions is converted into the final products on treatment with various reagents.



R = Ph, 4-MeC_6H_4, 4-ClC_6H_4, 2-$NO_2C_6H_4$, 2,4-$(NO_2)_2C_6H_3$.

III. Sulfonium reagents

A characteristic feature of divalent sulfur compounds, for example sulfides, is their ability to react with electrophiles, which is due to the presence of a free electron pair at the sulfur atom by virtue of which the atom can participate in the formation of a third covalent bond. The positive charge arising at the sulfur atom is as a rule stabilised by the negative charge of the anion. The compounds formed under these conditions have the general name of sulfonium salts and are divided into several types depending on the nature of the groups surrounding the sulfonium centre: trialkyl(aryl)sulfonium, halosulfonium, aminosulfonium, alkoxysulfonium, aryloxysulfonium, acyloxysulfonium, alkyl(aryl)thiosulfonium salts, etc.



R = Alk, Ar; Y = Cl, Br, BF_4, ClO_4 etc.;

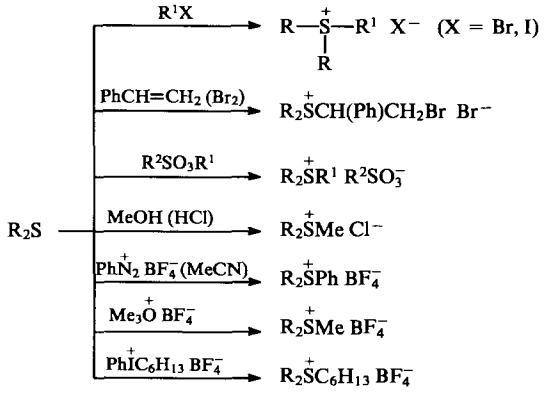
X = Alk, Ar, Cl, Br, I, F, OAc, NR'_2, OR', SR' (R' = Alk, Ar).

1. Trialkyl(aryl)sulfonium salts

a. Methods of synthesis of trialkyl(aryl)sulfonium salts

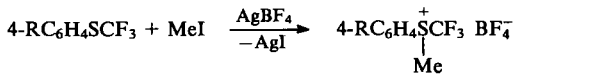
Preparation from sulfides. The alkylation (arylation) of sulfides by aryl halides,[12,17–19] alkenes,[2,20] sulfonic acid esters,[21,22] alcohols,[23] and diazonium,[2] oxonium,[2] and iodonium[24] salts is very frequently used to obtain trialkyl(aryl)sulfonium salts (Scheme 2).

Scheme 2



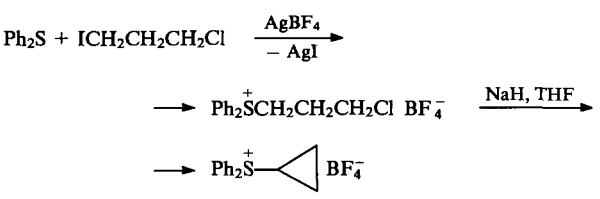
Dialkyl sulfides react with alkyl halides relatively easily, whereas diarylsulfides, as well as sulfides containing strongly electron-accepting groups at the sulfur atom, are alkylated by alkyl halides only in the presence of catalysts ($FeCl_3$, $AgBF_4$, etc.). For example, despite the reduced nucleophilicity of the sulfur atom in aryl trifluoromethyl sulfides, the latter were methylated by methyl iodide in methylene chloride in the presence of $AgBF_4$ (Scheme 3).[25,26]

Scheme 3

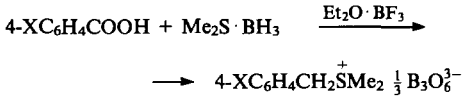


R = H, Me, Cl, NO_2.

The same catalyst has been used in the synthesis of cyclopropyldiphenylsulfonium tetrafluoroborate.[27,28]

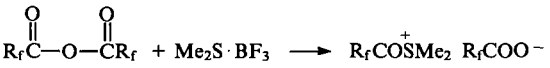


In the synthesis of trialkyl(aryl)sulfonium salts, the complexes of sulfides with BH_3 and BF_3 as well as various systems based on sulfides are used instead of the sulfides themselves. The reduction of aromatic carboxylic acids by the borane–dimethyl sulfide complex has been described.[29] The reduction products then react with dimethyl sulfide in the presence of boron trifluoride etherate to form the corresponding sulfonium salts.

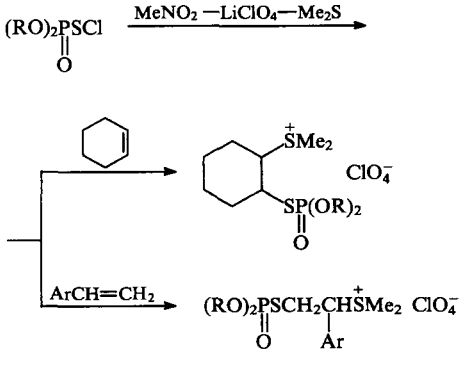


X = MeO, HO, H_2N.

The complex between Me_2S and BF_3 reacts relatively easily with the anhydrides of perfluorocarboxylic acids to form the corresponding sulfonium salts.[30]

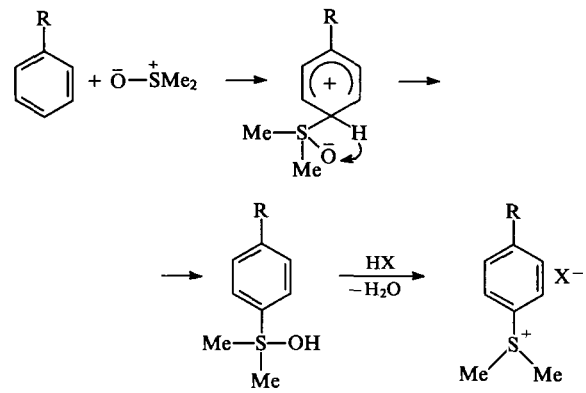


It has been shown[31] that the addition of dialkoxyphosphonylsulfenyl chlorides to ethene hydrocarbons in the presence of the $MeNO_2$–$LiClO_4$–Me_2S system leads to sulfonium salts containing dialkoxythiophosphonyl groups.



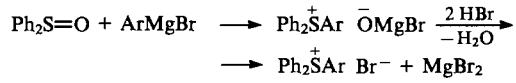
R = Me, Pr^i; Ar = Ph, 4-$MeOC_6H_4$.

Preparation from sulfoxides. By virtue of the presence of the electron-deficient sulfur atom, dialkyl sulfoxides react as electrophiles with an aromatic ring activated by electron-donating groups (OH, OR, etc.), forming dialkylarylsulfonium salts.[1] The reaction is catalysed by a strong inorganic acid (HCl, H_2SO_4, etc.).



R = OH, OR; X = Cl, HSO_4.

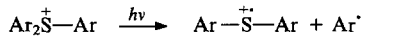
Triarylsulfonium salts are formed in the reaction of diphenyl sulfoxides with arylmagnesium bromides.[1,2]



It has been noted[32] that, in the interaction of dimethyl sulfoxides with 5-R-6-methyl-2,4-diphenyl-3-azapyrylium perchlorate in acetic anhydride, the product is a sulfonium salt, which is converted on heating in alcohol into the salt $PhCH_2NHC(Ph)=C(R)COCH_2S^+Me_2\ ClO_4^-$.

b. Applications of trialkyl(aryl)sulfonium salts in organic synthesis.

Generation of sulfonium radical-cations. One of the characteristic features of trialkyl(aryl)sulfonium salts is their photolytic instability. On irradiation with UV light at a certain wavelength, they are cleaved, affording a mixture of products. The primary step in the photolytic process is the homolysis of one of the three C–S bonds with formation of sulfonium radical-cations, which give rise to secondary photolysis products on interaction with the solvent or solutes. For example, on pulsed laser irradiation, the photolytic cleavage of triarylsulfonium salts begins with the homolysis of the Ar–S bond.[33]



The diarylsulfonium radical-cations formed in this process are initiators of the polymerisation of alkenes.[33]

On irradiation of the sulfonium salt $(4\text{-}Bu^tOCOOC_6H_4)_3S^+.CF_3SO_3^-$ with light at wavelengths of 254 and 266 nm in acetonitrile or dimethylformamide (DMF), the sulfonium radical-cation $(4\text{-}Bu^tOCOOC_6H_4)_2S^{\cdot+}$ and trifluoromethanesulfonic acid are formed as the primary reaction products. Their further reactions lead to the sulfide $(4\text{-}HOC_6H_4)_2S$ and the sulfonium ions $(4\text{-}Bu^tOCOOC_6H_4)_2S^+(C_6H_4OH\text{-}4)$, $(4\text{-}HOC_6H_4)_3S^+$, and $(4\text{-}HOC_6H_4)_2S^+(C_6H_4OOCOBu^t\text{-}4)$.[34]

The photolysis of the isomeric sulfonium salts $RMeS^+PhSbF_6^-$ (R = 1-, 2-, 9-$C_{14}H_9$), which proceeds on UV irradiation at wavelengths in the range from 260 to 400 nm, has been described.[35] The primary step in the photolysis is the homolysis of the Me–S bond accompanied by the formation of the sulfonium radical-cation $PhRS^{\cdot+}$, the interaction of which with the solvent leads to acid products.

Generation of sulfonium ylides. The deprotonation of trialkylsulfonium salts by a base B is one of the commonest methods for the generation of sulfonium ylides.[36]

$$Me_3S^+ + B \rightleftharpoons Me_2\overset{+}{S}-\bar{C}H_2 + BH^+$$

The mobility of the proton in the alkyl group of the sulfonium salt depends on many factors and in the first place on its acidity, the nature of the solvent, and also on the presence of other substances in the solution. Various combinations of bases and solvents, such as aqueous solutions of NaOH or KOH in the presence of tetraalkylammonium halides,[36,37] KOH in dimethyl sulfoxide (DMSO),[28,30] sodium hydride in tetrahydrofuran (THF)[28] or in DMSO,[36] *tert*-butyllithium in THF,[38] potassium *tert*-butoxide in THF,[2,28] and sodium dimethyl sulfoxide in DMSO or THF [36,39] are used to increase the mobility. In the presence of strongly electron-accepting groups in the α-position in the alkylsulfonium salt, the ylide may be formed even on treatment with organic bases, such as, for example, 1,5-diazabicyclo[5.4.0]undec-5-ene.[40]

In the preparation of an ylide from triarylsulfonium salts, one aryl group is replaced by an alkyl group (for example, the butyl group) with its subsequent deprotonation.[36]

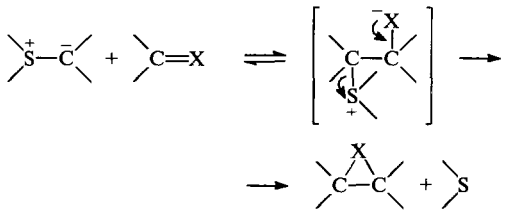
$$Ph_3S^+BF_4^- + BuLi \xrightarrow[-PhLi]{THF} Ph_2\overset{+}{S}Bu\ BF_4^- \longrightarrow Ph_2\overset{+}{S}-\bar{C}HPr$$

Sulfonium ylides are also obtained by adding nucleophiles to vinylsulfonium salts.[2]

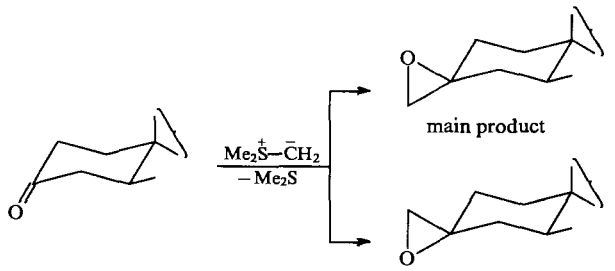
$$R_2\overset{+}{S}-CH=CR^1_2 + \bar{N}u \rightleftharpoons R_2\overset{+}{S}-\underset{\displaystyle Nu}{\bar{C}H}CR^1_2$$

When R = Me and R^1 = H, the methylation of the nucleophile via an S_N2 reaction competes with the addition reaction.

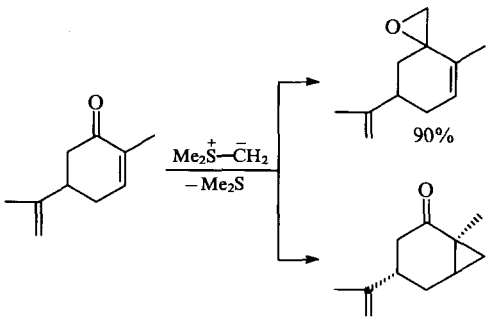
The high nucleophilicity of the carbon atom in the ylide group and also the tendency of the sulfonium centre to be converted into the readily eliminated sulfide group, are responsible for the principal application of sulfonium ylides in organic synthesis, namely the transfer of alkylidene groups to an electrophilic double bond via the intermediate formation of a betaine, which cyclises via direct substitution at the carbon atom.[2,41]



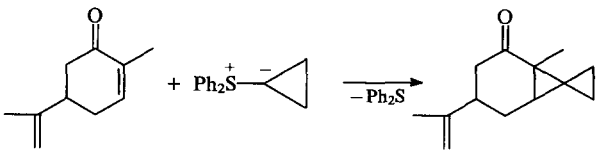
Depending on the structure of the ylide and the alkene, their addition to one another may lead to the formation of diastereoisomeric or structurally isomeric betaines. The cyclisation of such betaines gives various combinations of products. For example, the interaction of dimethylsulfonium methylide with cholestan-3-one leads to two isomeric products, with the isomer having an axial disposition of the epoxide substituent predominating.[2]



The addition of dimethylsulfonium methylide to carvone leads to two different products, with the epoxide predominating.[2]

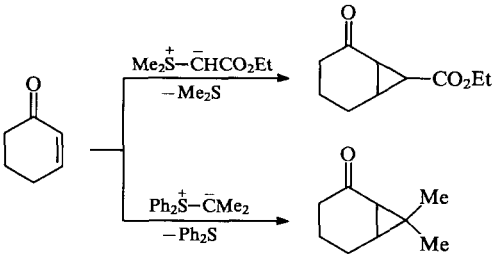


On the other hand, the addition of the diphenylsulfonium cyclopropylide to carvone takes place at the C=C bond with formation of one product.

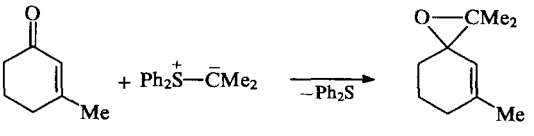


The addition of dimethylsulfonium ethoxycarbonylmethylide and diphenylsulfonium dimethylmethylide to cyclohexen-2-one also takes place at the C=C bond[2] (Scheme 4).

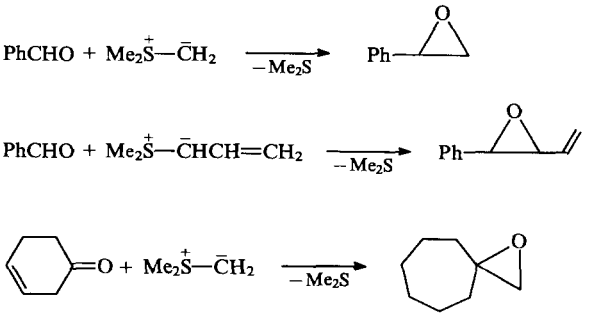
Scheme 4

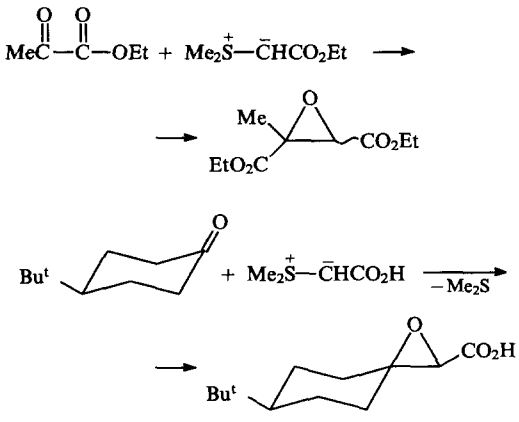


The introduction of an alkyl group in the 3-position in cyclohex-2-enone alters the mode of addition.[2]

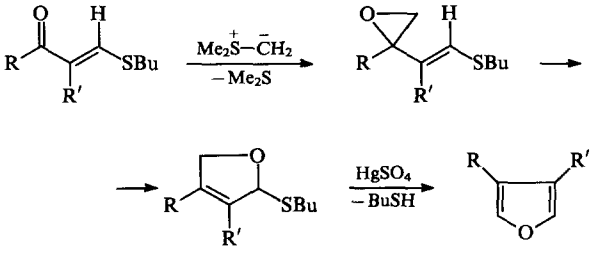


As a result of the diversity and ready availability of aldehydes and ketones, their condensation with sulfur ylides has become the most important synthetic method for the preparation of oxiranes with a wide variety of structures.[2,36,42,43]



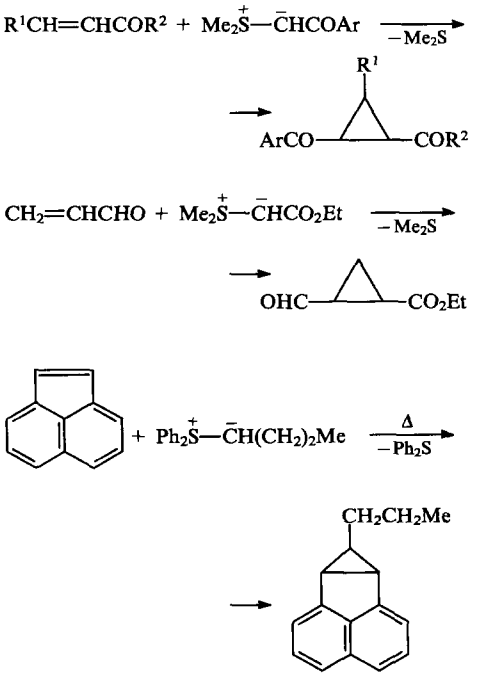


In the presence of a mobile hydrogen atom in the substrate molecule, the oxirane ring formed may be opened with subsequent formation of a five-membered ring, which is used in the synthesis of furans from dimethylsulfonium methylide and unsaturated ketones.[28]



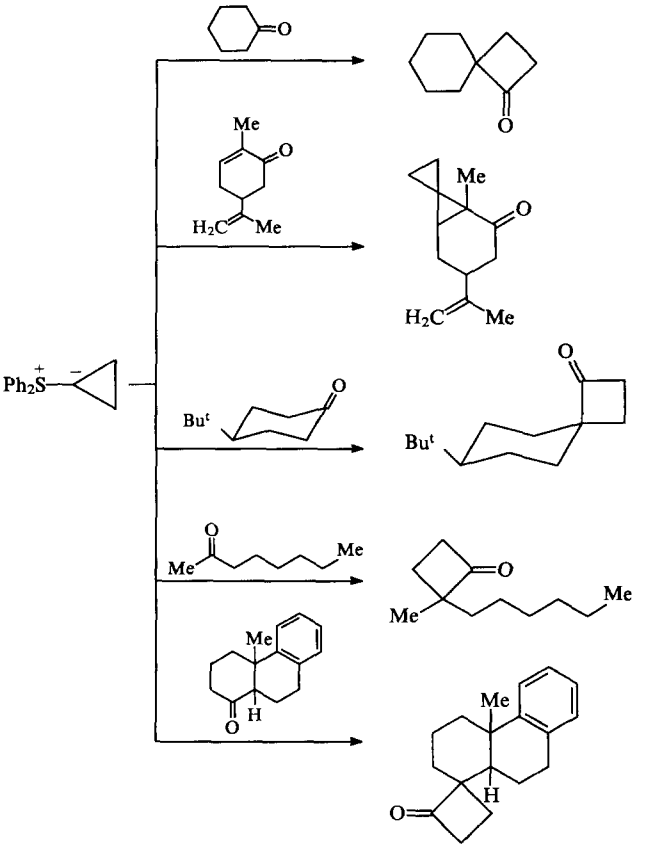
The availability of unsaturated compounds with a wide variety of structures makes it possible to employ the ylides for the synthesis of cyclopropanes (Scheme 5).

Scheme 5

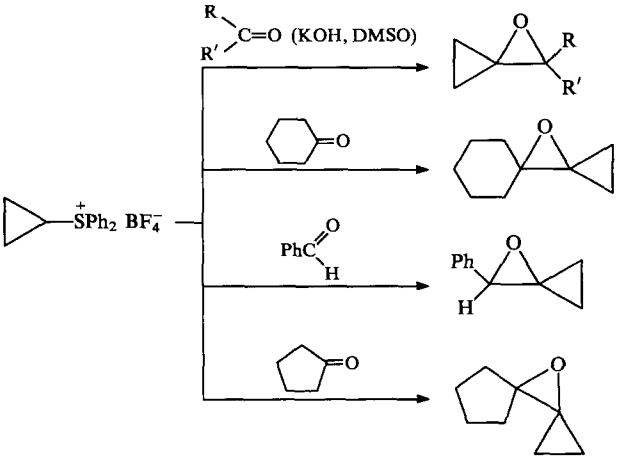


It has been suggested[44] that the biosynthesis of the cyclopropane ring in many natural products proceeds via the copper-catalysed transfer of the methylene group from the sulfonium methylide formed from *S*-adenosylmethionine.

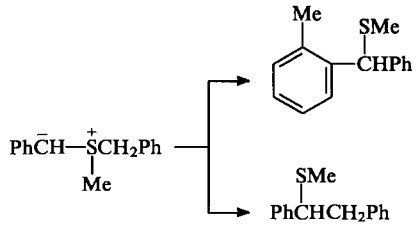
Diphenylsulfonium cyclopropylide, formed when cyclopropyldiphenylsulfonium tetrafluoroborate is treated with sodium dimethyl sulfoxide in THF, is widely used in the transfer of the cyclopropylidene group in preparative organic chemistry.[28] The interaction of this reagent with aldehydes and ketones and also with α,β-unsaturated ketones affords spirocycloalkanones and cyclic ketones.[27,28,44,45]



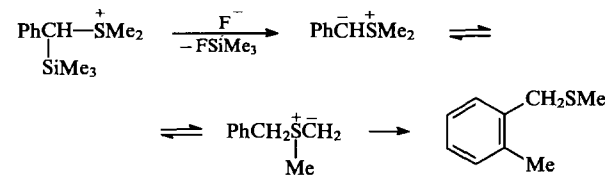
Oxaspiropentanes are intermediates in some of these reactions. They have been isolated by treating the carbonyl compounds with cyclopropyldiphenylsulfonium tetrafluoroborate.[46,47]



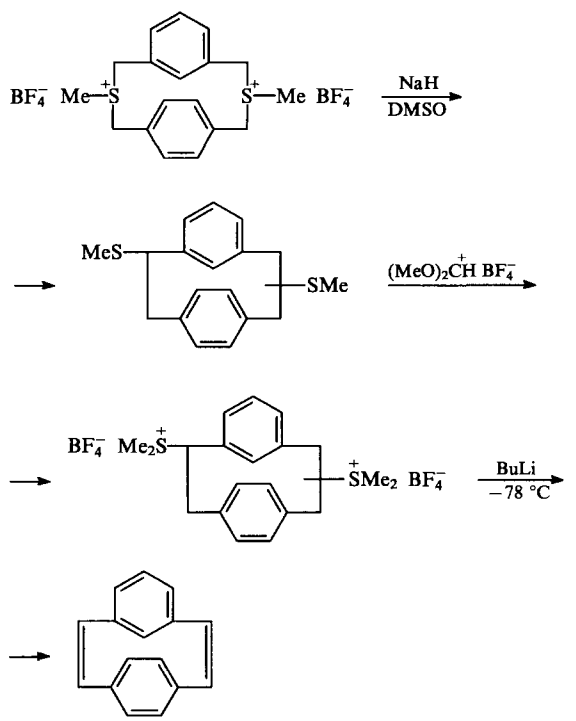
The tendency of sulfonium ylides to undergo rearrangements is frequently employed in the syntheses of various sulfides. For example, in the presence of strong bases, benzylsulfonium ylides undergo the [2,3]-sigmatropic rearrangement and also 1,2-shift rearrangements with formation of the corresponding sulfides.[2,15,48,49]



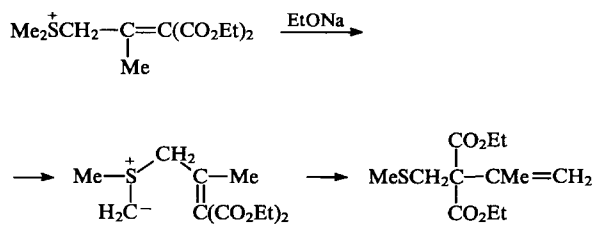
The [2,3]-sigmatropic rearrangement of the benzylsulfonium ylide, formed as a result of the desilylation of a α-trimethylsilylbenzylsulfonium salt by the fluoride anion, has been described.[50]

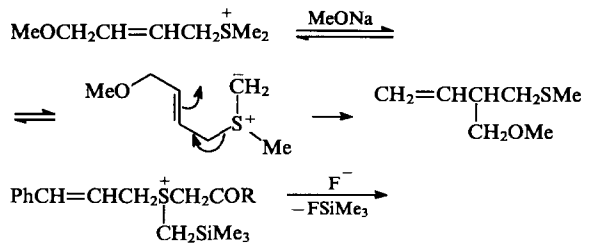


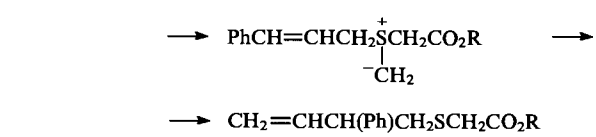
The 1,2-shift rearrangement of benzylsulfonium ylides constitutes the basis of the synthesis of cyclophanes.[36,51]



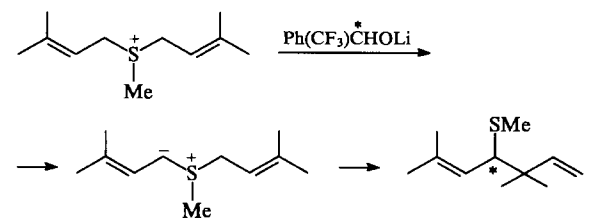
The [2,3]-sigmatropic rearrangements of allylsulfonium ylides, which take place on heating or on treatment with basic reagents, are used in the syntheses of but-3-enyl sulfides.[52-54]





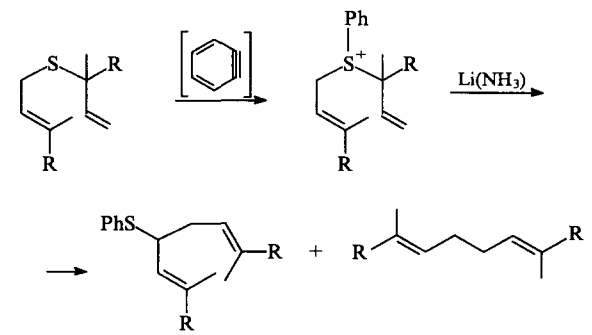


Thus the [2,3]-sigmatropic rearrangement of the sulfonium ylide generated from *S*-methyl-*S*,*S*-di(α,α-dimethylallyl)-sulfonium tetrafluoroborate in the presence of an optically active base led to an optically active sulfide.[54]



The synthesis of squalene has been achieved with the aid of the [2,3]-sigmatropic rearrangement of the corresponding allylsulfonium ylide (Scheme 6).[2]

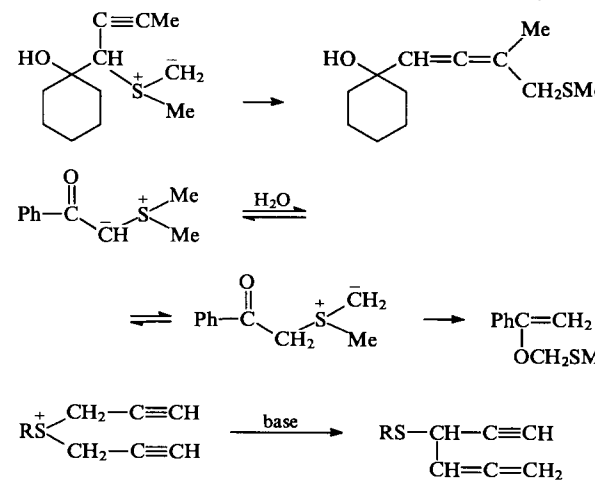
Scheme 6



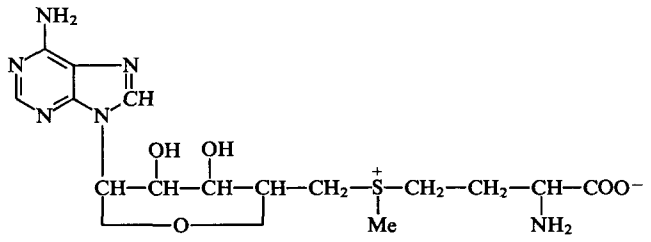
R = $Me_2C{=}CHCH_2CH_2C(Me){=}CHCH_2CH_2$.

Ylides and sulfonium salts containing triple bonds and heteroatoms can also participate in similar rearrangements (Scheme 7).[36,55]

Scheme 7



The transfer of alkyl and acyl groups. The high lability of the C–S bond in sulfonium salts makes possible their use as alkyl group transfer reagents, which has found application in biological methylation reactions[56] and in the biomimetic transalkylation of alkenes.[57] It has been suggested[1] that methylation in living organisms takes place with participation of the adenosylsulfonium salt of methionine.



The transfer of an alkyl groups to the sulfur atom of a thiolate anion[56,58,59] or sulfides[17,24,60] is used in the syntheses of asymmetric sulfides.

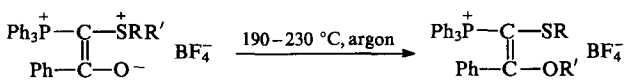
$$4\text{-}ClC_6H_4\overset{+}{S}(Me)\text{-}C_6H_4OMe\text{-}4\ SbF_6^- + 4\text{-}NO_2C_6H_4SNa \longrightarrow 4\text{-}NO_2C_6H_4SMe + 4\text{-}ClC_6H_4SC_6H_4OMe\text{-}4$$

$$Me_2\overset{+}{S}C_6H_{13}\ BF_4^- + Me_2S \longrightarrow MeSC_6H_{13} + Me_3\overset{+}{S}\ BF_4^-$$

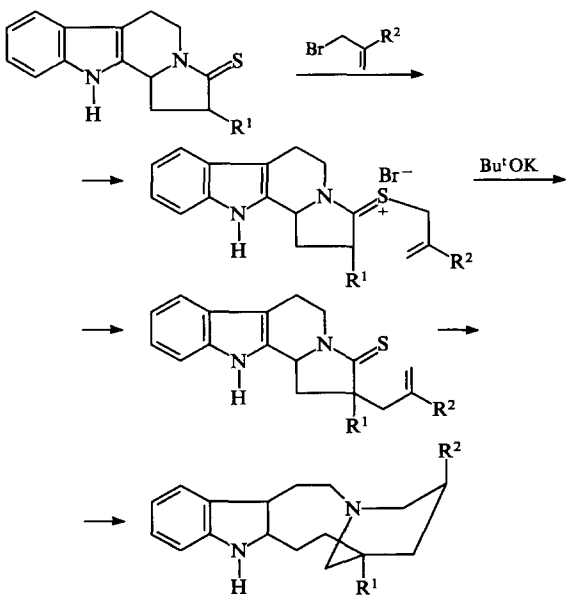
$$Me_2S + Me_2CHBr \longrightarrow Me_2\overset{+}{S}\text{—}CHMe_2\ Br^- \xrightarrow{Me_2S} Me_2CHSMe + Me_3\overset{+}{S}\ Br^-$$

$$Me_2S + Me_3SiCH_2\overset{+}{S}Me_2\ I^- \longrightarrow Me_3SiCH_2SMe + Me_3\overset{+}{S}\ I^-$$

An example of the intramolecular transfer of an alkyl group from the sulfonium centre to an oxygen atom is provided by the isomerisation of dialkylsulfonium salts containing the triphenylphosphonium group, which takes place at 190–230 °C under an argon atmosphere.[61] This leads to the preferential formation of the (*E*)-isomer of the corresponding α,β-disubstituted styryltriphenylphosphonium tetrafluoroborate.



The Claisen thio-rearrangement of sulfonium salts, used in the syntheses of certain alkaloids, is also of the type involving the intramolecular transfer of an alkylallyl group.[54]



It has been noted[62] that sulfonium salts containing a nitro-group at a carbon atom adjoining the sulfonium centre are capable of being cleaved also in the presence of electrophiles. The cleavage then takes place at the S–C(NO_2) bond with transfer of the nitroalkyl fragment to the electrophilic part of the reagent.

$$R_2\overset{+}{S}\text{—}C(NO_2)_2Z\ A^- + \bar{Y}\text{—}\bar{X} \longrightarrow YC(NO_2)_2Z + R_2S\overset{+}{X}\ A^-$$

Y—X = Cl–Cl, Cl–N(COR)$_2$, Cl–SO_2Cl, Cl–RS.

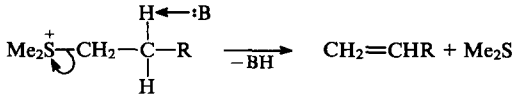
Z = COR, H.

It has been shown[63–65] that the dimethylacylsulfonium salts $RCOS^+Me_2BF_4^-$ (R = Me, Bu^t, CF_3) act as acylating agents in reactions with alkenes, dienes, and ethynes, which is used in the synthesis of α,β-unsaturated ketones.

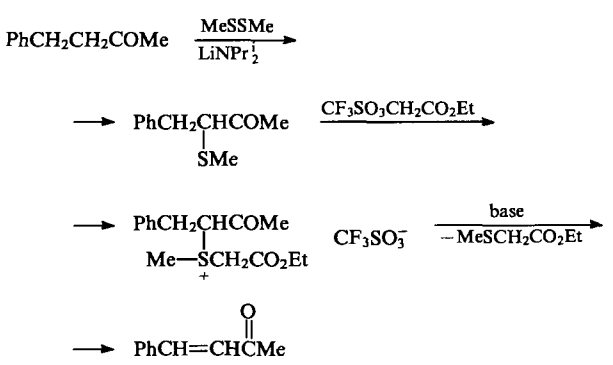
$$RCO\overset{+}{S}Me_2\ BF_4^- + CH_2{=}CHR' \xrightarrow[-HBF_4]{} RCOCH{=}CHR' + Me_2S$$

R = Me, Bu^t; R′ = Ph, CH_2=CMe.

Elimination of the sulfonium group. The sulfonium centre activates the β-hydrogen atoms in alkyl groups; the sulfonium group can also be the leaving nucleophile in elimination reactions. These factors have in fact determined the use of sulfonium salt in the syntheses of unsaturated compounds.[66]

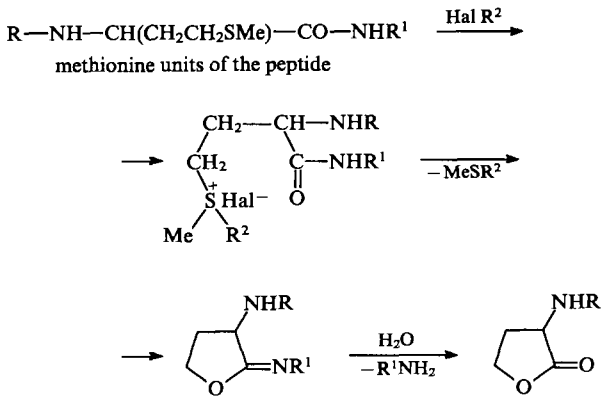


The conversion of a sulfide functional group into a sulfonium group and the elimination of the latter are used as a method for the introduction of a carbon–carbon double bond, for example in the conversion of saturated ketones into α,β-unsaturated ketones.[66–68]



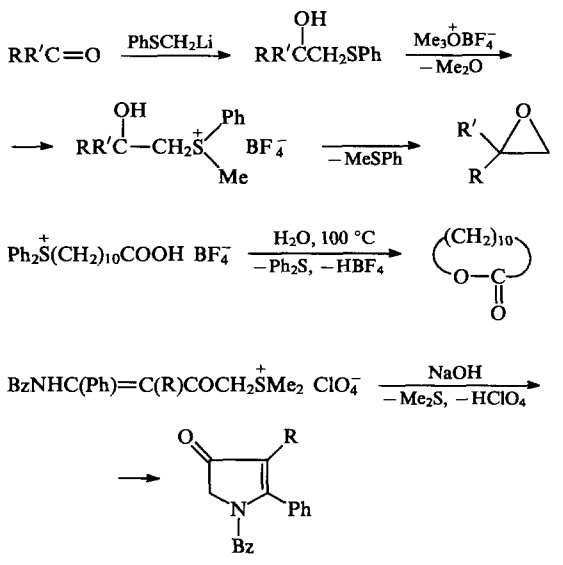
One of the methods for protecting the carboxyl group involves its conversion into an alkylthiomethyl ester group $-CO_2CH_2SR$, which is resistant to the action of weak alkalis and reductants. This is frequently employed in peptide and phosphatide syntheses.[66] In order to remove the alkylthiomethyl group, it is initially converted into a sulfonium group by treatment with methyl iodide and is then cleaved with a weak solution of alkali.

The intramolecular displacement of the sulfonium group by other nucleophilic groups with formation of cyclic products has come to be widely employed in organic synthesis. For example, a method has been developed for the specific cleavage of peptides in the methionine units, involving the intramolecular displacement of the sulfonium group by the oxygen atom of a neighbouring amide group.[66]

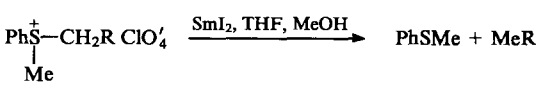


$HalR^2$ = BrCN, ICH_2CONH_2.

The intramolecular displacement of the sulfonium group is also used in the synthesis of oxiranes,[2] lactones,[68] and other heterocyclic compounds.[69]



The reduction of the sulfonium group by samarium diiodide in THF at 20 °C in the presence of 2 equiv. of methanol leads to the formation of the corresponding hydrocarbons and sulfides in quantitative yields.[70]

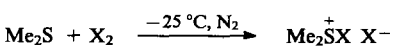


R = CN, 4-BrC_6H_4CO.

2. Halosulfonium salts

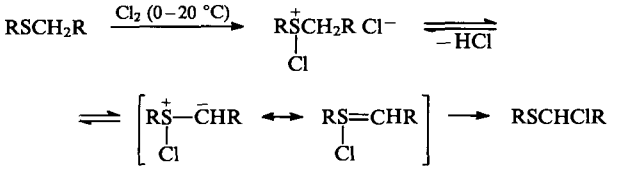
a. Methods for the generation of halosulfonium salts

Generation from sulfides. The interaction of sulfides with the halogens is one of the commonest methods for the generation of halosulfonium salts. The reaction is carried out at low temperatures (−50 to −25 °C) in anhydrous inert solvents (CCl_4, CH_2Cl_2, $CHCl_3$, etc.).[28,71,72]



X = Cl, Br

The solutions of the halosulfonium salts obtained may be stored in the dark without access of moisture for several weeks. At higher temperatures (0–20 °C), the halogenation of alkyl sulfides by the halogens leads to the formation of α-haloalkyl sulfides,[2,73] halosulfonium salts being formed as intermediates in this process.

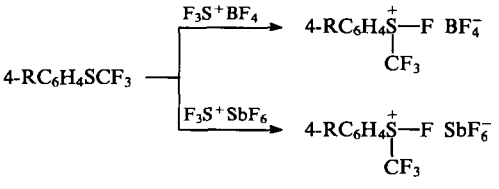


Apart from the halogens, *tert*-butyl hypochlorite,[74–78] sulfuryl chloride,[79] and sulfonic acid *N*-chloroamides[76,80,81] are also used as halogenating agents.

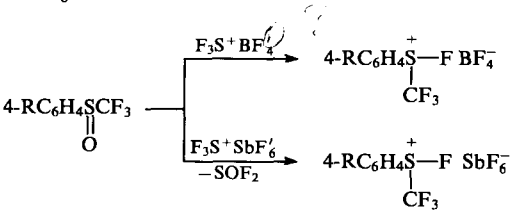


Z = BuO, SO_2Cl, $ArSO_2NH$.

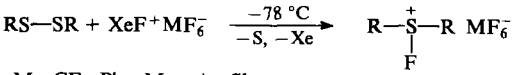
When aryl trifluoromethyl sulfides are treated with the complexes $F_3S^+BF_4^-$ and $F_3S^+SbF_6^-$, arylfluoro(trifluoromethyl)sulfonium salts are formed.[82]



Generation from sulfoxides. Arylfluoro(trifluoromethyl)-sulfonium salts are also formed when aryl trifluoromethyl sulfoxides are treated with the complexes $F_3S^+BF_4^-$ and $F_3S^+SbF_6^-$.[82]



Generation from disulfides. It has been noted[83] that, when disulfides interact with the complexes $FXe^+MF_6^-$ (M = As, Sb), the S–S and C–S bonds are cleaved with formation of fluorosulfonium salts.

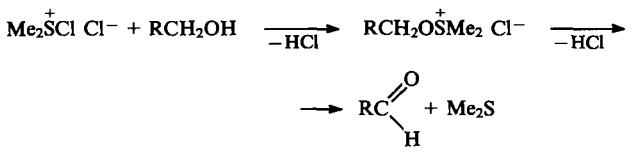


R = Me, CF_3, Ph; M = As, Sb.

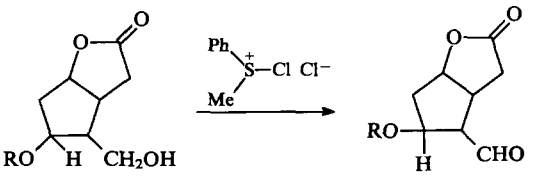
The interaction of the complex $FXe^+SbF_6^-$ with hydrogen sulfide at −78 °C leads to the formation of the fluorosulfonium salt $H_2S^+FSbF_6^-$.[83]

b. The use of halosulfonium salts in organic synthesis

Oxidation of alcohols. Chlorodimethylsulfonium chloride is widely used in organic synthesis as a mild oxidant which oxidises primary and secondary alcohols to carbonyl compounds.[28]



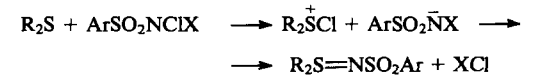
Chloro(methyl)phenylsulfonium chloride is used as a mild oxidant for the conversion of hydroxylactones into aldehydrolactones.[28]



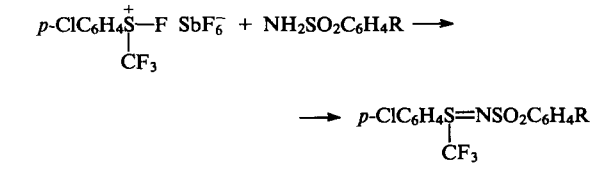
R = 4-PhC_6H_4CO.

Preparation of alkyl bromides. Bromodimethylsulfonium bromide is widely used for the replacement of the OH group in an alcohol by bromine.[28] For this purpose, the sulfonium salt is treated with an excess of the alcohol for 4–5 h at 80 °C. The reaction takes place with inversion of the configuration.

Synthesis of sulfimides (sulfilimines). *N*-Arenesulfonylsulfimides[80,81,84–89] are obtained by the reaction of sulfimides with sulfonic acid *N*-chloroamides via the intermediate formation of the chlorosulfonium cation R_2S^+Cl and the sulfonamide anion $ArSO_2N^-X$ (X = H, Cl).



Arylfluoro(trifluoromethyl)sulfonium salts give rise relatively easily to *N*-arenesulfimides on interaction with sulfonic acid amides.[26,90]

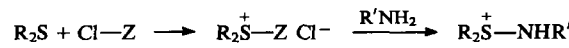


R = H, 4-Me.

3. Aminosulfonium salts

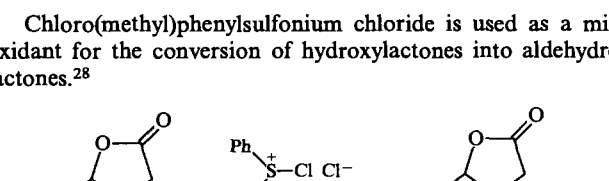
a. Methods for the generation of aminosulfonium salts

Generation from sulfides. Several variants of the generation of aminosulfonium salts from sulfides have been developed. According to one of them, the sulfides are converted into sulfonium salts by treatment with halogenating agents. The interaction of the sulfonium salts with amines leads to aminosulfonium salts.[80,91–98]

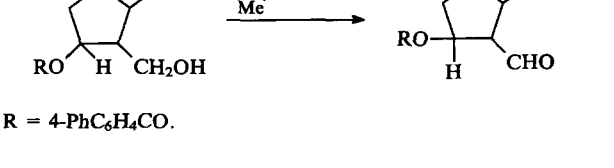


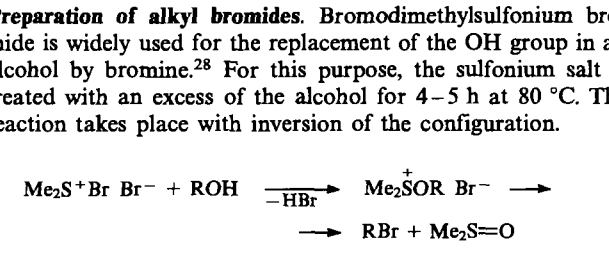
Z = Cl, Bu^{t}O, SO_2Cl, etc.

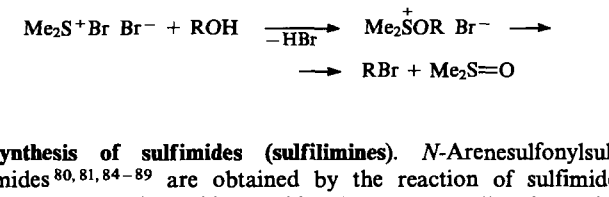
Another method is based on the reaction of sulfides with *N*-halo-compounds such as *N*-chloramine,[99] *N*-bromoacetamide,[100] *N*-chlorourethane,[100,101] *N*-chloramidines,[102] *N*-chloroguanidines,[102] *N*-chlorourea and its derivatives,[103,104] *N*-chlorosuccinimide,[28] *N*-chlorobenzotriazine,[105] and iminosulfonic acid *N*-chloroamides.[106]

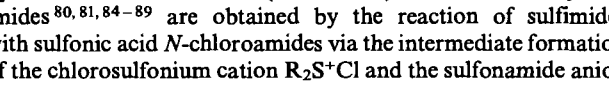


X = Cl, Br; Z = H, MeCO, EtOCO, PhC(=NH)–, $NH_2NHC(=O)$–, $NH_2C(=O)$–, NH_2–CH(OMe)–.

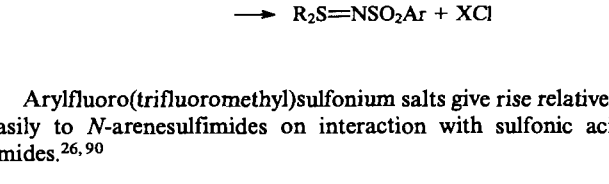




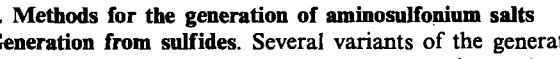




One of the modifications of these two variants for the generation of aminosulfonium salts involves the halogenation of sulfides in the presence of amines by halogenating agents such as *N*-chlorosuccinimide[107,108] and *tert*-butyl hypochlorite.[109]



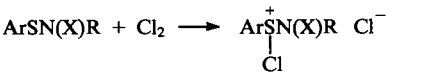
The third method for the generation of aminosulfonium salts from sulfides involves the interaction of the latter with certain derivatives of hydroxylamine, for example with hydroxyaminosulfonic acid,[80] *N*-arenesulfonyl-*O*-(*p*-nitrobenzenesulfonyl)-hydroxylamine,[80] *N*-ethoxycarbonyl-*O*-(*p*-nitrobenzenesulfonyl)hydroxylamine.[80] *O*-mesitylenesulfonylhydroxylamine,[110] and (+)-*O*-(α-bromocamphorsulfonyl)hydroxylamine.[111]



R = Alk; X = H, $ArSO_2$, EtOCO;

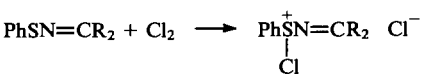
Y = HSO_3, 2,4,6-$Me_3C_6H_2SO_2$, 4-$NO_2C_6H_4SO_2$.

Generation from sulfenamides. The formation of aminosulfonium salts as intermediates in the reactions of sulfenamides with chlorine,[112–116] *N*-chloro- and *N*-dichloro-amides,[117–119] *N*-halosuccinimides,[120,121] *N*-chlorobenzotriazine,[122] and other halogenating agents has been noted.

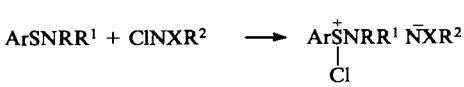


Ar = Ph, 4-MeC_6H_4, 2-$NO_2C_6H_4$, 4-$NO_2C_6H_4$;

R = Bu^t, $PhSO_2$; X = H, Na.

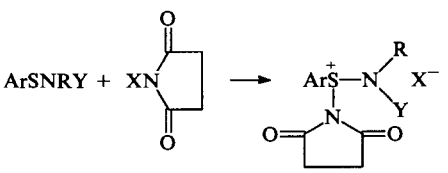


R = Ph, CF_3.



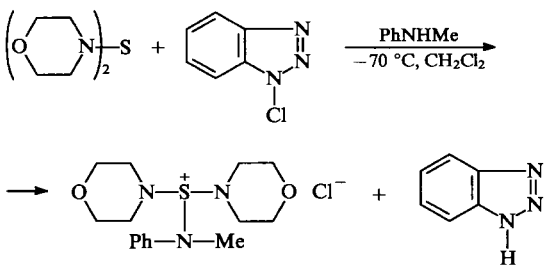
R = H, Alk; R^1 = Alk, Ar, $ArSO_2$;

X = H, Cl; R^2 = ArCO, $ArSO_2$.

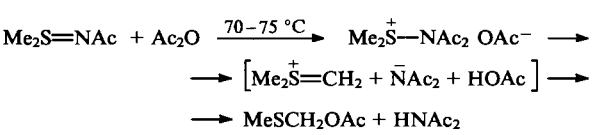


Ar = Ph, 2-$NO_2C_6H_4$;

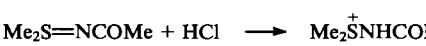
R = Me, $PhSO_2$; Y = Me, Na; X = Cl, Br.



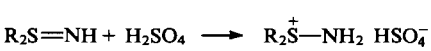
Generation from sulfimides. On heating in acetic anhydride, *N*-acyl-*S*,*S*-dimethylsulfimides enter into the Pummerer reaction, which proceeds via an intermediate stage involving the generation of aminosulfonium salts.[123]



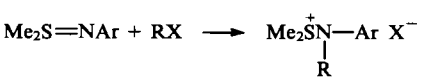
N-Acetyl-*S*,*S*-dimethylsulfimide is converted into an aminosulfonium salt on interaction with gaseous hydrogen chloride.[124]



Sulfimides unsubstituted at the nitrogen atom give rise to aminosulfonium salts on interaction with strong inorganic acids, for example with sulfuric acid.[125]



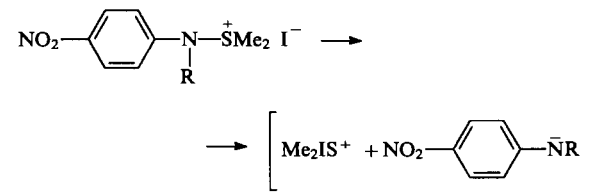
Unstable aminosulfonium salts have been obtained by the interaction of *N*-arenesulfilimides with alkylating or acylating agents.[80,81,126]



R = Me, X = Cl; R = EtOCO, X = Cl;

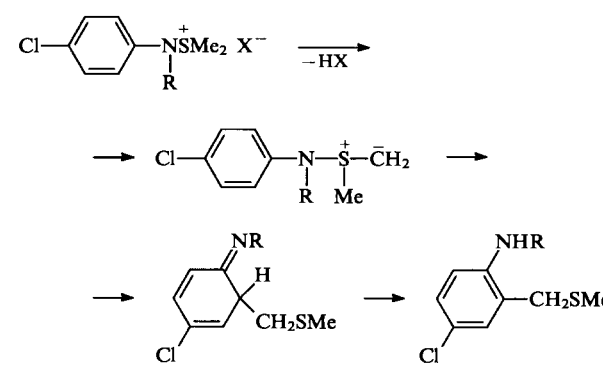
R = MeCO, X = MeOCO; Ar = *p*-$NO_2C_6H_4$, *p*-ClC_6H_4.

Further reactions of these salts are determined by the nature of the substituents in the benzene ring of the aryl group and by the basicity of X^-. In the case of strongly electron-accepting substituents (for example, NO_2) and highly basic X^-, X^- attacks the positively charged sulfur atom with subsequent dissociation of the S–N bond.



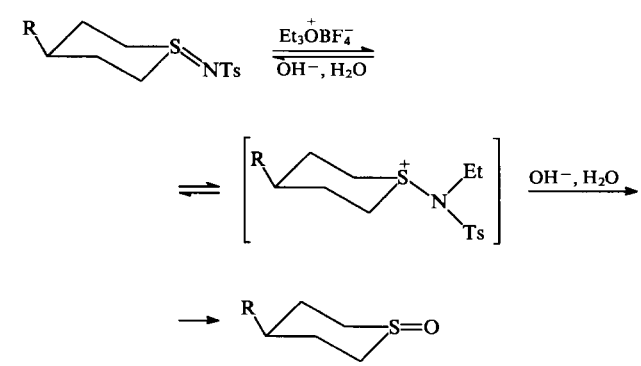
In the case of weakly electron-accepting or electron-donating substituents, the anion X^- abstracts a proton from the MeS group, giving rise to an intermediate ylide. The ylide then undergoes an intramolecular sigmatropic rearrangement, which leads to unstable cyclohexadiene derivatives and these are converted into the more stable benzene derivatives.

The replacement of one methyl group at the sulfur atom by the ethyl or propyl group does not alter the mode of abstraction of a proton — it is abstracted from the Me group as before, while on replacement of the methyl group by the benzyl group it is abstracted only from the latter, which is correlated with the decrease in acidity in the sequence $PhCH_2S$ > MeS > $AlkCH_2S$.



N-Arenesulfonylsulfimides give rise to aminosulfonium salts only on interaction with highly active acylating and alkylating agents such as oxonium salts,[80,81] methyl fluorosulfonate,[127] and complexes of carboxylic acid chlorides with $SbCl_5$.[127] The aminosulfonium salts formed in this case are relatively stable and undergo further reactions only on treatment with inorganic and organic bases (Scheme 8).

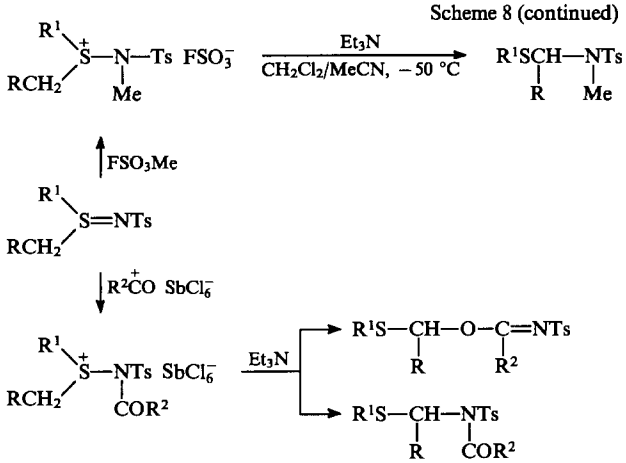
Scheme 8



R = Bu^t.

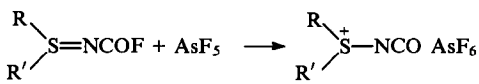
(continued over)

Scheme 8 (continued)



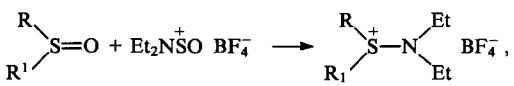
R = H, R^1 = R^2 = Me; R = H, R^1 = Me, R^2 = Et;
R = Ph, R^1 = Et, R^2 = Me;
R = H, R^1 = Me, R^2 = Ph; R = H, R^1 = Et, R^2 = Me.

It has been shown [128] that the reaction of fluorocarbonylsulfimide with arsenic pentafluoride proceeds with abstraction of a fluoride anion and the formation of an aminosulfonium salt.

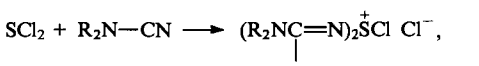


R = F; R′ = CF_3, NMe_2; R = CF_3; R′ = NMe_2.

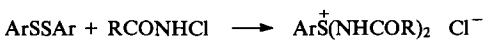
Other generation methods. Among other methods, mention should be made of the interaction of sulfoxides with *N*-sulfinyldialkylimmonium salts [129]



the reaction of sulfur dichloride with dialkylcyanamide [130]

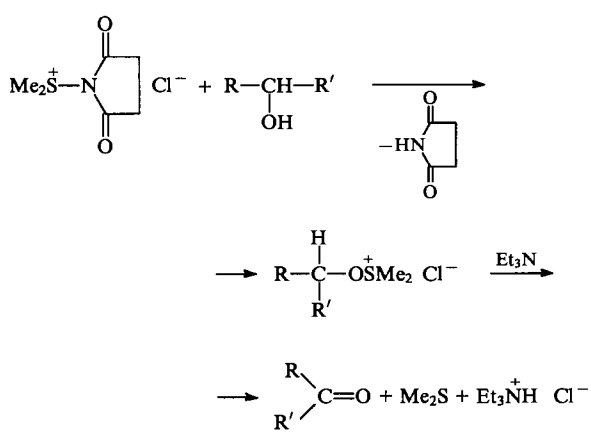


and the interaction of disulfides with carboxylic acid *N*-chloroamides; [131]

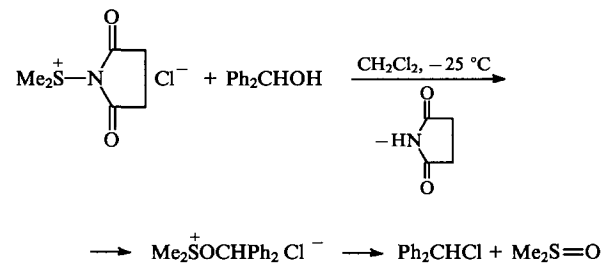


b. The use of aminosulfonium salts in organic synthesis

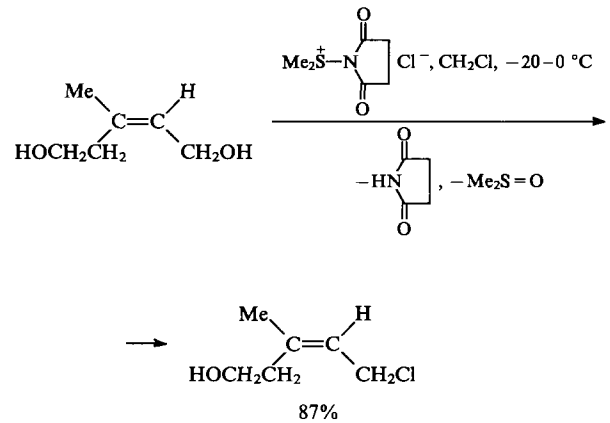
Dimethyl-*N*-succinylsulfonium chloride (the Corey–Kim reagent) has found extensive application in organic synthesis as a mild oxidant for alcohols,[28] which is superior in this respect to chlorodimethylsulfonium chloride.



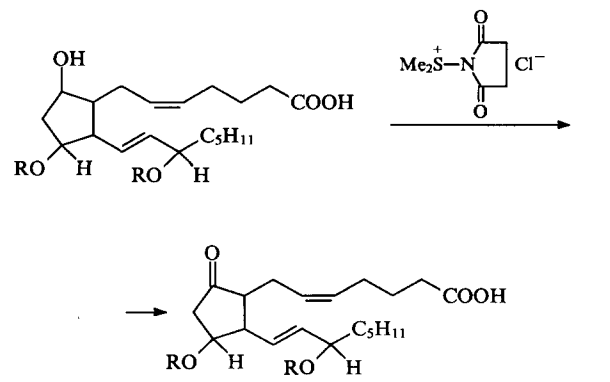
As an oxidant, the Corey–Kim reagent exhibits a high selectivity. For example, in contrast to primary and secondary aliphatic alcohols, allyl and benzyl alcohols are not oxidised by this reagent but are converted into the corresponding chlorides. In the case of diphenylmethanol, the yield of diphenylmethyl chloride reaches 95% in this reaction.[28]



Under the same conditions, cyclohex-1-en-3-ol is converted into 3-chlorocyclohexene in a yield exceeding 95%. The conversion of (*Z*)-3-methylpent-2-ene-1,5-diol into the allyl monochloride in 87% yield can also serve as a clear example of the selectivity of the Corey–Kim reagent.[28]

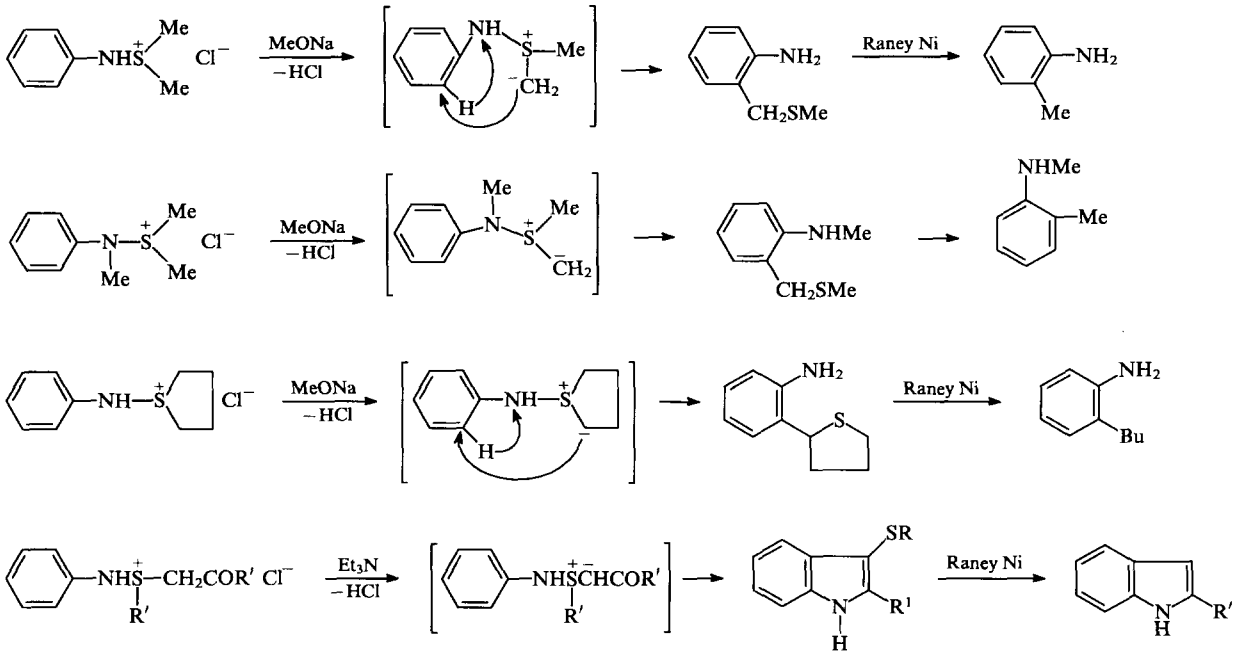


The Corey–Kim reagent is also used in an improved synthesis of prostaglandins for the conversion of a hydroxy-group into a keto-group in a yield exceeding 90%.[28]

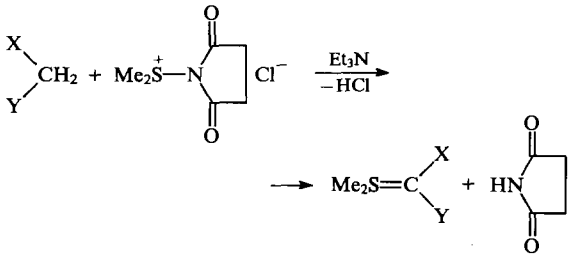


Generation of sulfur ylides. In the presence of bases, dialkylaminosulfonium salts may undergo C-deprotonation with formation of aminosulfonium ylides, which is also used in organic synthesis. For example, the conversion of dialkylaminosulfonium salts into aminosulfonium ylides with subsequent rearrangement of the latter is employed in the orthoalkylation or anilines [132] and in the synthesis of indoles (Scheme 9).[133]

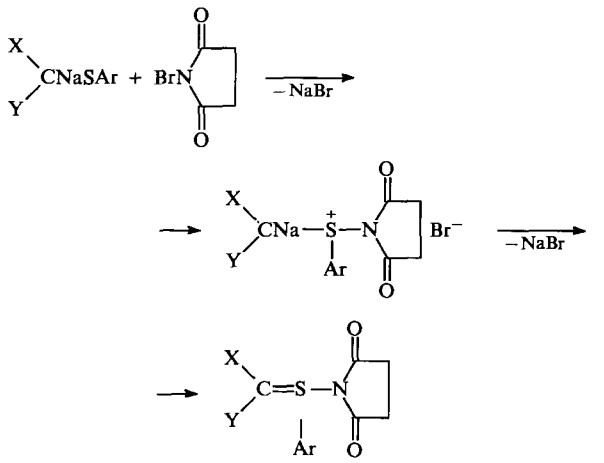
Scheme 9



It is worth noting that, in the case of aminosulfonium salts containing a hydrogen atom at the nitrogen atom, the formation of sulfur ylides may be accompanied by a side reaction — the formation of sulfimides. The rearrangement of aminosulfonium salts in the presence of bases, which results in the formation of sulfides,[134] also proceeds via a sulfonium ylide generation stage. The formation of sulfur ylides has also likewise been observed in the interaction of Corey–Kim reagents with CH acids in the presence of triethylamine.[135]



X = Br, Ac, CN;
Y = Br, Ac, CO_2Et, CO_2Me, Ph.

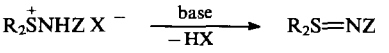


X = MeCO, Y = EtOCO, Ar = 2-$NO_2C_6H_4$;

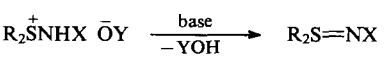
X = $PhSO_2$, Y = Ph, Ar = 4-$NO_2C_6H_4$.

It has been suggested[136] that the interaction of sodium salts of arylthio-CH acids with *N*-bromosuccinimide, which results in the formation of stable *S*-aryl-*S*-succinimidosulfonium methylides, proceeds via a stage involving the formation of aminosulfonium salts.

Synthesis of sulfimides. The N-deprotonation of aminosulfonium salts containing a hydrogen atom at the nitrogen atom is one of the commonest methods of synthesis of sulfimides.[80,81] Both organic and inorganic bases (Et_3N, NaOH, etc.) are used as the deprotonating agents.



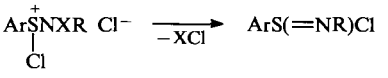
R = Alk, Ar, Het, X = Cl, Br; Z = H, MeCO, EtOCO, etc.



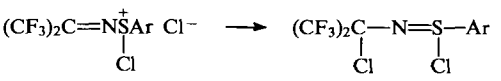
R = Alk, Ar; X = H, $ArSO_2$, EtOCO;

Y = HSO_3, 4-$NO_2C_6H_4SO_2$, 2,4,6-$Me_3C_6H_2SO_2$.

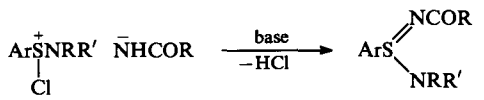
Synthesis of derivatives of iminosulfinic acids. The aminosulfonium salts formed on chlorination of *N*-substituted sulfenamides[112] or their sodium salts[113] are readily converted into iminosulfinic acid chlorides as a result of the elimination of HCl or NaCl.



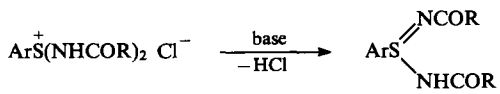
R = Bu^t, $PhSO_2$, ArCO; X = Na, H.



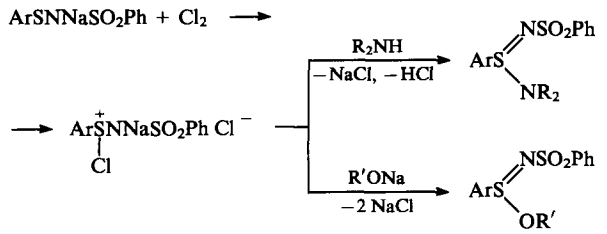
The dehydrochlorination of the aminosulfonium salts formed on interaction of *N*-chloroamides with sulfenamides[119] and disulfides[131] leads to the amides of iminosulfinic acids.



R = H, Alk; R′ = Alk, Ar, RCO



One cannot rule out the possibility that the chlorination of the sodium salts of *N*-arenesulfonylarenesulfenamides in the presence of various nucleophiles, which results in the formation of the amides[137] and esters[138,139] of iminosulfinic acids, also proceeds via a stage involving the formation of aminosulfonium salts.



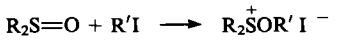
Ar = 2-$NO_2C_6H_4$, 4-$NO_2C_6H_4$;

R = Et, Bu, C_5H_{11}; R′ = Me, Et, Pr, Bu^i, Bu^n

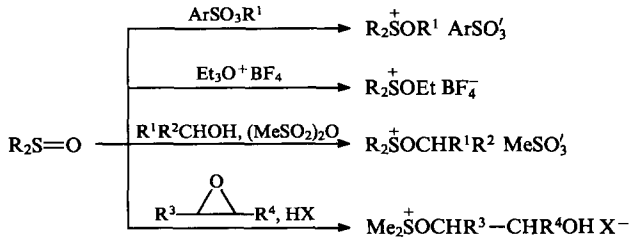
4. Alkoxy-, aryloxy-, and acyloxy-sulfonium salts

a. Methods for the generation of alkoxy-, aryloxy-, and acyloxy-sulfonium salts

Generation from sulfoxides. The commonest method for the generation of alkoxysulfonium salts involves the interaction of sulfoxides with alkyl halides.[1,2]



The alkyl esters of sulfonic acids,[28] triethyloxonium tetrafluoroborate,[2] alcohols (in the presence of the anhydride of methanesulfonic acid),[2] and epoxides (in the presence of strong acids)[2] are used as other alkylating agents.[2]

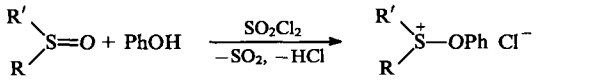


R = Alk, R^1 = Alk, Ar = 4-MeC_6H_4, 4-$NO_2C_6H_4$;

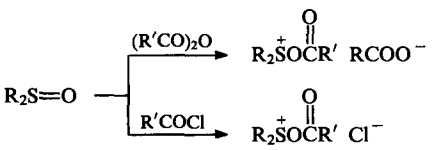
R^2 = Alk; R^3 = H, Alk, Ph; R^4 = H, Alk;

X = 2,4,6-$(NO_2)_3C_6H_2SO_3$.

The synthesis of a phenoxysulfonium salt by the reaction of sulfoxides with phenol in the presence of sulfuryl chloride has been described.[140]

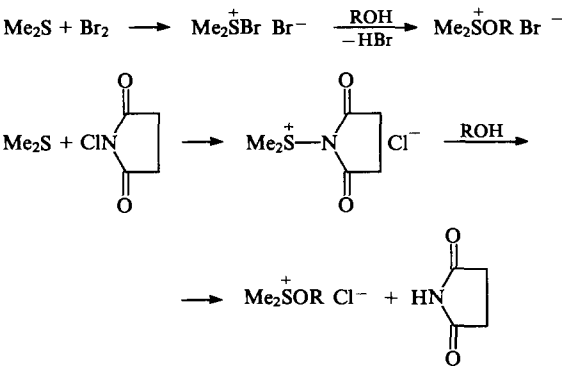


The interaction of the sulfoxides with carboxylic acid anhydrides[2,141,142] of halides[28] leads to the formation of acyloxysulfonium salts.

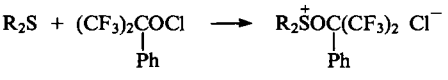


R = Me, Ph, CH_2=CH, etc.; R′ = Me, CF_3.

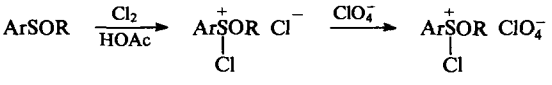
Generation from sulfides. Two alternative methods for the generation of alkoxysulfonium salts from sulfides have been developed. In the first method, the sulfide is converted into halo- or amino-sulfonium salts, which are subsequently treated with alcohols.[28]



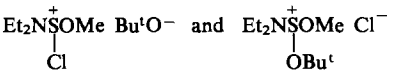
The second method involves the interaction of sulfides with alkyl hypochlorites.[105]



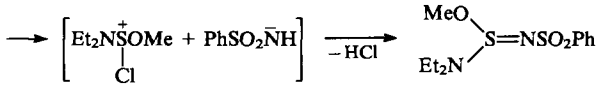
Generation from sulfenic and sulfinic acid esters. Alkoxysulfonium salts are formed on interaction of the alkyl esters of sulfenic acids with chlorine in acetic acid.[2]



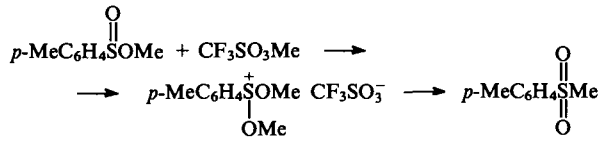
It has been noted[143,144] that the oxidation of *O*-methyl-*N*,*N*-dimethylaminosulfenates by *tert*-butyl hypochlorite to aminosulfinates proceeds via a stage involving the formation of alkoxysulfonium salts.



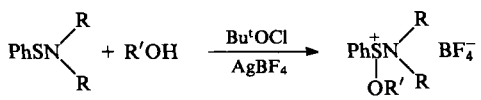
Evidently the oxidative imination of these compounds by the sodium derivatives of sulfonic acid chloramides[145] also proceeds via a stage in which alkoxysulfonium salts are generated.



The formation of a dimethoxysulfonium salt in the alkylation of methyl toluene-*p*-sulfinate by methyl trifluoromethanesulfonate has been postulated.[146]



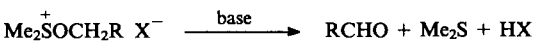
Generation from sulfenamides. It has been shown[147] that *N,N*-dialkylarenesulfenamides react with *tert*-butyl hypochlorite in the presence of alcohols and $AgBF_4$ to form alkoxyaryldialkylaminosulfonium salts.



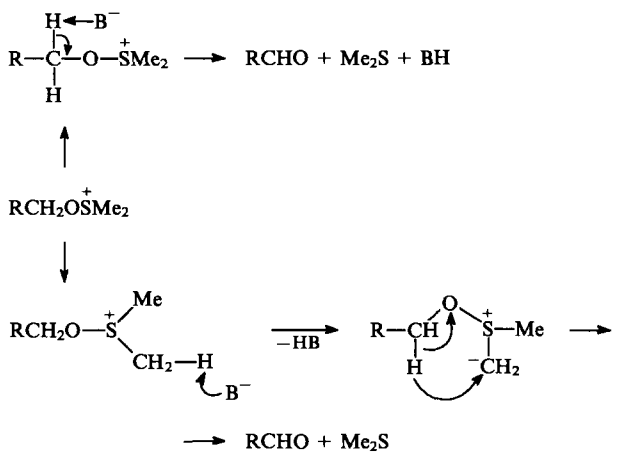
R = Me, $(CH_2)_5$, $(CH_2)_2O(CH_2)_2$; R′ = Me, Et, Pr^i, iso-C_6H_{11}.

b. Applications of alkoxysulfonium salts in organic synthesis

Synthesis of carbonyl compounds. On treatment with bases, alkoxysulfonium salts are cleaved, affording carbonyl compounds in relatively high yields.

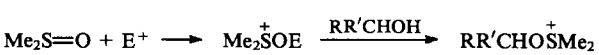


The cleavage can proceed in two ways.

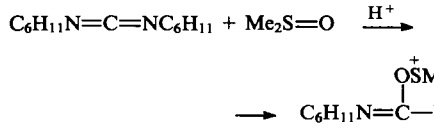


A whole series of convenient methods for the conversion of primary and secondary alcohols and also alkyl halides and tosylates into carbonyl compounds have been developed on the basis of this reaction. As a rule, alkoxysulfonium salts based on DMSO are used in these methods, which is evidently associated with their greatest availability. The advantage of these methods of synthesis of carbonyl compounds consist not only in the high yields of the target products but also in the fact that the oxidation of the aldehyde group to a carboxy-group is ruled out and other readily oxidised fragments, such as C=C and C–S–C, are not affected.

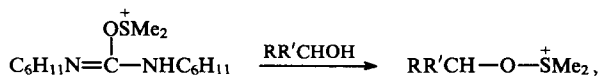
Depending on the method of generation of alkoxysulfonium salts, all these methods can be divided into several groups. The first group includes methods in which the alkoxysulfonium salt is formed as a result of the interaction of an alcohol with the alkoxysulfonium salt generated by the interaction of DMSO with the electrophilic species E^+ present in the reaction medium.[2]



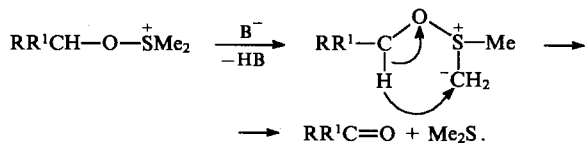
Here it is essential that the electrophilic species should react with DMSO faster than with the alcohol and that the OE group should be readily eliminated. Dicyclohexylcarbodiimide (DCC) combined with proton sources, for example pyridinium fluoroacetate, acetic anhydride, trifluoroacetic anhydride, and methanesulfonic acid anhydride is most often employed as the electrophile. When the last two compounds are used, the alcohol is introduced into the reaction medium after the reaction of dimethyl sulfoxide with the electrophile. The oxidation of the alcohol by the DMSO–DCC system includes three stages: the activation of DMSO by the electrophile with formation of a primary alkoxysulfonium salt:



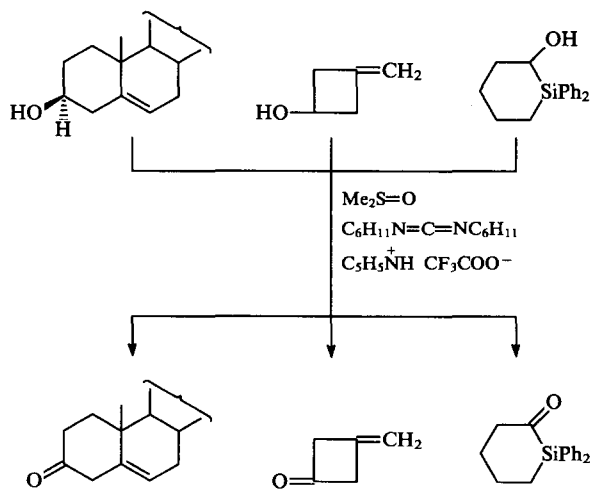
the interaction of the alkoxysulfonium salt with the alcohol to form a secondary alkoxysulfonium salt:



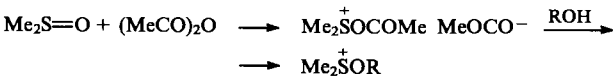
the decomposition of the secondary alkoxysulfonium salt:



Cholesterol, 3-methylenecyclobutanol, and 1,1-diphenylsilacyclohexan-2-ol have been oxidised to the corresponding ketones by means of the DMSO–DCC system.[2]

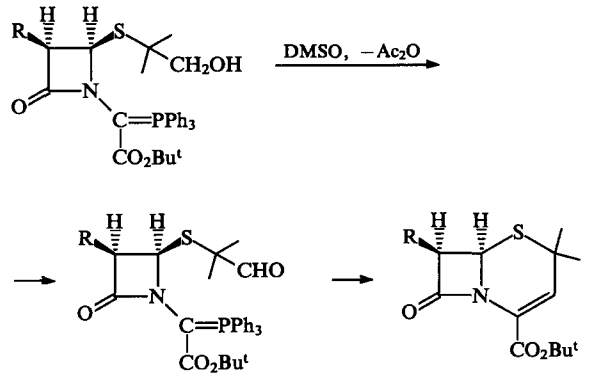


The acylsulfonium salt formed in the DMSO–$(MeCO)_2O$ system is converted into an alkoxysulfonium salt as a result of its interaction with the alcohol.[2]



This system is also used in the oxidation of hydrocarbons, sterically hindered alcohols, and also alcohols with readily oxidisible functional groups such as the sulfide and phosphorus-containing groups. For example, the conversion of a phosphorane, containing the β-lactam group, into a bicyclic

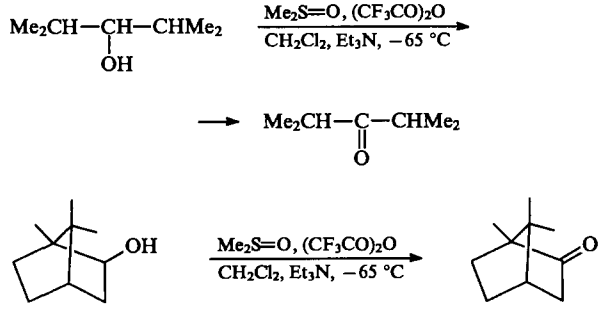
product takes place as a result of the Wittig reaction with participation of the aldehyde group formed on oxidation of an alcoholic group by the DMSO–$(MeCO)_2O$ system without change in the phosphorane and sulfide functional groups.



R = $NHC(O)CH_2Ph$.

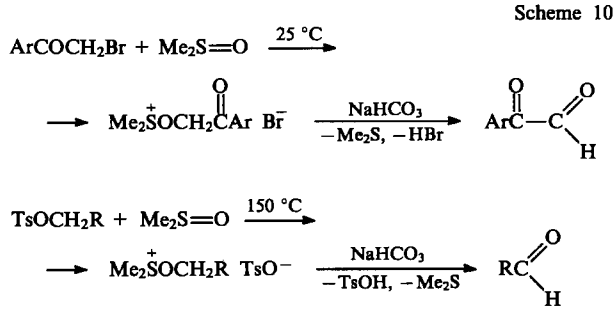
The formation of side products – acetates and methylthiomethyl ethers – must be regarded as a disadvantage of this system.

Among other methods, mention should be made of the use of the DMSO–methanesulfonic acid anhydride system in DMF for the oxidation of testosterone to androst-4-ene-2,17-dione and of the DMSO–trifluoroacetic anhydride system in CH_2Cl_2.[148] The latter method has been used in the oxidation of sterically hindered alcohols. For example, in the presence of this system 2,4-dimethylpentan-3-ol and isoborneol are converted into diisopropyl ketone and camphor in 86% and 93% yields respectively.[149]



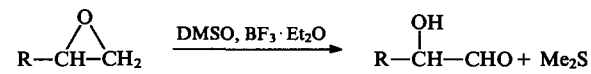
Methods in which the alkoxysulfonium salts are generated by the interaction of DMSO with halo-derivatives or tosylates in the presence of $NaHCO_3$ or collidine, which not only decompose the intermediate alkoxysulfonium salt but also neutralise the acid side products, are included in the second group of methods of synthesis of carbonyl compounds from alkoxysulfonium salts (Scheme 10).[2]

Scheme 10

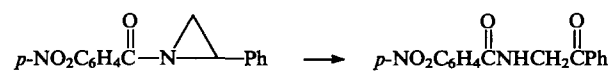


These methods are especially suitable in the case of halo-derivatives and tosylates, which tend to undergo S_N2 substitution reactions (α-halogenated esters and acids, phenacyl and benzyl halides, primary alkyl iodides, sulfonates). However, one should note that, when secondary halo-derivatives and tosylates are employed, the yields of the carbonyl compounds are low owing to the competing elimination reactions.

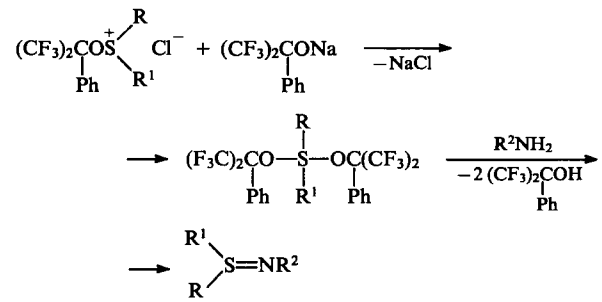
The third group comprises methods in which the intermediate alkoxysulfonium salts are the products of the interaction of DMSO with three-membered heterocyclic compounds in the presence of acid catalysts. For example, the interaction of DMSO with epoxides in the presence of $BF_3.Et_2O$ leads to the formation of α-hydroxyaldehydes.



On heating in DMSO at 115–120 °C, the ring in *N*-acylaziridines is opened with conversion into *N*-substituted amides.



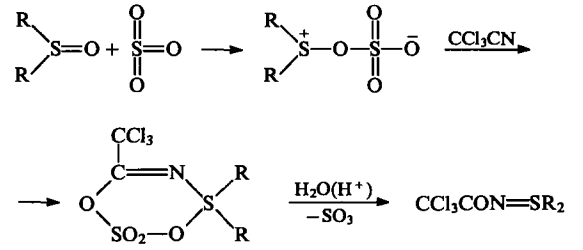
Synthesis of sulfimides. Several methods have been developed for the preparation of sulfimides from alkoxysulfonium salts. One of them involves the conversion of alkoxysulfonium salts by alkoxides into sulfuranes, which give rise to sulfimides on interaction with amines.[105]



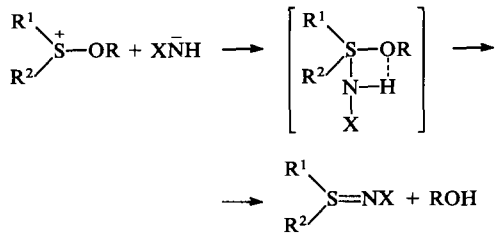
Another method is based on the interaction of alkoxysulfonium salts, generated from sulfoxides and active electrophiles E^+, with N-nucleophiles.[80,81]



The activating electrophiles employed are P_2O_5, $(CF_3CO)_2O$, SO_3, H_2SO_4, and BF_3.[80,81] Amines and amides of sulfonic and carboxylic acids are employed as the N-nucleophiles. The sulfonium salts formed in the reactions of sulfoxides with SO_3 also react with nitriles to form sulfimides.[149] The proposed reaction mechanism involves the attack by the electron-deficient carbon atom of the nitrile group on one of the oxygen atoms of the sulfonium salt, which occurs only in the case of nitriles containing strongly electron-accepting groups.



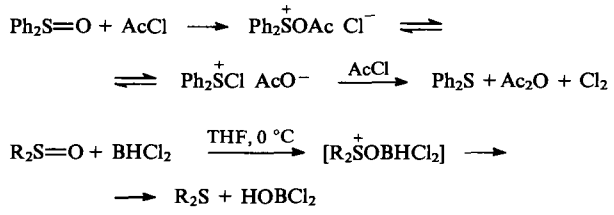
The synthesis of sulfimides by the reactions of the sodium derivatives of the amides and sulfonic and carboxylic acids with alkoxysulfonium salts has been described.[150] According to the authors, the reaction is stereospecific and proceeds with retention of configuration of the sulfur atom, which is due to the formation of an intermediate four-membered cyclic compound stabilised by an intramolecular hydrogen bond.



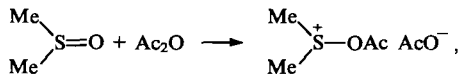
R = Me–C6H4–CHMe2, R^1 = 2-$MeOC_6H_4$, R^2 = Ph

X = $ArSO_2$, CH_2ClCO, $CHCl_2CO$, CF_3CO

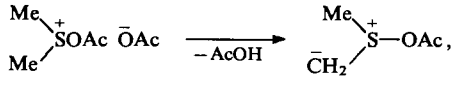
Synthesis of sulfides. Several methods have been developed for the synthesis of sulfides from sulfoxides involving an intermediate stage in which alkoxy- or acyloxy-sulfonium salts are generated. One of them amounts to the reduction of sulfoxides by an excess of acetyl chloride[151] and by dichloroborane.[152]



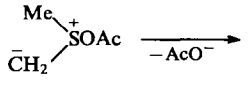
However, the method has not found extensive application, since more effective and convenient procedures have been developed for the reduction of sulfoxides and sulfides. Reactions leading to the formation of sulfides differing in structure from those employed for the synthesis of the sulfoxides are frequently used. One of them is based on the Pummerer rearrangement, which takes place when sulfoxides are heated in acetic anhydride.[2,153] The mechanism of this rearrangement includes the following stages:
the formation of an acyloxysulfonium salt:



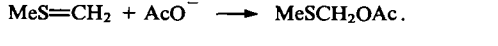
the conversion of the acyloxysulfonium salt into an ylide:



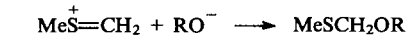
the formation of a sulfonium cation:



the interaction of the sulfonium cation with the acetate anion:

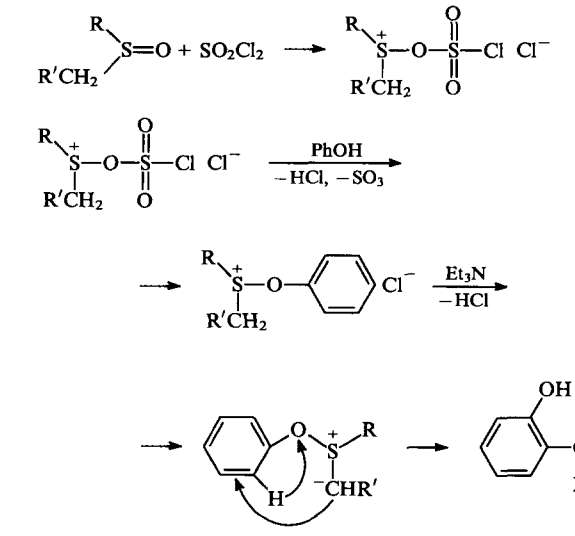


The presence of alkoxide anions in the reaction mixture leads to the formation of a methylthiomethyl ether or an alkoxymethyl methyl sulfide, which makes it possible to explain the formation of this compound as a side product in the oxidation of alcohols by the DMSO–$(MeCO)_2O$ system.

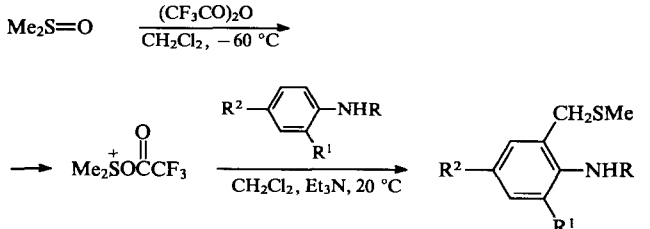


The regioselectivity of the Pummerer rearrangement, observed for asymmetric sulfoxides, can be predicted on the basis of the comparison of the relative acidities of the two α-protons in the acyloxysulfonium salt. Bearing in mind the ease of the conversion of sulfides into sulfoxides, the Pummerer rearrangement is a very important method for the conversion of one set of sulfides into another.

Other methods for the conversion of sulfoxides into sulfides are based on the intramolecular rearrangement of aryloxysulfonium salts proceeding via an ylide generation stage.[140] The final result of such 2,3-sigmatropic rearrangement is the introduction of an alkylthiomethylene group into the *ortho*-position in phenols.



An alkylthiomethylene group is introduced similarly into the *ortho*-position in aromatic amines.[141]

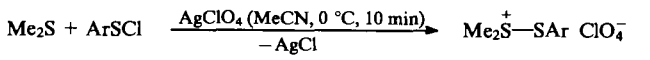


R = H, Me, Ph; R^1 = H, MeO; R^2 = H, Me, MeO

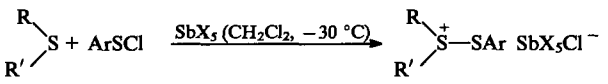
5. Alkyl(aryl)thiosulfonium and [dialkyl(aryl)]alkyl(aryl)-thiosulfonium salts

a. Methods of generation

Generation from sulfides. Dialkyl sulfides and certain diaryl sulfides react relatively easily with arenesulfenyl chlorides in the presence of silver perchlorate[154] or Lewis acids,[155] forming (dialkyl)arylthiosulfonium salts.



Ar = Ph, 4-MeC_6H_4

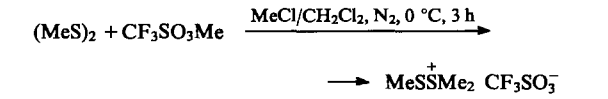


R = R′ = Me, Ph; R = Me, R′ = 4-ClC_6H_4; X = Cl, F

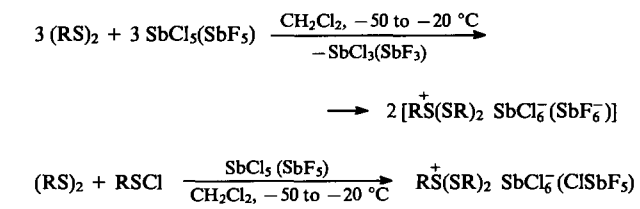
Ar = Ph, 4-MeC_6H_4, 4-ClC_6H_4, 2,4,6-$Me_3C_6H_2$, 4-$CF_3C_6H_4$.

Some of these salts are relatively stable and can be isolated in a crystalline state and analysed by ^1H and ^{13}C NMR spectroscopy.[155]

Generation from disulfides. (Dialkyl)alkylthiosulfonium salts have also been obtained by the interaction of dialkyl disulfides with methyl trifluoromethanesulfonate.[156]



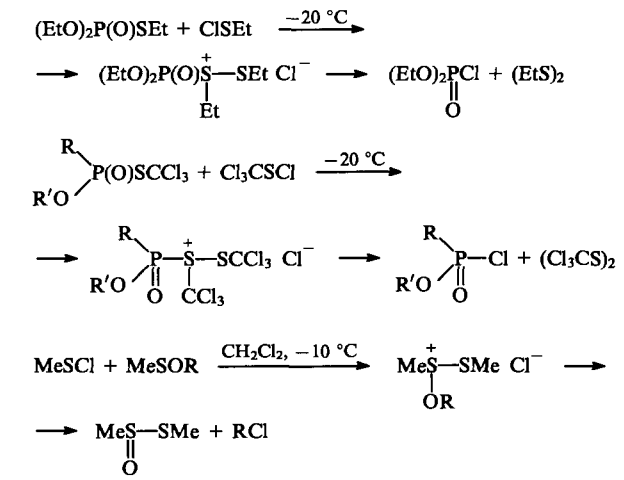
The interaction of dialkyl disulfides[157,158] and diaryl disulfides[159–161] with Lewis acids ($SbCl_5$, SbF_5) or with sulfenyl chlorides leads to the formation of [dialkyl(aryl)]alkyl(aryl)-thiosulfonium salts.



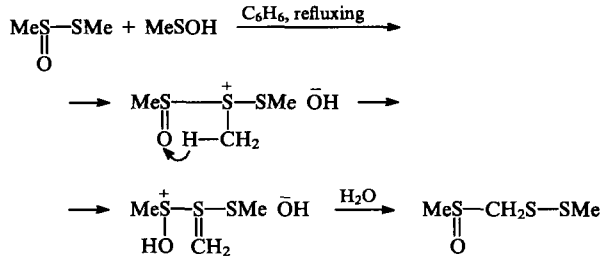
R = Me, Ph, 4-ClC_6H_4, 4-MeC_6H_4, 2,4,6-$Me_3C_6H_2$.

The salt solutions obtained can be stored without change for several hours at −50 to −20 °C. The formation of intermediates of analogous structure in the disproportionation of disulfides in an acid medium has been postulated.[162]

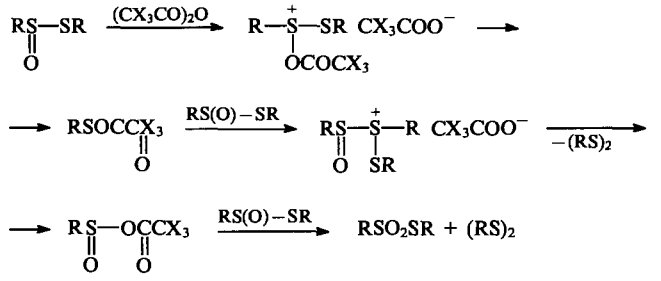
Other methods of generation. The formation of alkylthiosulfonium intermediates has been observed in the reactions of alkanesulfenyl chlorides with phosphorothiolates[163] and sulfenates.[2]



It has been suggested[164] that the sulfenic acids formed in the thermal dissociation of thiolosulfinates in the absence of trapping agents may react with the thiolosulfinates to form sulfinylthiosulfonium intermediates, which are converted into alkane-α-sulfinyl disulfides as a result of the Pummerer rearrangement.



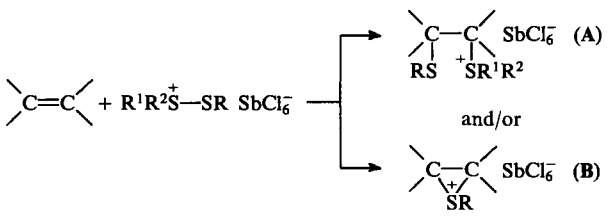
The probable mechanism of the rearrangement of thiolosulfinates on treatment with the anhydrides of trichloro- and trifluoro-acetic acids, described in the literature,[165] also involves the generation of thiosulfonium intermediates.



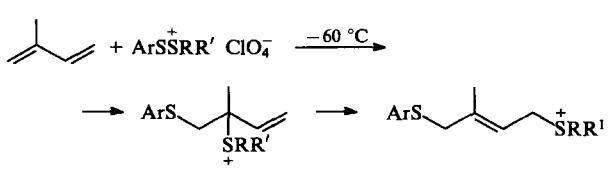
R = Me, $PhCH_2$; X = Cl, F.

b. The applications of alkyl(aryl)thiosulfonium and [dialkyl(aryl)]-alkylthiosulfonium salts in organic synthesis

It has been noted[155,157,158,166] that alkyl(aryl)thiosulfonium salts are effective agents for transferring the RS^+ groups to the double bond in Ad_E reactions with alkenes such as cyclohexene, 1-methylcyclohexene, tetramethylethene, cyclooctene, styrene, isoprene, etc. These reactions take place relatively easily even at −10 to −30 °C and lead to the formation β-alkyl(aryl)-thiosulfonium salts **A**[155,157,158,166] and/or *S*-alkyl(aryl)episulfonium salts **B**.[155–158]



According to Kal'yan et al.,[155] the interaction of alkenes with the salts RR′S^+–SAr $SbCl_6^-$ (R = R′ = Me; Ar = Ph, 4-MeC_6H_4, 4-ClC_6H_4, 2,4,6-$Me_3C_6H_2$, 4-$CF_3C_6H_4$, C_6F_5) and RR′S^+SAr $SbCl_6^-$ [R + R′ = $-(CH_2)_4-$, Ar = 4-ClC_6H_4, 2,4,6-$Me_3C_6H_2$] proceeds most unambiguously. In the reactions of these salts with cyclohexene, styrene, and isoprene, the formation of only β-arylthioalkylsulfonium salts A, readily isolated in the form of substances fairly stable in the solid state, has been observed. According to ^1H NMR data, the salts obtained under these conditions from isoprene have the structure of 1,4-adducts formed as a result of the rearrangement of the 1,2-adducts.

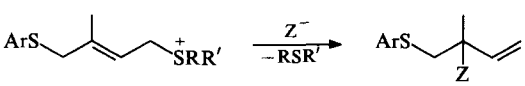


The formation of the episulfonium salt **B** has been observed in the reaction of ($RR'S^+-SC_6H_4Me$-4) $SbCl_6^-$ (R = Me, R′ = C_6H_4Cl-4) with cyclohexene, but, when the methyl group in the *S*-aryl fragment of the initial salt is replaced by CF_3 or Cl, a 1 : 1 mixture of the salts **A** and **B** is obtained. This enabled the authors[155] to postulate the primary formation of the episulfonium salt **B**, the interaction of which with the sulfide present in the reaction mixture leads to the salt **A**. The reactivity of the episulfonium salt **B** is then determined by the nature of the substituents in the *S*-aryl fragment. In terms of their reactivity in relation to nucleophiles, certain salts **A** are close to the episulfonium salt **B**. Thus the reactions of these salts with the acetate anion lead to the corresponding acetoxy-adducts.

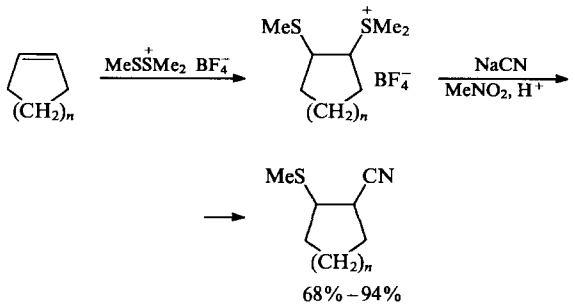


R = Me, Ph; R′ = Ph, 4-ClC_6H_4.

Salts of type **A** based on isoprene react in an unusual manner with the acetate anion and other nucleophiles. In this case, the reaction proceeds exclusively in accordance with an S_N2 mechanism with formation of β-acetoxysulfides.

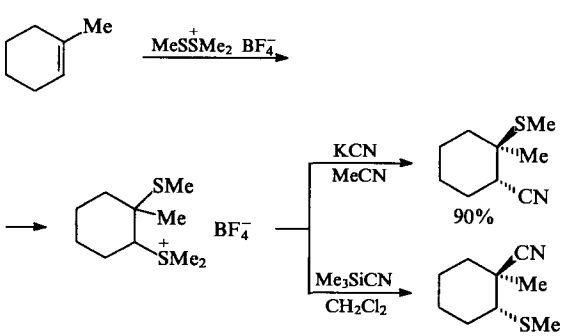


It has been noted[9] that β-alkyl(aryl)thiosubstituted salts **A** are effective electrophiles for the transfer of the β-alkyl(aryl)thioalkyl group in reactions with anionic C-nucleophiles. For example, it has been shown that the adducts of different alkenes with $MeS\overset{+}{S}Me_2$ BF_4^- react fairly readily with the cyanide ion, which has made it possible to develop a general method for the cyanosulfenylation of alkenes under mild conditions.

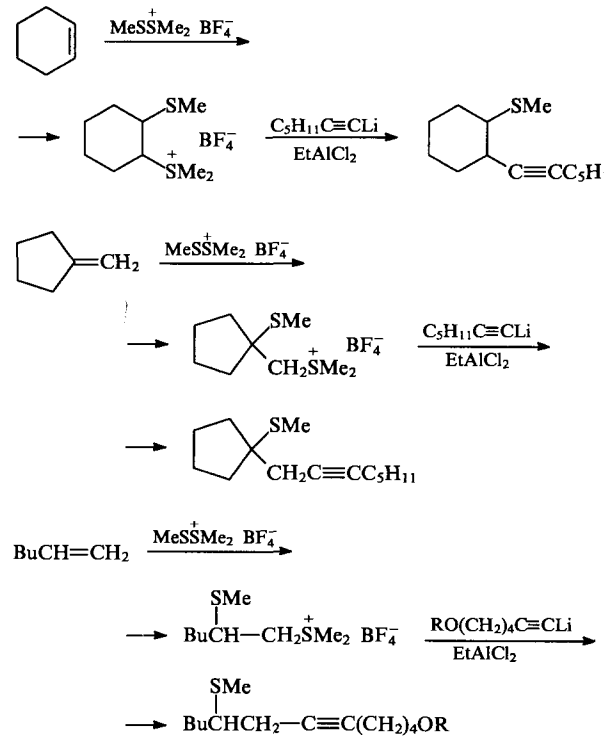


68%–94%

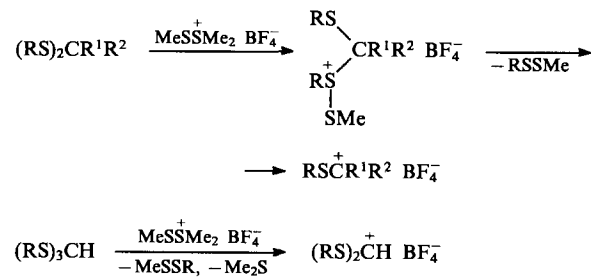
When the reaction conditions are altered, both regioisomers may be obtained.



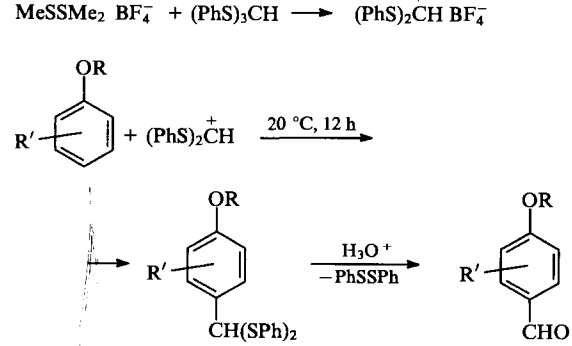
Complexes of acetylides with organoaluminium compounds are also used as the C-nucleophiles.[9]



One of the very important aspects of the use of alkyl(aryl)-thiosulfonium salts in organic synthesis is the generation of α-thio-substituted[167] and α,α-dithio-substituted[168] carbonium ion intermediates.

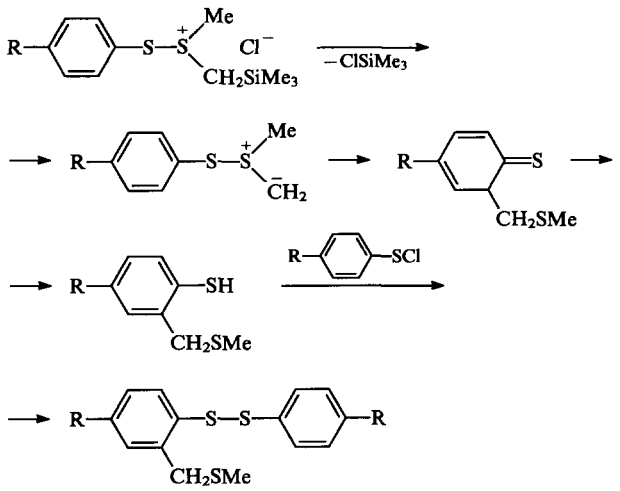


In a regioselective method[169] for the formylation of phenols and naphthols, a α,α-diphenylthio-substituted carbonium ion is generated with the aid of the salt $MeSS^+Me_2$ BF_4^-.

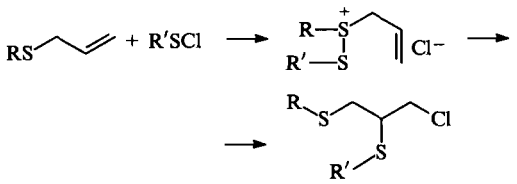


The rearrangements of alkyl(aryl)thiosulfonium salts are frequently employed to synthesise various sulfur-containing compounds. For example,[170] the spontaneous 2,3-sigmatropic rearrangement of the salts $RR'S^+SAr$ Cl^- (R = Me; R′ = CH_2SiMe_3; Ar = Ph; 4-MeC_6H_4, 4-ClC_6H_4), formed in the

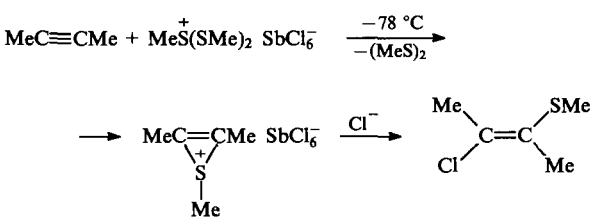
reactions of arenesulfenyl chlorides with methylthiomethyl(trimethyl)silane, has been described.[170] The authors suggest[170] that the rearrangement proceeds via an ylide formation stage.



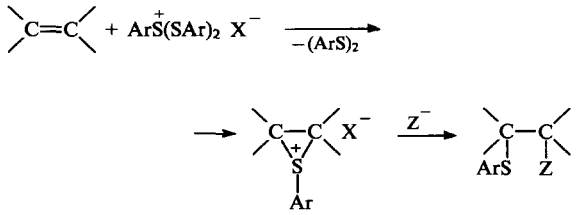
An interesting case of a degenerate 2.3-sigmatropic rearrangement has been observed in the interaction of sulfenyl chloride with allyl sulfides.[54,171]



[Dialkyl(aryl)]alkyl(aryl)thiosulfonium salts are also effective agents for the transfer of the RS^+ group in Ad_E reactions with unsaturated hydrocarbons. The interaction of such salts with ethyne hydrocarbons leads to the formation of thiirenium salts, the reactions of which with nucleophiles involve ring opening and the formation of unsaturated sulfides.[172]



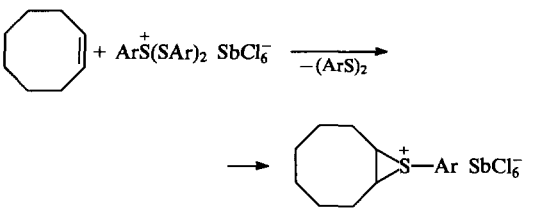
(Diaryl)arylthiosulfonium salts react rapidly with alkenes even at −60 °C, affording the corresponding *S*-arylepisulfonium salts, which are converted into β-substituted aryl sulfides on treatment with nucleophiles.[159–161]



Ar = Ph, 4-ClC_6H_4, 4-MeC_6H_4, 2,4,6-$Me_3C_6H_2$.

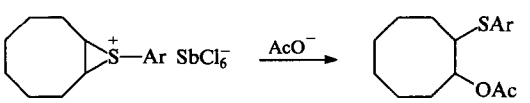
X = $SbCl_6$, SbF_5Cl, Z = OAc.

The reaction of (diaryl)arylthiosulfonium salts with cyclooctene has been studied in greatest detail. In this case, the authors[161] were able to isolate *S*-arylcyclooctenoepisulfonium hexachloroantimonates in a crystalline state in 100% yield.

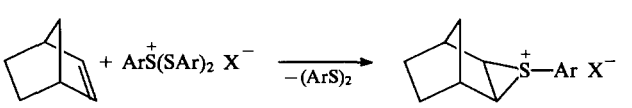


Ar = Ph, 4-ClC_6H_4, 4-MeC_6H_4, 2,4,6-$Me_3C_6H_2$.

The reactions of these salts with the acetate anion lead to the formation of 2-acetoxycyclooctyl aryl sulfides.



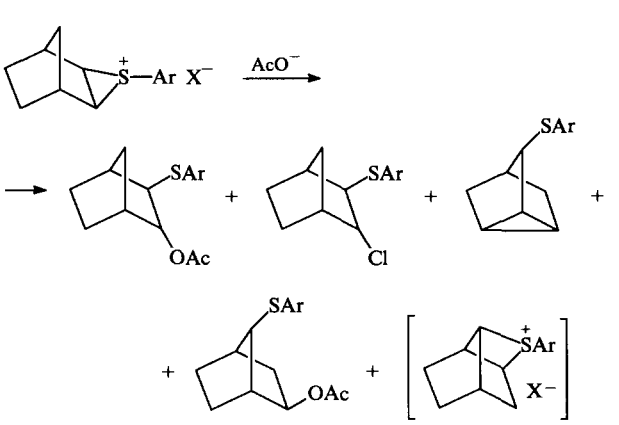
The corresponding *S*-arylnorbornylideneepisulfonium salts have also been isolated in the solid state and characterised.[161]



X = $SbCl_6$; Ar = 4-ClC_6H_4, 4-MeC_6H_4, 2,4,6-$Me_3C_6H_2$.

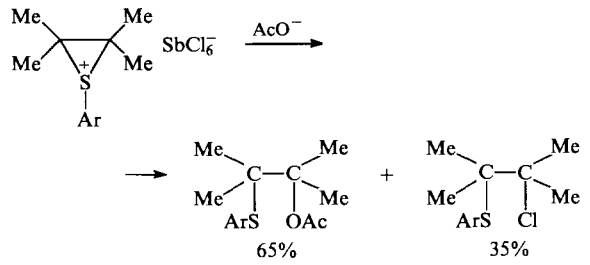
X = SbF_6; Ar = 4-ClC_6H_4, 2,4,6-$Me_3C_6H_2$.

The interaction of these salts with the acetate anion results in the formation of a mixture of several products, which, according to the authors,[161] is due to their instability in solution.

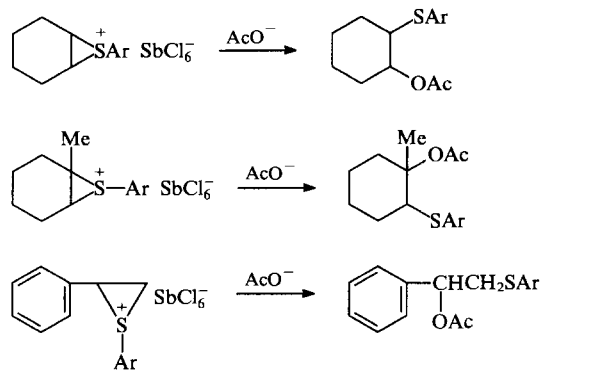


The composition and structure of the final products of this reaction are influenced significantly also by the nature of the initial episulfonium salt. For example, the reaction of the *S*-methylnorbornylideneepisulfonium salt with the acetate anion leads to the formation of only one product—2-acetoxy-3-methylthionorbornane in 95% yield.[161]

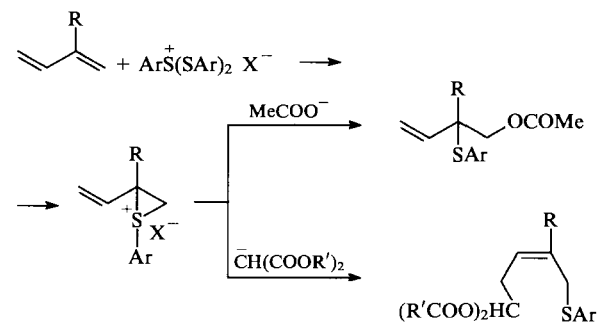
In the reaction of the $ArS^+(SAr)_2$ (Ar = 2,4,6-$Me_3C_6H_2$) salt with tetramethylethene, the authors[161] were able to isolate the episulfonium salt in the crystalline state in 89% yield. The interaction of this salt with the acetate anion leads to the formation of a mixture of two products—2-acetoxy-3-mesitylthio-2,3-dimethylbutane and 2-chloro-3-mesitylthio-2,3-dimethylbutane.



The episulfonium salts formed in the reactions of cyclohexene, 1-methylcyclohexene, and styrene with $ArS^+(SAr)_2\ SbCl_6^-$ (Ar = 2,4,6-$Me_3C_6H_2$) are unstable and it was not possible to isolate them in the crystalline state. Their presence was demonstrated by their reactions with the acetate anion, which resulted in the formation of the corresponding β-acetoxysulfides.



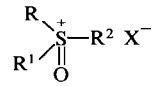
The interaction of (diaryl)arylthiosulfonium salts with butadiene and isoprene[173] afforded the corresponding *S*-aryl-episulfonium salts, which were isolated in a free state. They are hygroscopic crystalline substances stable at temperatures below 0 °C. The reactions of these salts with the acetate anion lead to 1,2-acetoxyarylthio-adducts (yield up to 90%), whilst their interaction with sodiomalonic ester proceeds via a different mechanism and the formation of 1,4-adducts (yield up to 60%).



R = H, Me; R′ = Me, Et; X = BF_4, SbF_6, $SbCl_6$;
Ar = Ph, 4-ClC_6H_4, 4-MeC_6H_4, 2,4,6-$Me_3C_6H_2$, 4-$CF_3C_6H_4$, C_6F_5.

IV. Sulfoxonium (oxosulfonium) reagents

Oxosulfonium salts having the general formula



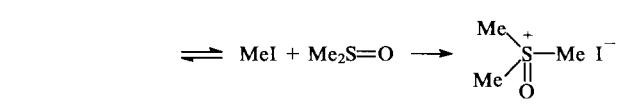
R = Alk, Ar; R^1 = Alk, Ar; R^2 = Alk, Ar, $NAlk_2$;
X = Cl, Br, I, BF_4, etc.;

as well as some of their derivatives are the principal members of the class of oxosulfonium reagents.

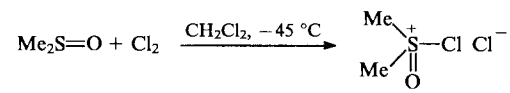
1. Methods for the generation of oxosulfonium salts

a. Generation from sulfoxides

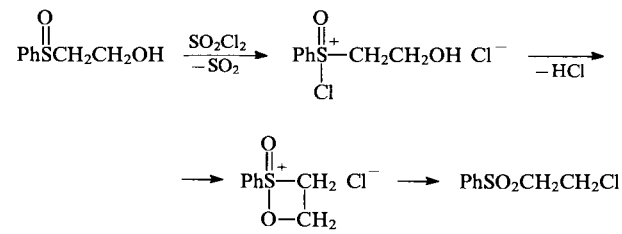
The reaction of dimethyl sulfoxide with methyl iodide results in the formation of dimethylmethoxysulfonium iodide, which is slowly converted into the thermodynamically more stable trimethyloxosulfonium iodide.[2]



Optically active oxosulfonium salts are obtained from optically active sulfoxides by their interaction with the MeI–HgI_2 system.[173] Dimethyl sulfoxide reacts with chlorine in methylene chloride at −45 °C, forming a relatively unstable chlorodimethyloxosulfonium salt.[174]

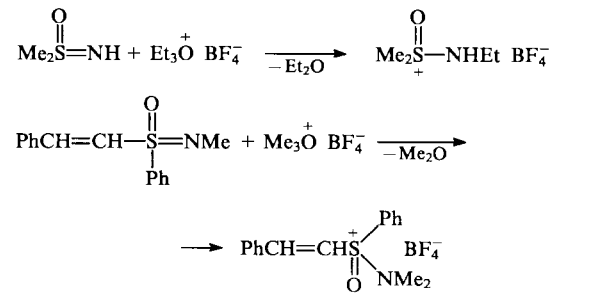


Chlorooxosulfonium salts are also obtained at an intermediate stage in the oxidative chlorination of β-hydroxysulfoxides.[175]



b. Generation from sulfoximides

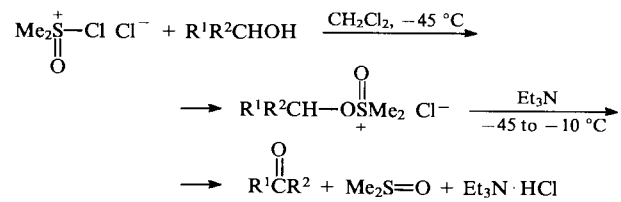
Sulfoximides which are unsubstituted or substituted at the nitrogen atom react relatively easily with trialkyloxonium salts to form oxosulfonium salts.[2]



2. Applications of oxosulfonium salts in organic synthesis

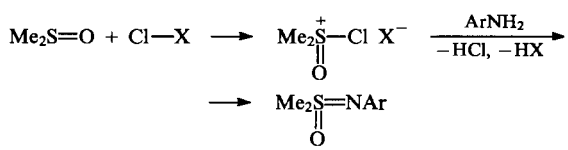
a. Oxidation of alcohols

Chlorodimethyloxosulfonium salts, formed as a result of the chlorination of dimethyl sulfoxide by chlorine, are used to oxidise primary and secondary alcohols to carbonyl compounds.[176]



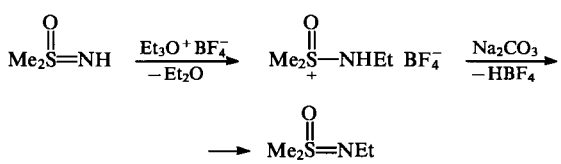
b. Synthesis of sulfoximides

The interaction of chlorooxosulfonium salts with aromatic amine entails the replacement of the chlorine atom at the sulfur atom by the imido-group with formation of sulfoximides.[91]



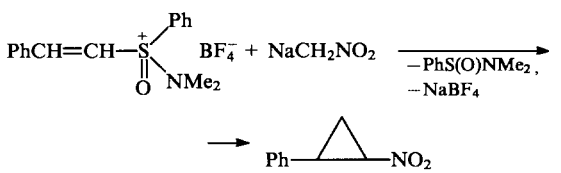
X = Cl, Bu^{t}O.

Sulfoximides are also formed when dialkylaminooxosulfonium salts are treated with bases, which, bearing in mind the ability of unsubstituted sulfoximides to be alkylated by trialkyloxonium salts, may be used to convert unsubstituted sulfoximides into *N*-substituted ones.

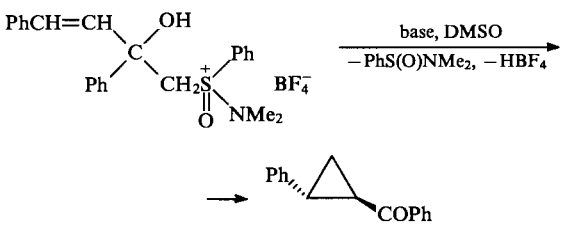


c. Synthesis of cyclopropanes

The interaction of substituted vinyloxosulfonium salts with C-nucleophiles, for example with sodionitromethane, results in the formation of cyclopropanes.[2]

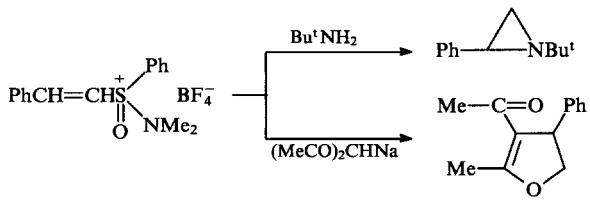


The intramolecular cyclisation of oxosulfonium salts containing an activated double bond also leads to cyclopropanes.[177] It has been suggested that in this case an oxonsulfonium ylide is generated with subsequent transfer of the methylene group to the C=C bond.



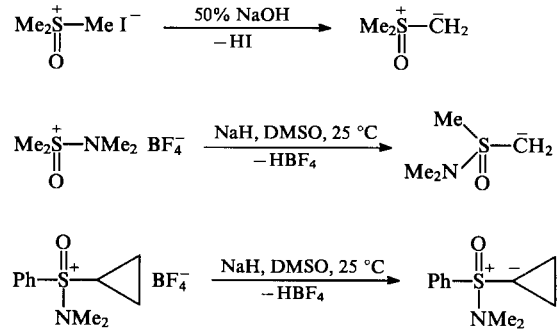
d. Synthesis of heterocyclic compounds

On interaction with primary amines, substituted vinyloxosulfonium salts afford aziridines, whilst their interaction with the sodium salt of acetylacetone leads to dihydrofuran derivatives.[178]

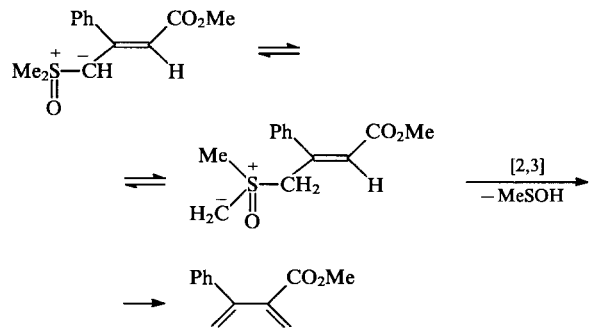


e. Generation of oxosulfonium ylides

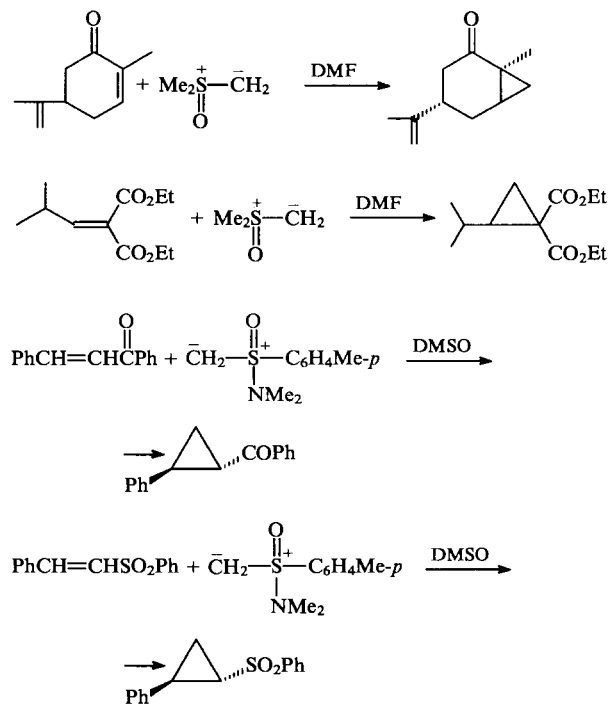
Treatment of dialkyloxosulfonium salts with deprotonating agents leads to the formation of oxosulfonium ylides,[36] which are more stable than dialkylsulfonium ylides.



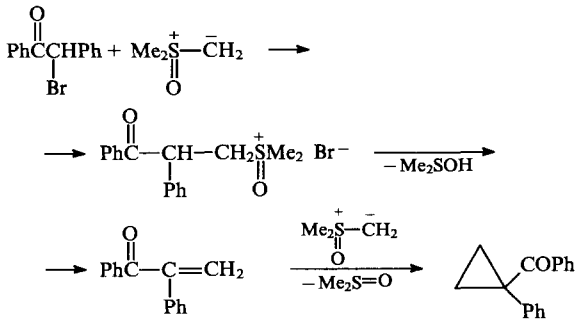
Together with oxosulfonium salts, oxosulfonium ylides have found extensive application in the synthesis of dienes, cycloalkanes, epoxy-compounds, spiro-compounds, and other products of fine organic synthesis. For example, the thermal rearrangement of certain alkenyloxosulfonium ylides is used in the synthesis of dienes.[2]



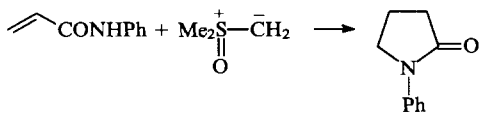
Oxosulfonium ylides are selective agents for the transfer of the methylene group to the electrophilic double bond. As a rule, these reactions lead to the formation of cyclopropanes. In the case of α,β-unsaturated carbonyl compounds, the methylene group adds not to the carbonyl group but to the C=C bond.



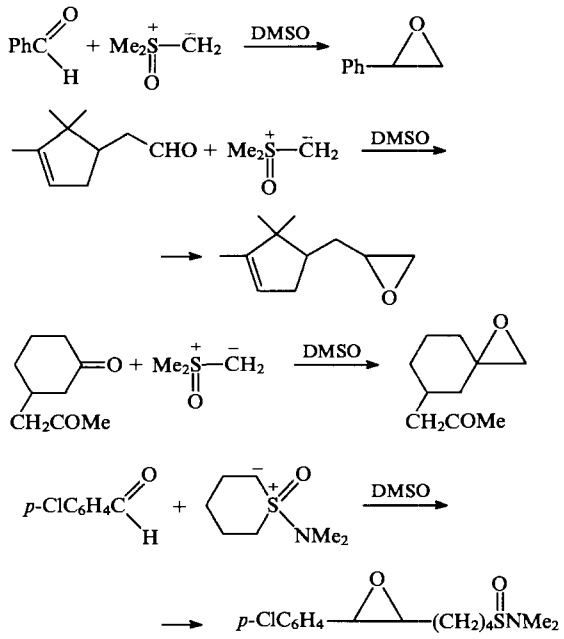
In the interaction of oxosulfonium ylides with α-bromoketones or esters, cyclopropanes are formed as a result of a sequence of alkylation, elimination, and methylene group transfer reactions.



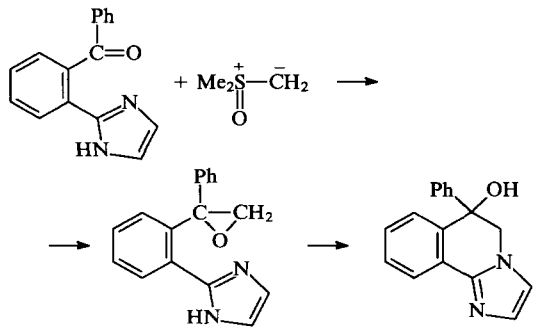
The transfer of the methylene group to the double bond in *N*-substituted amides of α,β-unsaturated carboxylic acids is accompanied by a prototropic shift and subsequent cyclisation with formation of γ-lactams.[2]



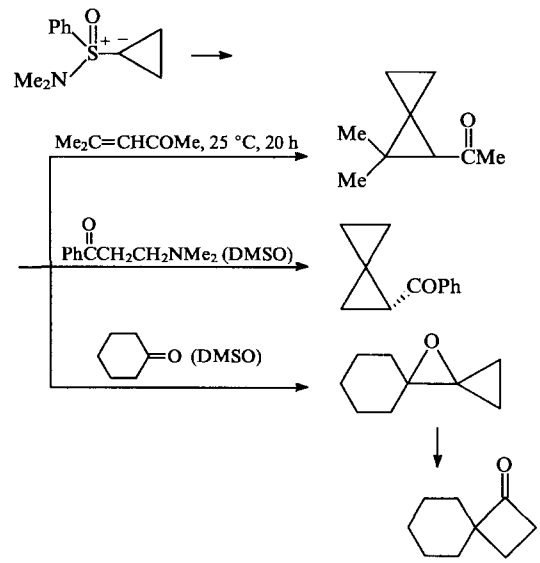
The addition of the methylene group to the C=O bond in aldehydes and ketones has found extensive application in the synthesis of epoxy-compounds with a wide variety of structures.[36]



In those cases where the epoxide molecule contains other reaction centres as well as the oxygen atom, there is a possibility of structural isomerisation.



The transfer of the cyclopropylidene group to the C=C and C=O bonds with the aid of cyclopropyloxosulfonium ylides is to a large extent analogous to the effect of diphenylsulfonium cyclopropylide (see above) and is used in the synthesis of spiro-compounds.[28]



* * *

It is seen from the present review that the application of S-cationoid reagents in fine organic synthesis has become very common during the last 10–15 years. It is based on the ability of such reagents to participate in the transfer of thiyl, methylene, and other functional groups and also on their involvement in the generation of radical-cations and ylides, in the selective oxidation of alcohols, and in other very important processes. This property is used widely in the syntheses of sulfides, cyclopropanes, epoxides, carbonyl compounds, spiro-compounds, sulfimides, sulfoximides, derivatives of iminosulfinic acids, and other important products of fine organic synthesis with functional group substituents.

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Intermediates and mechanisms of heterogeneous catalytic reactions. Oxidation reactions involving molecular oxygen and sulfur

O V Krylov, V A Matyshak

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Abstract. The structure of the intermediate surface compounds in heterogeneous catalytic oxidation reactions involving molecular oxygen and sulfur is discussed. The degrees of reliability of the role of various proposed structures in catalysis are evaluated. The reaction mechanisms derived from information on the surface complexes are presented. The bibliography includes 141 references.

I. Introduction

In our previous review[1,2] we have discussed the intermediate surface compounds observed during spectroscopic surface studies under the conditions of various heterogeneous catalytic reactions. The present review, which concludes the series, deals with oxidation reactions involving oxygen and sulfur. These reactions differ from those previously considered[1,2] by strongly involving atoms from the catalyst lattice.

The problem of the intermediate form of both the oxygen and the substance to be oxidised, and of the mechanism of their activation, invariably arises in studies of the mechanism of oxidation reactions.

Oxygen can be incorporated in an oxide lattice, or convert a metal into an oxide. In these cases the lattice can be treated as an intermediate form. The ionic forms O_2^-, O^{2-}, and O^- were observed by EPR and Raman spectroscopy during the reduction of the O_2 molecule to the regular lattice of O^{2-}. They were treated as compounds taking part in the catalytic reaction.

O V Krylov, V A Matyshak Complex Heterogeneous Catalyst Laboratory, N N Semenov Institute of Chemical Physics of the Russian Academy of Sciences, ul. Kosygina 4, 117977, Moscow.
Fax (7-095) 938 21 56

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II. Oxidation of carbon monoxide

The simplest oxidation reaction is the oxidation of CO. Its mechanism has been studied by many workers both on metals and on nonmetals. In particular, detailed studies have been made of the oxidation of CO on the faces of single crystals of the metals Pt, Pd, Ir, Ru, and Rh.[3]

On Pd(111) this reaction has been studied at low pressures (1.5 Torr) by absorption-reflection IR spectroscopy combined with kinetic measurements.[4] The rate of the reaction depended on the coverage of the surface by carbon monoxide.

The adsorption of CO and O_2 was also studied by low-energy electron diffraction (LEED), electron energy loss spectroscopy (EELS), and X-ray photoelectron spectroscopy (XPES). It is widely thought that at temperatures close to or below that of the catalytic reaction CO is adsorbed as bridging or linear carbonyls. Oxygen is adsorbed in a molecular or an atomic form. The mechanism of their interaction can include the following steps:

$$CO \rightleftharpoons CO_{ads},$$

$$O_2 \longrightarrow 2\,O_{ads},$$

$$O_{ads} + CO_{ads} \longrightarrow CO_2,$$

$$O_{ads} + CO \longrightarrow CO_2,$$

$$O_2 + 2\,CO_{ads} \longrightarrow 2\,CO_2.$$

The last of these reactions can be ignored, because the formation of CO_2 is not observed on a surface saturated with CO and exposed to gaseous oxygen. The interaction of CO with O_{ads} can take place with CO either in the gas phase (the Eley–Rideal mechanism) or in the adsorption layer (the Langmuir–Hinshelwood mechanism).

In the various mechanisms for the interaction of CO with C_{ads} it is assumed that the reaction takes place between neighbouring O_{ads} and CO_{ads} species, between more distant species (when the reaction is made possible by surface diffusion), or on the boundary of surface islets consisting of O_{ads} and CO_{ads}.

It is not self-evident that the effects observed at very low pressures can occur also at the higher pressures more commonly used in catalysis. It has been suggested[3] that since the pressure ratio

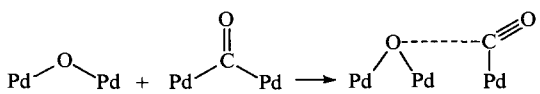
$$r = k\frac{P_{O_2}}{P_{CO}},$$

occurs in the rate equation for the reaction the rate should be independent of the total pressure, and therefore all the features of the reaction should be the same at low and at high pressures.

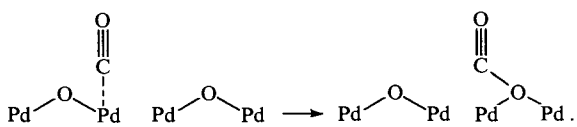
The same forms of adsorbed CO and oxygen were observed in a study by IR spectroscopy of the oxidation of CO on Pd at steady state.[5]

Bridging and linear forms of adsorbed CO, located both on terraces and on steps, were observed[6] on a Pt(335) surface by IR absorption–reflection spectroscopy. The carbon monoxide on the steps was oxidised substantially faster than the carbon monoxide on the terraces.

The oxidation of CO on Pd supported on a layer of SiO_2 deposited on a Mo(110) crystal face was studied by absorption–reflection IR spectroscopy and by temperature programmed desorption (TPD) over a wide range of pressure (10^{-9}–10^{15} Torr) and temperature (70–700 °C).[7] At low pressures the CO and the oxygen were adsorbed separately, probably as islets. In order to induce the reaction a CO molecule must diffuse into an islet of O_{ads}, surmounting the opposing barrier as a result of the exothermic reaction



At high pressures and relatively low temperatures a shift in the CO frequencies was observed in the stationary state, and attributed[7] to the simultaneous adsorption of CO and O on the same atom of Pd (O–Pd–CO), or to the formation of the weakly adsorbed precursor



The transition state is reminiscent of the CO_2 molecule. We know[8] that the vibrational excitation of the CO_2 molecule is strongest when the molecule is formed in a layer strongly covered with oxygen before being desorbed. Under certain conditions this can give rise to a 'pressure gap': a large difference between the effects observed at high and at low pressures.

A study of the EELS spectra during the oxidation of CO on Rh(111) showed[9] that the Rh–O–CO_2 complex, stabilised by OH groups, is formed on oxidised rhodium (i.e. in an excess of O_2). Carbon dioxide adsorbed on a clean Rh–O surface is desorbed at a temperature 100 K lower than from a Rh–OH surface.[9] It was concluded that the decomposition of the carbonate species could be rate-limiting.

Many studies of the oxidation mechanism of CO were carried out on supported metals,[10–21] because in these systems the specific surface of the catalyst is much greater and the intensity of the IR bands is correspondingly high.

According to Cant and Donaldson[10] the CO absorption band at 2075 cm^{-1} is unchanged during the interaction of CO with O_2 on Pt/SiO_2 at 40–50 °C. The kinetic order of the reaction (first order) with respect to the coverage of the surface with CO molecules (θ_{CO}) is attributed[10] to the location of the reaction at the boundary between CO_{ads} and O_{ads} islets.

A study of the IR spectra in the transition regime during the oxidation of CO on a 9.1% Pt/SiO_2 catalyst at 100–160 °C detected[11] a transition from the Eley–Rideal to the Langmuir–Hinshelwood mechanism as the adsorption of CO increased. However, unambiguous spectroscopic studies (i.e. studies of the kinetics of the intensity changes of the IR bands of the adsorbed species) were not attempted.

A study in which the rate of the reaction on Pt/SiO_2 was compared with the kinetics of the change in the Fourier transform IR (FTIR) spectra has been reported.[12] At 300 °C, when the rate of the reaction was high, the coverage θ_{CO} was less than 1% (i.e. below the sensitivity limit of the apparatus). Linearly bound CO was observed under conditions of low catalyst activity.

Simultaneous measurements of the band intensities in the FTIR spectra with one-second resolution and of the rate of the reaction in the transition regime were carried out[13] on Pt/Al_2O_3 at 140 °C. Self-oscillations were observed, with four linear forms of adsorbed CO and one bridging form. The linear CO–Pt form (2073 cm^{-1}) responds most rapidly to a change in composition of the gas phase. The yield of CO_2 is most accurately correlated with the intensity of the absorption band of the linear form (2092 cm^{-1}), which corresponds to the adsorption of CO on a Pt atom adjacent to a Pt–O bond. The following mechanism has been proposed for the oxidation mechanism of CO on Pt:

$$O_2 + 2\,Pt_n \overset{(1)}{\rightleftharpoons} 2\,Pt_nO,$$

$$O_2 + 2\,Pt \xrightarrow{(2)} 2\,PtO,$$

$$CO + Pt_nO^* \xrightarrow{(3)} CO^*Pt_nO^*,$$

$$CO^*Pt_nO^* \xrightarrow{(4)} Pt_n + CO_2,$$

$$CO + Pt \overset{(5)}{\rightleftharpoons} PtCO^*,$$

$$CO + 2\,Pt \overset{(6)}{\rightleftharpoons} Pt_2CO^*,$$

$$CO + PtO \overset{(7)}{\rightleftharpoons} PtOCO^*,$$

$$PtOCO^* \xrightarrow{(8)} Pt + CO_2,$$

$$PtCO^* + Pt_nO \xrightarrow{(9)} CO^*Pt_{n+1}O^*,$$

$$CO^*Pt_{n+1}O^* \xrightarrow{(10)} Pt_{n+1} + CO_2,$$

$n > 2$, surface compounds are shown by an asterisk.

Reactive oxygen is formed with the participation of at least two Pt atoms. The monoxide is easily formed, but when adsorbed on PtO it is inactive in this reaction. The reaction between O* and CO* can take place if the O* diffuses to a CO* centre or if gaseous CO interacts with PtO*. The reaction is possible also at the boundaries of the CO islets, where the linearly adsorbed CO can react, though this species has no activity when located within the islet.[14]

Also the oxidation of CO on Pt/SiO_2 and Pd/SiO_2 at 80–320 °C has been studied by FTIR spectroscopy with one-second resolution, and the kinetics of the reaction were studied with a quadrupole mass spectrometer.[15] It was found that the dissociation of O_2 is probably the rate-limiting step, and the adsorption of CO is a fast process. All three forms of CO react with O_2 at the same rate. The model proposed for the reaction assumes the presence of CO islets with very reactive boundaries.

In a study of the reaction of CO with O_2 on Ru/SiO_2, Rh/SiO_2, and Pd/SiO_2 it was found that the linear and the bridging forms of CO react faster than the dicarbonyl forms.[16] On Pt supported on graphite the bridging forms of CO have a greater reactivity than the linear forms (Pt–C≡O).[17] Conversely, it was reported[20] that on Pd–Rh/SiO_2 the linear forms of CO are more active than the bridging forms. According to Anderson[18] on Pt–Rh/Al_2O_3 only the linear forms adsorbed on the Pt can contribute to the reaction. The $Rh(CO)_2$ forms are not active in this reaction.

Six forms of surface carbonyl were detected on Rh supported on SiO_2, Al_2O_3, or La_2O_3: Rh–CO, Rh_2–CO, Rh^+–CO, $ORh^+(CO)_2$, ORh^+CO, and $Rh^+(CO)_2$.[19] The following reaction mechanism was proposed:

$$Rh^0 + CO \xrightarrow{(1)} Rh^0CO,$$

$$Rh^0 + \tfrac{1}{2}O_2 \xrightarrow{(2)} Rh^+O_l \rightleftharpoons Rh^+O_s \rightleftharpoons Rh^0O_s,$$

$$Rh^+O_s + Rh^0CO \xrightarrow{(3)} CO_2,$$

$$Rh^+O_s + CO \xrightarrow{(4)} O_sRh^+CO \xrightleftharpoons{CO} O_sRh^+(CO)_2,$$

$$Rh^+ + O_2 \xrightarrow{(5)} Rh^{n+}O_s \xrightarrow{CO} Rh^+ + CO_2,$$

$$O_sRh^+(CO)_2 \xrightarrow{(6)} Rh^0CO + CO_2,$$

$$O_sRh^+CO \xrightarrow{(6a)} Rh^0 + CO_2.$$

Here O_s is oxygen on the surface, and O_l is oxygen in the lattice.

The breakdown of the complexes with formation of CO_2 takes place at high temperatures. When transition metal oxides are added to the supported metals the lattice oxygen also contributes to the oxidation of CO. On $Pd-CeO_x/Al_2O_3$ the kinetics of the oxidation of CO have been studied by EPR.[21,22] It was found that the low-temperature (100–150 °C) reaction takes place only on catalysts which contain the reactive $O_2^- - Ce^{4+}$ ion. The kinetics of the change in concentration of the O_2^- ion at 100 °C correspond to the kinetics of the oxidation of the CO. In the high-temperature region (> 200 °C) the O_2^- form is not observed. As reported,[21] in this case the lattice oxygen $O^{\delta-}$ takes part in the reaction.

In a study by FTIR spectroscopy of the oxidation of CO on Au supported on Co_3O_4, α-Fe_2O_3, or TiO_2 carboxylate and CO_3^{2-} groups were seen on the catalyst surface, and the last names disappeared during the reaction.[23] Nevertheless a mechanism which ascribed the formation of CO_2 to the decomposition of carboxylates was proposed.

The oxidation of CO at 20 °C on Ag/Y_2O_3 and Cu/Y_2O_3 has been studied by EPR.[24] At low concentrations of Cu and Ag the reaction followed the mechanism

$$e \longrightarrow \square_O^- \xrightarrow{2\,CO} (CO)_2^- \xrightarrow[-CO_2]{O_2} O_2^- \xrightarrow[-CO_2]{2\,CO} CO_2^- \longrightarrow CO_2 + \square_O + e,$$

$$CO + 2\,O_2^- \longrightarrow CO_3^{2-} + \square_O,$$

$$e + Ag^{2+}(Cu^{2+}) \longrightarrow Ag^+(Cu^+).$$

$\square_O$ is an oxygen vacancy.

At high concentrations of Ag or Cu the reaction follows a different path:

$$Ag^+(Cu^+) + CO + 2\,O^- \longrightarrow Ag^{2+}(Cu^{2+}) + CO_3^- + 2e + \square_O,$$

$$CO_3^- \longrightarrow O^- + CO_2,$$

$$e + Ag^{2+}(Cu^{2+}) \longrightarrow Ag^+(Cu^+),$$

$$Ag^+(Cu^+) + CO \longrightarrow Ag^+(Cu^+)–CO,$$

$$\tfrac{1}{2}O_2 + 2e + \square_O \longrightarrow O^{2-}.$$

The participation of conduction electrons and of lattice oxygen is stipulated also for the oxidation of CO on oxides. The oxidation of CO on ZnO after exposure to light was studied[25] by EPR between −50 and +80 °C, and the following reactions were observed:

$$Zn–O^- + CO \longrightarrow Zn–CO_2^-,$$

$$Zn–CO_2^- \longrightarrow Zn–CO_2 + e,$$

$$Zn–CO_2^- + O_2 \longrightarrow Zn–CO_2 + O_2^-,$$

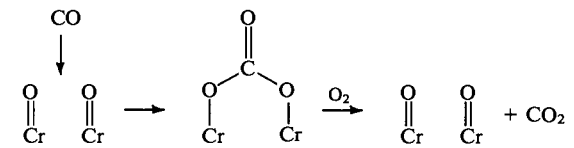
$$Zn–\square–Zn + 2e \longrightarrow Zn–O–Zn + Zn_i^0,$$

$$Zn–\square–Zn + \tfrac{1}{2}O_2 \longrightarrow Zn–O–Zn,$$

Zn_i^0 is an interstitial zinc atom.

According to data on the potentiometric monitoring of the state of an MnO_x surface[26] a metastable state of the oxide is produced under the condition of CO oxidation at 138–310 °C. The oxygen does not fill the anion vacancies on the surface but takes part in the catalytic reaction.

The mechanism of the oxidation of CO on Cr_2O_3,[27,28] ZnO,[29] and CuO,[30,31] was studied by IR spectroscopy (but not in situ). On Cr_2O_3 surface carbonates of type **1** are formed after the admission of a CO + O_2 mixture at low temperatures. At 150 °C their rate of decomposition with formation of CO_2 is quite high. In a flow of CO + O_2 the rate of decomposition of the carbonates is two orders of magnitude higher in the absence of O_2. In both cases the rate of decomposition of the carbonates is close to the rate of formation of CO_2. The following associative mechanism has been proposed[27,28] for the reaction:



1

Above 300 °C almost no carbonate groups are formed on the Cr_2O_3 surface. At this temperature the increase in the reactivity of the lattice oxygen produces a transition from an associative to a dissociative mechanism. The oxidation of CO can also take place without the participation of molecular oxygen from the gas phase. The acceleration of the decomposition of carbonates in the presence of O_2 has been observed also on ZnO.[29] According to EPR data the O_2^- ion radical contributes to this decomposition (oxidation). On the surface of CuO both carbonyl and carbonate compounds can exist.[30,31] The Cu^{2+}–CO carbonyl complexes are formed only at subzero temperatures. They are then oxidised according to the scheme:

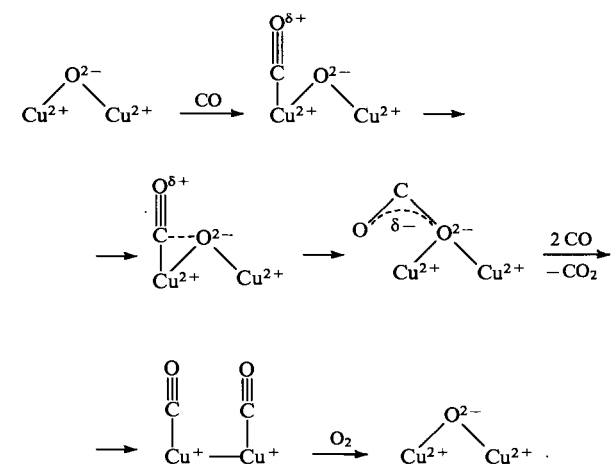
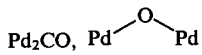
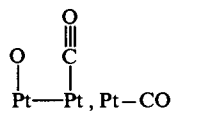
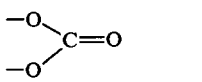
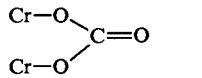
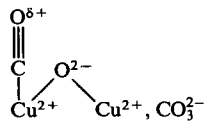
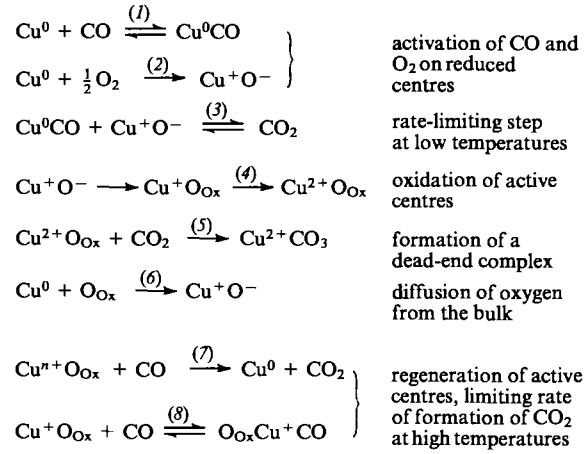


Table 1. Intermediate compounds in the oxidation of CO.

Catalyst	Intermediate complex	Reliability[a]	Ref.
Pt, Pd, Rh, Ir	M–CO, M_2CO, M–O	M	5,6
Pd/SiO_2-MoO_3	Pd–O–Pd–CO, Pd_2CO, 	H	7
Pd(111)	Pd–CO	H	4
Rh(111)	HO–Rh–O–CO_2	M	9
Pt/SiO_2	Pt–CO, Pt_2CO	H	10–12
Pt/Al_2O_3		H	13
Pt, Pd, Ru, Rh on SiO_2	M–CO, M_2CO	H	15,16
Pt/graphite	Pt_2CO	L	17
$Pd-Rh/SiO_2$	Pd–CO, Rh–CO	M	20
$Pd-Rh/SiO_2$	Pd–CO	M	18
Rh on SiO_2, Al_2O_3, La_2O_3	Rh^0CO, Rh^+CO, $ORh^+(CO)_2$, ORh^+CO, Rh_2CO, $Rh^+(CO)_2$	L	19
$Pd-CeO_2/Al_2O_3$	$Ce-O_2^-$	M	21,22
Au on Co_3O_4, Fe_2O_3, TiO_2		L	23
Cu/Y_2O_3, Ag/Y_2O_3,	O_2^-, CO_2^-	M	24
ZnO	$Zn-O^-$, $Zn-CO_2^-$	M	25,29
Cr_2O_3		M	27,28
CuO		L	30,31
CuO	Cu–CO, Cu^+-O_{ads}	H	32,33

[a] Here and elsewhere the symbol H denotes a high level of reliability, M a medium level, and L a low level.

In the presence of O_2 the surface carbonates are decomposed, possibly by a displacement mechanism (associative substitution). The overall rate of formation of CO_2 by the dissociation of all the carbonates is close to the observed rate of oxidation of CO on CuO. In spite of statements to the contrary,[30] a study by FTIR spectroscopy failed to detect surface carbonates under the conditions of the oxidation of CO on CuO.[32] It was suggested that the surface carbonates are formed by the readsorption of CO_2, i.e. they are dead-end forms. The following reaction mechanism was proposed:



A similar conclusion (that the carbonates are dead-end compounds) was reached in a study[33] of the oxidation of CO on a $CoO-Co_3O_4$ catalyst.

The intermediate compounds observed in the oxidation of CO are listed in Table 1. Thus, it has been shown fairly reliably that surface carbonyls and atomic oxygen take part in the oxidation of CO on both metals and oxides. Apparently the carbonates are dead-end compounds. At low temperatures we can observe the formation of associative complexes, in which O_{ads} and CO_{ads} are bound to the same or to neighbouring metal atoms on the surface.

III. Oxidation of ammonia

The oxidation of ammonia to NO and H_2O takes place on the platinum metals at high temperatures (800–1000 °C), when the reaction follows mainly a heterogeneous–homogeneous mechanism. Spectroscopic studies were carried out at lower temperatures. Under these conditions the reaction products include nitrogen and the nitrogen oxides N_2O and NO. On massive platinum the oxidation of ammonia was studied by emission IR spectroscopy,[34] which detected the formation of NH_2 species. The complex $Ag(NH_3)_x(NO)_y$ was observed on a silver surface, and NO_{ads} on an iron surface. On catalysts having a high activation energy for NH_3 a complex corresponding to the initial stages of the reaction is formed (in the case of Pt, the NH_2 entity). On the other hand if the catalyst has a low activation energy the species adsorbed on its surface participate in the later stages, closer to the stages which take the reaction to completion (in the case of Fe this is the adsorbed NO molecule). The formation of HNO, which apparently dissociates into OH and N_{ads}, has been observed[35] by EELS and thermal desorption methods during the oxidation of ammonia on Pt(111).

After carrying out the $NH_3 + O_2$ reaction on an MgO–CoO catalyst spectral bands corresponding to the NO_2^- and NO_3^- groups were observed[36] in the IR spectra measured at room temperature. The following mechanism for the formation of these groups was proposed:

$$Co^{2+}O^{2-} + NH_3 \longrightarrow NH_2^- Co^{2+}OH^-,$$

$$Co^{2+} + O_2 \rightleftharpoons Co^{3+}O_2^- \text{ (from EPR data)},$$

$$2\,NH_2^- + 3\,Co^{3+}O_2^- + 2\,O^{2-} \longrightarrow$$

$$\longrightarrow 2\,NO_2^- + 4\,OH^- + 3\,Co^{2+},$$

$$NH_2^- + 2\,Co^{3+}O_2^- + O^{2-} \longrightarrow$$

$$\longrightarrow NO_3^- + 2\,OH^- + 2\,Co^{2+}.$$

The following reactions are also possible:

$$2\,NH_3 + 3\,Co^{3+}O_2^- + 4\,O^{2-} \longrightarrow \longrightarrow 2\,NO_2^- + 6\,OH^- + 3\,Co^{2+},$$

$$2\,NH_3 + 4\,Co^{3+}O_2^- + 4\,O^{2-} \longrightarrow \longrightarrow 2\,NO_3^- + 6\,OH^- + 4\,Co^{2+}.$$

The formation of NO^- also cannot be excluded, but the NO^- bands in the IR spectrum are obscured by those of NO_2^- and NO_3^-.

An IR spectroscopic study[37] of the interaction of NH_3 with O_2 on MgO detected the NH_2^- complex on the surface. The $Si-NH_2$ and $Fe-NH_2$ complexes formed during the oxidation of ammonia on Fe_2O_3/SiO_2 have been described.[38] In the oxidation of NH_3 under the influence of NO on NaY zeolite Naito and Tamaru[39] observed the double complex $Ag(NH_3)_x(NO)_y$, which decomposes into N_2 and H_2O. It was shown[40-42] that the surface ammonium ion is an intermediate in the oxidation of ammonia by nitrogen oxides on V_2O_5 catalysts. We note that the information on the surface compounds given in the latter reports was obtained under conditions far removed from those of a practical catalytic reaction. Therefore it is doubtful whether or not the specified complexes have any relevance to actual reactions. The only exception is a group of papers[43-45] in which the role of the surface complexes is determined on the basis of simultaneous measurements of the reaction rate and of the rate of conversion of the surface compounds.

Table 2. Intermediate compounds in the oxidation of ammonia.

Catalyst	Intermediate complex	Reliability	Ref.
Pt	NH_2	M	34
Ag	$Ag(NH_3)_x(NO)_y$	M	34
Fe	NO_{ads}	M	34
Pt(111)	HNO	L	35
CoO–MgO	NO_2^-, NO_3^-	L	36
MoO_3	NH_4^+	H	43
ZnO	N_2O(ads)	H	44
Fe_2O_3	OH, NH_3(ads), NH_4^+, NH_2	M	45
Fe_2O_3/SiO_2	$FeNH_2$	L	38
V_2O_5	NH_4^+	L	40–42

Exposing MoO_3 to an $NH_3 + O_2$ mixture at 25–400 °C produces NH_4^+ ions on the surface.[43] A study of this catalytic reaction by the response method provide a quantitative proof that the ammonia is an intermediate compound. In the case of ZnO (see Ref. 44) N_2O(ads) is formed on the surface, and on α-Fe_2O_3 the OH group is formed (see Ref. 45) with coordinately bound ammonia, NH_4^+, and the NH_2 group. The following self-consistent chain of conversions of these complexes can be suggested:

$$NH_3 \longrightarrow NH_4^+ \longrightarrow NH_2\,(ads) \longrightarrow \longrightarrow N_2O(ads) \longrightarrow N_2 + NO.$$

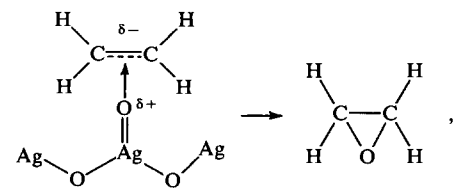
As in the case of metals the activation energy for the overall reaction (oxidation of NH_3) is lower for the catalysts on which intermediates formed in stages close to the final stage of the reaction are adsorbed.[43] Data on the intermediate compounds taking part in the oxidation of NH_3 are summarised in Table 2.

IV. Partial oxidation of olefins

The oxidation of hydrocarbons takes place by two main paths: to compounds containing oxygen (partial oxidation) and to CO_2 and H_2O (extensive oxidation). We shall first examine a partial oxidation reaction in which the main skeleton of the molecule is not broken down, and one or two oxygen atoms are added to the molecule with formation of compounds containing oxygen.

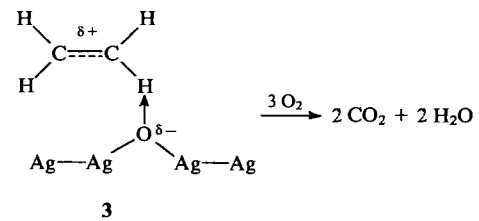
The simplest olefin (ethylene) gives ethylene oxide (C_2H_4O) after partial oxidation. Both weakly and strongly bound acetaldehyde, and also silver acetate, have been detected[46] on an Ag/α-Al_2O_3 catalyst by diffuse reflectance FTIR spectroscopy combined with kinetic measurements in the transitional regime under conditions conducive to the oxidation of C_2H_4 to C_2H_4O. An analogous study on an Ag/γ-Al_2O_3 catalyst revealed adsorbed ethylene,[47] carbonates, and Ag–CO, which are probable precursors of the extensive oxidation products.[48]

New possibilities in the study of intermediate compounds were offered by the development of the TAP (temporal analysis of products) reactor, in which the product directly desorbed from the surface can be analysed by using special attachments, thus avoiding the problem of readsorption. This development also allowed the use of millisecond (and even microsecond) measurement times, well beyond the limits of the characteristic catalysis times (10^{-2}–10^2 s) (see Gleaves et al.[49]). The application of the TAP reactor to the study of the oxidation mechanism of ethylene on powdered Ag showed[50] that the deep and the partial oxidation reactions of ethylene involve the same surface complexes of ethylene but different forms of oxygen. Carbon monoxide is formed more rapidly than ethylene oxide, mainly because of the interaction with the more weakly bound surface oxygen. Ethylene oxide is formed from both the atomic oxygen on the surface and the subsurface oxygen, which keeps the silver in an intermediate charge state Ag^{n+} (probably Ag^{3+}). Svoboda et al.[50] confirmed a scheme[51] according to which 'electrophilic' oxygen $O^{\delta+}$ forms the complex **2**, which is a precursor of ethylene oxide,



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whereas 'nucleophilic' oxygen $O^{\delta-}$ gives the complex **3**, which is an intermediate in the deep oxidation reaction:

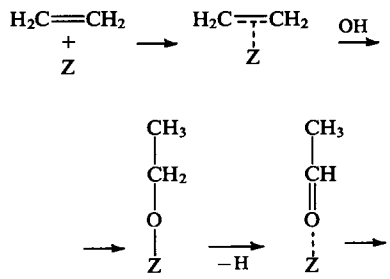


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This mechanism is further confirmed by an analysis of the Raman spectra obtained in situ during the oxidation of ethylene on Ag(111) and Ag(110). Under the catalysis conditions three Ag–O vibration bands were observed, corresponding to $Ag-O_{ads}$, the –Ag–O–Ag– subsurface group, and dissolved oxygen. The subsurface oxygen disappears as ethylene oxide is formed.

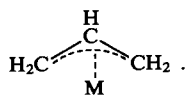
In the oxidation of ethylene to acetaldehyde on MoO_3/TiO_2 the complex π-$C_2H_4^+$ and adsorbed acetaldehyde have been observed, as well as a weak enolic complex.[52] It is assumed that

the reaction takes place with the participation of an OH surface group by a hydration–dehydrogenation mechanism:



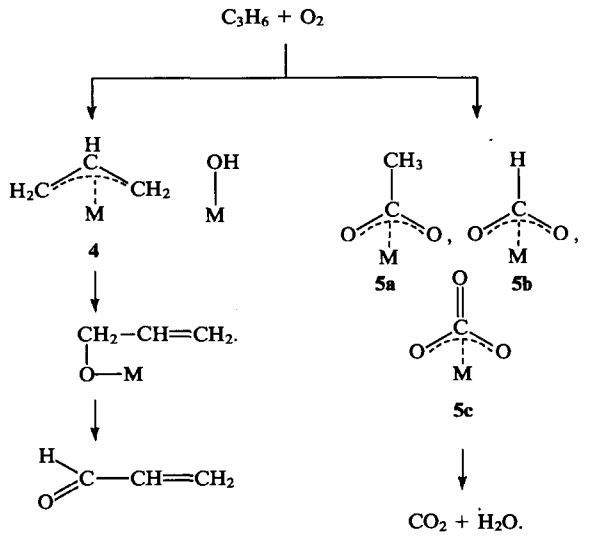
Under the conditions of the oxidation of C_3H_6 on Ag/SiO_2 a bidentate carbonate and polymeric surface formations were observed on the surface. An analysis of the in situ FTIR spectra also revealed the presence of adsorbed acrolein.[53]

The oxidation of propylene to acrolein on oxide catalysts takes place through the intermediate formation of a π-allyl complex. Many isotopic studies have established the indistinguishability of the C(1) and C(3) carbon atoms in the propylene molecule, and of the hydrogen atoms attached to them.[54] This is evidence for the symmetry of the complex:



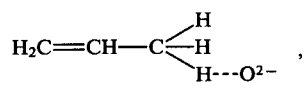
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The precursor of the π-allyl complex is a π-olefin complex. The adsorption centres for the olefin in the form of π-complexes on the oxides can be not only the metal ions but also surface acidic centres of the Brønsted type.[55] π-Allyl complexes **4** were detected spectroscopically on $Bi_2O_3-MoO_3$,[55] Cu_2O, and Ga molybdates.[56] On the other hand the carbonate–carboxylate complexes **5a–5c** are most often observed on the deep oxidation catalysts. This suggested the following general scheme for the oxidative transformations of C_3H_6:



On ZnO acrolein is not formed, and diallyl is obtained ($CH_2=CH-CH_2-CH_2-CH=CH_2$).[57] According to IR spectral studies in this case the π-allyl is converted into σ-allyl $[CH_2=CH-CH_2]^-$, which is probably anionic. Subsequent transformations give the dimer C_6H_{10}. On Bi–Mo oxide propene oxidation catalysts the π-allyl complex was observed under the conditions of the reaction.[58] The kinetics of the processes leading to its formation and decomposition were measured by in situ IR spectroscopy. Increasing the activity of the catalyst (by increasing its molybdenum content) lowers the activation energy for the consumption of π-allyl. We note that the number of cases in which the presence of π-allyl complexes on the surface has been truly established is small, and that the catalysts on which the observations were made were not good catalysts for the oxidation of propene to acrolein. Evidently the formation of the π-allyl complex (the initial rupture of a C–H bond) is the rate-limiting step of the reaction, after which the complex rapidly undergoes further transformations. Satisfactory spectroscopic studies of this process have not yet been reported. In the oxidation of C_3H_6 to acrolein on $USb_{4.6}O_{13.2}$ bands due to adsorbed acrolein were observed[59] in the IR spectra. It was concluded from isotopic data that the π-allyl complex takes part in the reaction.

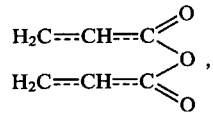
Weakly bound adsorbed forms of propene observed on Ti–Sb–O[60] and Fe–Sb–O catalysts,[61]



6

could be the precursors of acrolein. The process does not necessarily require activation of the double bond.[60,61] The acrolein can be formed immediately after the breaking of the C–H bond coordinated to O^{2-} in the complex **6** (see also Ref. 62). The participation of weakly bound forms of adsorbed propene in the oxidation to acrolein on $Bi_2O_3-MoO_3$ was detected during experiments with the TAP reactor.[63] Two forms of adsorbed oxygen were also observed: one contributes to the partial oxidation, the other does not contribute directly but exchanges readily with the oxygen from the gas phase.

A study by FTIR spectroscopy of the partial oxidation of propene and isobutene to acrolein on the industrial Co(Mg)–Mo–Bi–Fe oxide catalyst showed that under the conditions of the reaction 1% of the surface is occupied by the compound **7** of the acrylic anhydride type:

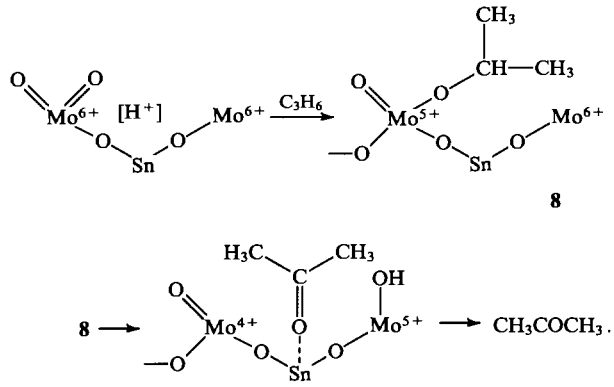


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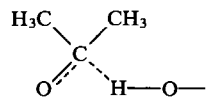
which is converted into an unsaturated aldehyde by reacting with a proton-donor reagent (i.e. with another olefin molecule, for example C_3H_6 or iso-C_4H_8).[64,65] This allows the associative substitution mechanism to take place.

The first stages of the oxidative ammonolysis of propylene with formation of acrylonitrile ($CH_2=CHCN$) are apparently similar to the first stages of the oxidation of propene to acrolein (through π-olefin and π-allyl complexes).[66] However, it was found that the rate of oxidative ammonolysis is always higher than the rate of oxidation of olefins to unsaturated aldehydes. Obviously, the ammonia gives intermediate forms which intercept (for example) the hydrogen from olefins. Bands due to NH_4^+ and to coordinatively bound ammonia have been observed in the IR spectra obtained after the oxidative ammonolysis of propene on a Co–Mo–Bi–Fe oxide catalyst.[67]

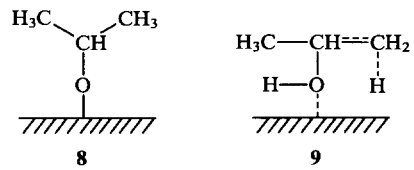
On oxide catalysts containing V and Mo propene can undergo partial oxidation to acetone but not to acrolein. A spectral study[68–71] of this reaction detected the surface isopropylates **8**. As reported,[68] the oxidative transformations of olefins on Sn–Mo–O catalysts take place by the scheme



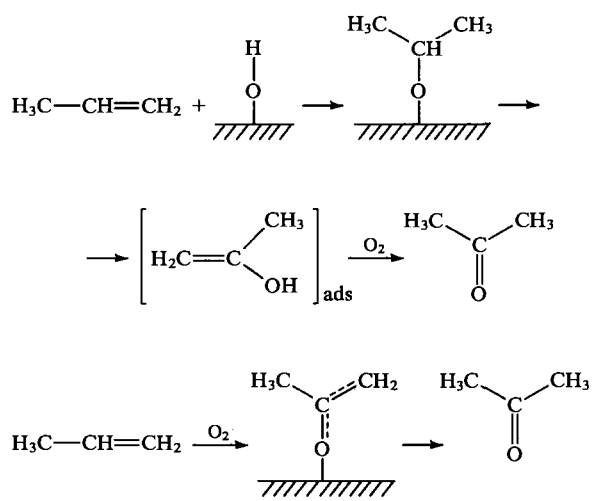
Here the rate-limiting step is the dehydrogenation of the surface isopropylates **8**, and the intermediate complex is



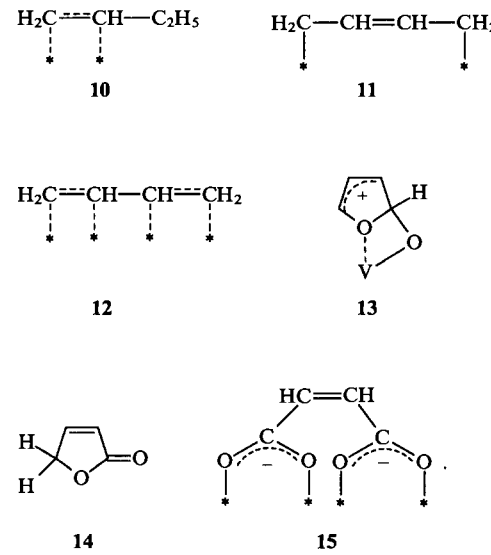
However, the reliability of these results is doubtful because the IR spectra were not measured under the conditions of the catalysis. An in situ study by IR spectroscopy on the Sn–Mo–O and Sn–V–O catalysts revealed the presence of two surface complexes:[71]



The intensity of the bands of the complex **8** on Sn–V–O increases with temperature up to 120 °C, and then decreases (while the yield of acetone increases). It was concluded that the complex **8** is an intermediate. On Sn–Mo–O the enol complex **9** contributes to the formation of some of the acetone. The following mechanism was proposed for the reaction:



In the oxidation of but-1-ene on $V_2O_5-P_2O_5/Al_2O_3$ at 100–150 °C (i.e. below the stationary reaction temperature) adsorbed 1-C_4H_8 (two π-complexes), 1,3-C_4H_6, furan, maleic anhydride, and 2,5-H-furanone were detected by IR spectroscopy.[72] Butadiene forms complexes of two types: the π-complexes **10** and **12** (interaction at the C=C bond) and the σ-complex **11** (1,4-addition). Furan is adsorbed at the C(2) atom (complex **13**), and 2,5-H-furanone forms the complex **14**. Maleic anhydride is chemisorbed as the stable complex **15**, but physisorbed maleic anhydride is also formed



The asterisks denote surface atoms.

Among the complexes which have been observed only 2,5-H-furanone (**14**) is active under the catalysis conditions.[72] Bands from π-allyl and adsorbed butadiene were observed[73] in the IR spectra during the oxidative dehydrogenation of butenes on the ferrites $MgFe_2O_4$, $CoFe_2O_4$, and $CuFe_2O_4$. The breaking of the C–H bond and the formation of the π-allyl are probably the rate-limiting step. The formates, carboxylates, and carbonates formed during the adsorption are intermediates in the deep oxidation reaction.

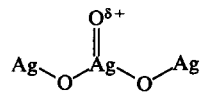
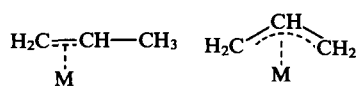
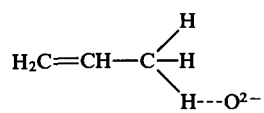
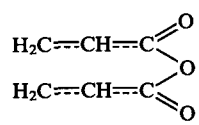
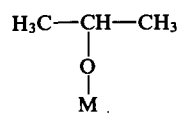
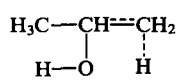
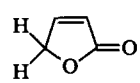
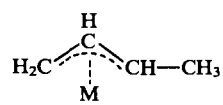
The oxidation of C_3H_6 and 1-C_4H_8 on γ-Bi_2MoO_6 was studied in the TAP reactor.[74] The reaction takes place by an oxidation–reduction mechanism. In spite of widely held views to the contrary there is no fast exchange of oxygen between the catalyst and $^{18}O_2$ from the gas phase. Therefore there can be no fast reversible chemisorption of O_2 with formation of O, O^-, or O_2^-. It is pointed out[74] that two types of centre are present on the surface: M and M′ (different oxygen vacancies). The M centres can be reoxidised by oxygen, and they can then reoxidise the M′ centres. The M′ centres are created by reduction and they cannot be directly reoxidised by oxygen. In the oxidation of C_3H_6 and iso-C_4H_8 no difference is found between the types of centre. Evidently these results can be explained in terms of our two- or three-phase catalyst model,[75] according to which the activation of olefins takes place on some centres, the activation of oxygen on others, and the diffusion of oxygen involves a third phase.

The intermediate oxygen forms produced in the oxidation of C_3H_6 on V_2O_5/SiO_2 were studied by EPR.[76] The products of the interaction of C_3H_6 with O_2^- and those of the oxidation of C_3H_6 in the stationary regime are identical, but the concentration of O_2^- under the reaction conditions is two orders of magnitude lower than the level required to achieve a stationary rate.

Table 3 summarises the data on the intermediate compounds which take part in the partial oxidation of olefins.

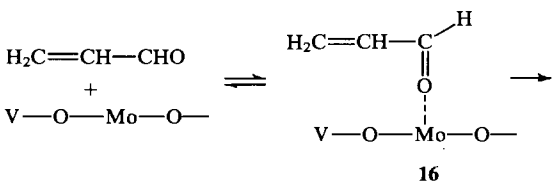
In conclusion we note that many published papers have dealt with the mechanism of the partial oxidation of olefins, and many surface forms have been observed, but so far there have been very few reports containing all the necessary spectral and kinetic data, and the existence of most of the suggested intermediates is hypothetical.

Table 3. Intermediate compounds in the partial oxidation of olefins.

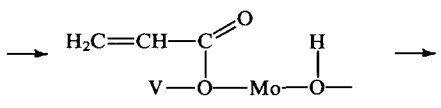
Reaction, catalyst	Intermediate complex	Reliability	Ref.
Oxidation of ethene on Ag/Al_2O_3	$CH_3CHO(ads)$	L	46
Oxidation of ethene on $Ag/\gamma\text{-}Al_2O_3$	$C_2H_4(ads)$	L	47
Oxidation of ethene on Ag		M	50–52
Oxidation of ethene and acetaldehyde on MoO_3/TiO_2	$H_2C{=}CH_2$, $CH_3CHO(ads)$,  $H_3CCHO-Z$	M	52
Oxidation of propene and acrolein on Ag/SiO_2	$H_2C=CHCHO(ads)$	M	53
Oxidation of propene and acrolein on $Bi_2O_3-MoO_3$, Cu_2O and Ga molybdates		L	55, 56
Oxidation of propene and diallyl on ZnO and Bi_2O_3	$H_2C=CH-CH_2-O-M$	M	57, 58
Oxidation of propene and acrolein on Ti–Sb–O and Fe–Sb–O		L	60, 61, 63
Oxidation of propene and acrolein on Co–Mo–Bi–Fe–O		M	64, 65
Oxidation of propene to acetone on Sn–Mo–O		L	68–70
		M	71
Partial oxidation of but-1-ene on $V_2O_5-P_2O_5/Al_2O_3$		L	72
Oxidative dehydrogenation of butenes on $MgFe_2O_4$, $CoFe_2O_4$, and $CuFe_2O_4$		L	74

V. Oxidation of aldehydes to unsaturated acids

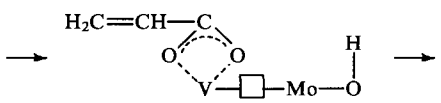
Unsaturated acids can be prepared by the further oxidation of unsaturated aldehydes produced from olefins. The reaction takes place on V–Mo oxide catalysts, including V–Mo–O heteropolycompounds and heteropolyacids. The oxidation of acrolein to acrylic acid was studied by in situ IR spectroscopy on VMo_3O_{11}[77] and on V–Mo–O/SiO_2.[78] Several complexes containing C=C bonds (complex **16**) and also COO^- (complexes **17** and **18**) and C=O (molecular adsorption of CH_2=CHCOOH, complex **19**) were seen. The rate constants for the transformations of these complexes were measured. The following reaction mechanism was proposed:



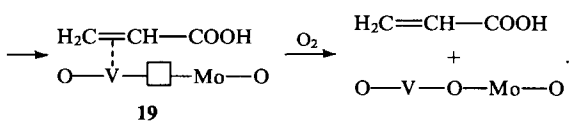
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17



18

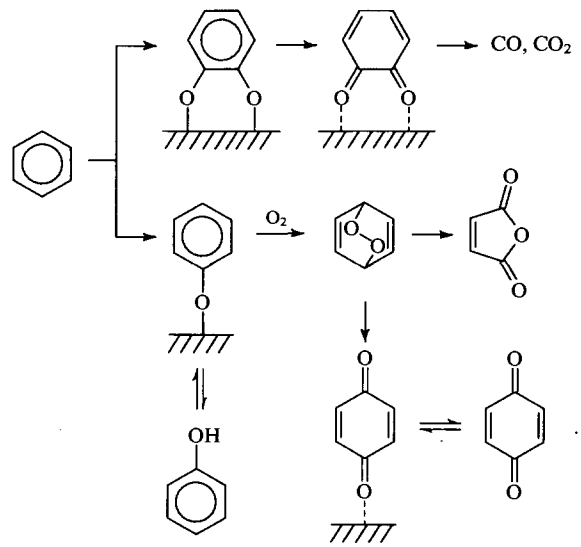


19

The rate-limiting step is the conversion of the complex **17** (which is not observed in practice) into the complex **18**. The catalyst should contain Mo^{6+} (or W^{6+}) ions for the σ-bonding of the acrolein, and V^{4+} (Mo^{4+} and Ti^{4+}) ions of the weakly basic or amphoteric type for the formation of salt-like acrylates. However, the degree of correspondence between the kinetics of the change in intensity of the IR lines and the kinetic curves describing the formation of acrylic acid is not stated. The reliability of the observed intermediate complexes can be classified as high (H).

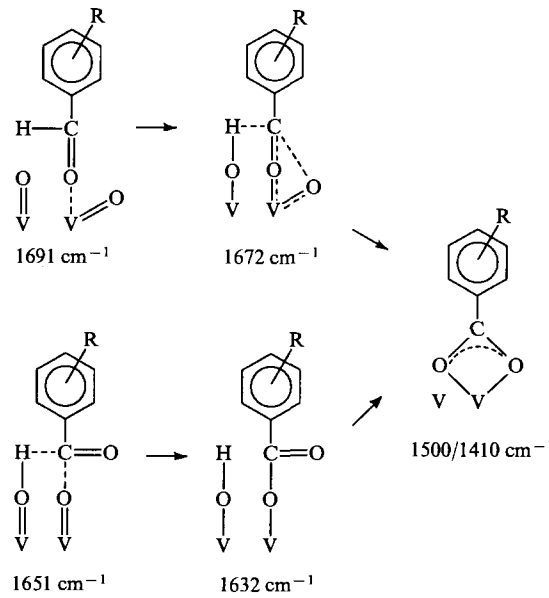
VI. Partial oxidation of aromatic hydrocarbons

Aromatic hydrocarbons undergo partial oxidation on the same catalysts as olefins. The surface compounds formed by the interaction of benzene with oxygen at 280 °C on a V_2O_5/TiO_2 catalyst have been studied by FTIR spectroscopy.[79] Adsorbed quinone, phenol, maleic anhydride, and carboxylates were detected on the surface. The following mechanism was proposed:

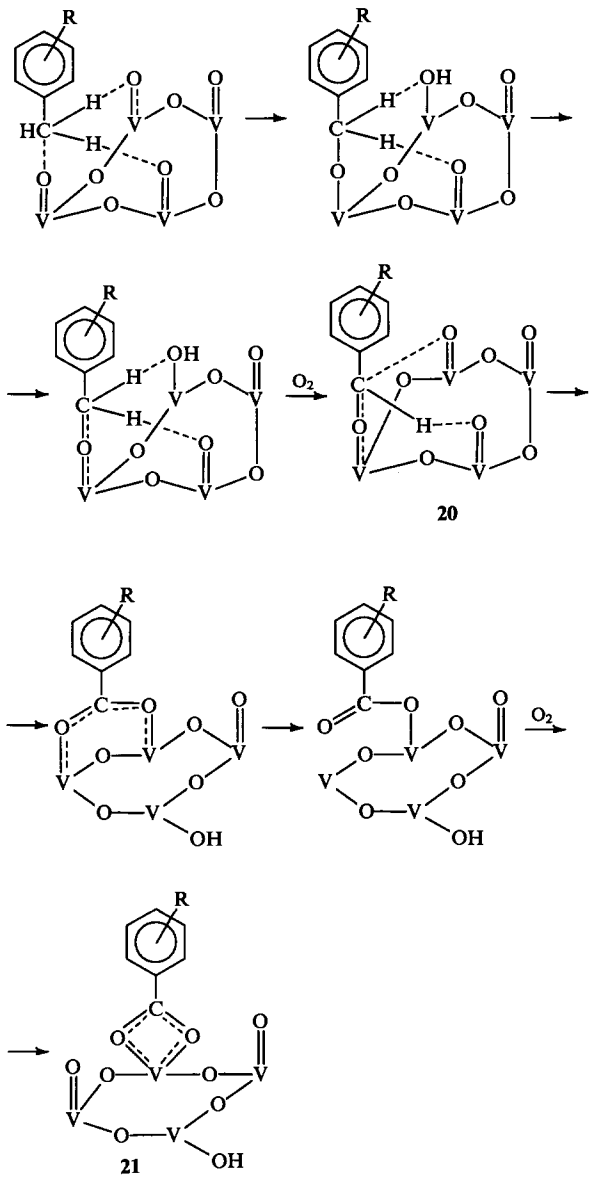


The IR spectra of the resulting surface compounds were recorded[80] at room temperature after the partial oxidation of toluene and *o*-xylene on V_2O_5/TiO_2. The $C_6H_5-CH_2-V$ and $C_6H_4(CH_3)CH_2-V$ complexes which were observed led to the conclusion that the first step of the reaction is the breaking of the C–H bond in the methyl group. In these complexes the aromatic ring is positioned parallel to the surface.

In situ FTIR spectra were obtained[81] during the selective oxidation of toluene to benzaldehyde and of *o*-xylene to α-toluyl aldehyde on V_2O_5/TiO_2. Complexes of aldehydes, carboxylates, and benzoates were observed on the surface.



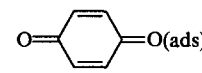
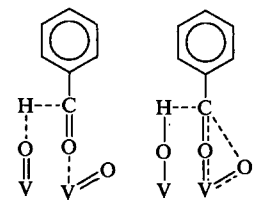
The following mechanism has been proposed for the oxidative transformations of toluene (or xylene) on the surface: it assumes that an aldehyde can be formed by the decomposition of the complex **20** without oxidation, and an acid by the decomposition of the complex **21**.



The oxidative ammonolysis of toluene on V–Sb–Bi–O/Al_2O_3 was studied by thermal desorption and IR spectroscopy.[82] NH_4^+ ions and ammonia coordinately bound to Lewis-acid centres were detected. Heating the system to 200 °C to 300 °C produced also NH_2. The adsorption of toluene leads to the formation of π-complexes and benzoate structures, and in the reaction with NH_3 benzamide and benzimide structures were also noted. The concentration of benzoate (unlike that of benzimines) is not correlated with the yield of the reaction products (nitriles). Adsorbed ammonia poisons the deep oxidation centres and thus prevents the formation of benzoates. The mechanism of the partial oxidation of benzene and phenol in the presence of N_2O has been studied on the Fe–ZSM-5 catalyst.[83] Bands of adsorbed phenol were seen in the diffuse reflectance IR spectra. Active oxygen O_{ads}, which has a very low bond energy, is formed during the decomposition of N_2O.

Table 4 shows the intermediate compounds which contribute to the partial oxidation of aromatic compounds.

Table 4. Intermediate compounds in the partial oxidation reactions of aromatic compounds.

Reaction, catalyst	Intermediate complex	Reliability	Ref.
Oxidation of benzene to oxygen compounds on $V_2O_5-TiO_2$	$M-OC_6H_5$, $M-OC_6H_4OH$, 	L	79
Oxidation of toluene to toluic aldehyde and of *o*-xylene to benzaldehyde on $V_2O_5-TiO_2$	$C_6H_5CH_2-V$, $C_6H_4(CH_3)CH_2-V$ 	L M	80 81
Oxidative ammonolysis of toluene on V–Sb–Bi–O/Al_2O_3	NH_4^+, NH_3-M, NH_2, π-$C_6H_5CH_3$, $C_6H_5-CH=NH$	L	82
Oxidation of benzene to phenol by N_2O on Fe–ZSM-5	O(ads), C_6H_5OH(ads)	M	83

VII. Partial oxidation of alkanes

Very detailed studies of the oxidation of methane with formation of C_2H_4, C_2H_6, CH_3OH, and CH_2O have recently been reported. Attempts to obtain the in situ spectra of surface compounds under the conditions of the partial oxidation of methane were unsuccessful.[84] This is evidently due to the fact that at high temperatures the reaction proceeds by a heterogeneous–homogeneous mechanism, and the lifetime of the intermediate species on the surface is very short. Under the conditions of its oxidative condensation (700–900 °C) methane interacts with the surface oxygen O_s, forming methyl radicals and OH groups on the surface.

$$CH_4 + O_s \longrightarrow CH_3^{\cdot} + OH_s,$$

$$2\,OH_s \longrightarrow H_2O + O_s.$$

The methyl radicals recombine in the gas phase, and are thus converted into ethane and (further) into ethylene.

$$2\,CH_3^{\cdot} \longrightarrow C_2H_6,$$

$$C_2H_6 + O_s \longrightarrow C_2H_4 + H_2O.$$

The interaction of methane with films of oxide catalysts under the conditions of adsorption at 300–500 °C and under the conditions of CH_4 oxidation was studied *in situ* by the new and very sensitive surface electromagnetic waves method.[85,86] Bands from OH and OCH_3 groups were detected in the IR range at 900–1100 °C. They are obviously associated with the compounds formed during the extensive oxidation of methane to CO_2 and H_2O.

$$CH_4 + O_s \longrightarrow CH_3 + OH_s,$$

$$CH_3 + O_s \longrightarrow OCH_3,$$

$$OCH_3 + O_2 \xrightarrow[-H_2O]{} \underset{\underset{O}{\|}}{\overset{O}{\|}}{>}CH \longrightarrow CO_2$$

Bands ascribed to OCH_3 and carbonate complexes were observed also in the FTIR spectra recorded after the oxidative condensation of methane into C_2 hydrocarbons on MgO.[87] These complexes take part in the extensive oxidation processes on the surface. Similar processes were observed by XPES during studies of the oxidation of CH_4 on NaOH/CaO and NaOH/(BaO, CaO).[88] It was found that methane interacts with surface carbonate (CO_3^{2-}) at 500–750 °C, forming a surface compound which rapidly disappears when the methane is pumped off. Possible intermediate complexes include the CH_3O and C=O groups, which are further oxidised to CO_2.

A study of the mechanism of oxidative condensation by combining the TAP reactor[89] with isotopic methods[90] showed that the methane taking part in the reaction is effectively not adsorbed on MgO and BaO/MgO surfaces. Apparently it reacts by the collision mechanism

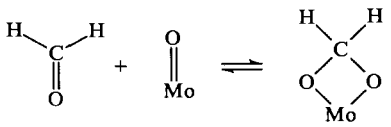
$$CH_4 + O_s \longrightarrow CH_3^{\cdot} + OH_s,$$

and initiates further oxidative processes in the gas phase.[84] On the other hand heterolytically adsorbed methane is involved in the $CH_4 + CD_4$ isotope exchange.[90] It forms complexes of the $CH_3-Mn^{n+}O^{2-}H^+$ type on the basic centres, which differ from the O^- centres involved in the homolytic breakdown of the CH_4 molecule.

The surface forms of oxygen created during the oxidative condensation of methane on BaO/MgO were studied by in situ Raman spectroscopy.[91,92] The peroxide groupings (O_2^{2-}) observed in this way at 844 cm^{-1} are stable in the presence of O_2, and at 740 °C they react with CH_4 over a period of several minutes. By using a TAP reactor it was shown that the lifetime of the adsorbed oxygen which reacts with methane on BaO/MgO is greater than 20 s. This species could also be the peroxide group. However, a longer-lived form of surface oxygen (O_s) is involved in the oxidative condensation of methane on MgO.

The oxidation of methane to formaldehyde takes place most selectively on catalysts which contain molybdenum, vanadium, or silicon oxides. A study by in situ laser-Raman spectroscopy of the partial oxidation of methane to formaldehyde on MoO_3 monocrystals led to the conclusion[93] that in this reaction the intermediate oxygen compounds are the Mo=O groups on a (100) MoO_3 face, whereas the Mo–O–Mo groups are involved in the extensive oxidation. A dispersed heteropolyacid is formed on the surface of the Mo–Si–O catalyst.[94] According to XPES and Raman spectroscopy Mo=O groups are formed as well under the catalysis conditions.

A study of the isotope exchange of O_2 under the conditions of the oxidation of methane to formaldehyde on MoO_3/SiO_2 showed[95] that not only the MoO_3 but also the SiO_2 contributes to the exchange. A very fast exchange between CH_2O and the oxygen of the catalyst was also noted: it was ascribed to the equilibrium



According to data obtained in a TAP reactor[96] a surface oxygen species with a lifetime between 5 and 60 s is responsible for the oxidation of CH_4 to CH_2O on V_2O_5/SiO_2. Compounds containing oxygen and related to the oxidative condensation or to the oxidation of methane to formaldehyde were not detected under the catalysis conditions. Intermediate compounds such as the $^{\cdot}CH_3$ and $CH_3O_2^{\cdot}$ radicals migrating from the surface into the gas phase[84,91] will not be considered here.

Dissociative forms of carbon on the surface of metals [C(ads), CH_x(ads)] are apparently intermediates in the oxidation of methane by oxygen[97] or by carbon dioxide[98] with formation of synthesis gas (CO + H_2). The vapour phase conversion of methane on Ni/NaY at 300 °C has also been studied by in situ IR spectroscopy.[99] Formate was found on the surface after the reaction. The following reaction mechanism was proposed:

$$H_2O + S \rightleftharpoons H_2O-S,$$

$$CH_4 + M \rightleftharpoons MC + 2H_2,$$

$$MC + H_2O-S \rightleftharpoons HCO-M + \tfrac{1}{2}H_2 + S,$$

$$HCO-M + H_2O-S \rightleftharpoons HCOO-M + H_2 + S,$$

$$HCOO-M \longrightarrow CO_2 + \tfrac{1}{2}H_2 + M.$$

The last step is rate-limiting.

In the oxidation of ethane on Pd/Al_2O_3 and Pd/SiO_2 in situ IR spectra obtained at 200–600 °C revealed acetate and carbonyl complexes acting as intermediates in the extensive oxidation reaction.[100] The oxidative dehydrogenation of ethane to ethylene apparently takes place by a heterogeneous–homogeneous mechanism.[101]

The oxidation of CH_4, C_2H_6, and C_2H_4 on Co_3O_4 and on Pd/TiO_2 has been studied.[102] The interaction of CH_4 with Co_3O_4 produces surface OH groups, carbonates of two types, and (apparently) Co–CH_2–Co groups. The formation of CH_3CHO and acetate adsorbed on the TiO_2 carrier has been observed in the reaction of C_2H_4 with O_2 on Pd/TiO_2. The ethane is first dehydrogenated to ethylene by an oxidation–reduction reaction, involving the $Pd^{2+}-O_2^{2-}$ ion pair, and then the C_2H_4 is rapidly oxidised to CH_3CHO, which undergoes decarbonylation with formation of Pd–CH_3 + CO. The Pd–CH_3 complex is formed also by the reaction between CH_4 and the $Pd^{2+}-O_2^{2-}$ pair. This is followed by the reactions

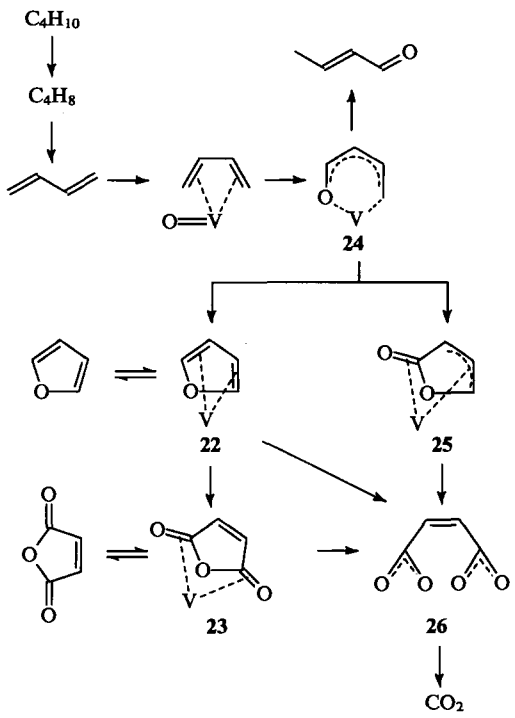
$$CH_3 \xrightarrow{O_2} CH_2 + H(OH) \xrightarrow{O_2} CH_2O \xrightarrow{O_2} CO + H_2O.$$

The final result is deep oxidation of the CH_4.

Many studies have been devoted to the partial oxidation of butane to maleic anhydride and other oxygen compounds on V–Ti and V–P oxide catalysts. The mechanism of the oxidation of butane on TiO_2 and $V_2O_5-TiO_2$ has been examined[103,104] by studying the FTIR spectra of C_4H_6, furan, and maleic anhydride on the catalysts in the presence and in the absence of O_2. The sequence of transformations on $V_2O_5-TiO_2$ shown in Scheme 1 was proposed. At room temperature the complex **22** (adsorbed furan) is first formed. At higher temperatures a strong band assigned to the complex **24** appears in the IR spectra. At 200 °C its intensity decreases, and an absorption band corresponding to the complex **26** appears. As a result of the interaction with oxygen the intensity of the band assigned to the complex **24** increases again. The absorption band which characterises the complex **24** disappears at 250–300 °C, and absorption bands due to the complexes **23** and **25** are produced. Maleic anhydride is formed only in the presence of oxygen: in the absence of oxygen the maleates **26** are obtained. Evidently, these decompose by associative interaction with O_2. On TiO_2 only the π complex of C_4H_8 (or C_4H_6) with Ti^{3+} is formed reversibly. On a V–P–O catalyst maleic anhydride is formed even in the absence of O_2, and maleates are not observed. Obviously, in this case the oxygen in the bulk of the catalyst has a higher mobility. The V–O–Ti bridging forms, which are more nucleophilic than V–O–P, may

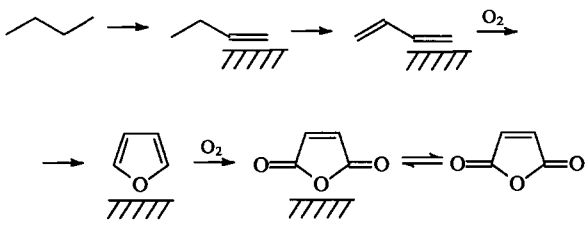
also contribute to the formation of the maleates. This leads to nonselective catalysis.

Scheme 1

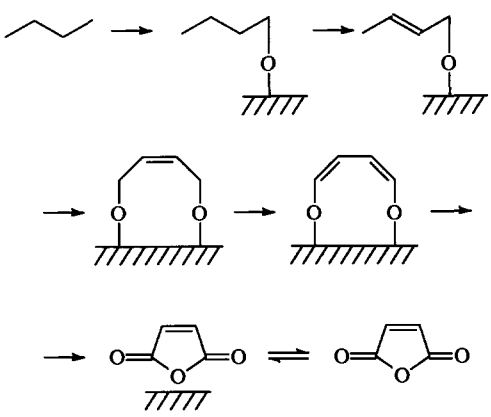


Two possible paths for the conversion of butane into maleic anhydride on a vanadium–phosphorus oxide catalyst have been considered:[105]

(a) the olefin path

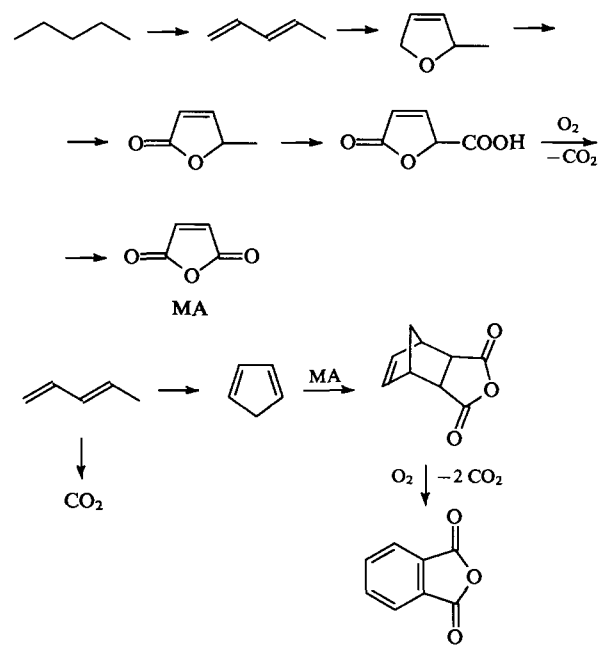


(b) the alkoxide path



The olefin path (a) has been called[105] the equilibrium path, because all the contributing intermediates are in adsorption equilibrium with the gas phase. The alkoxide path (b) is a nonequilibrium process: all the intermediates (except the last) remain on the surface, and only maleic anhydride is desorbed into the gas phase. However, the formation of the surface complexes listed above was not confirmed spectroscopically, and their structure was determined only from indirect data obtained by ^{31}P NMR and EPR methods.

The difference between the mechanisms of the partial oxidation of butane and butene (see Section IV) also suggests that the alkoxide path is preferable to the olefin path. It is assumed[106] that the oxidation of C_4H_{10} on $(VO)_2P_2O_7$ is characterised by a strong adsorption of the intermediate substances, which suppresses their desorption into the gas phase and limits their surface mobility. Under these conditions the number of free centres is also limited, leading to the geometric isolation of the active intermediates and thus suppressing the oxidation to CO and CO_2. On $(VO)_2P_2O_7$ the oxidation mechanism of butane and pentane to maleic anhydride was studied by in situ FTIR spectroscopy, and by using a TAP reactor.[106–108] Exposing the catalyst to a mixture of C_5H_{12} and O_2 produced a large number of IR spectroscopic bands for which only a tentative assignment was given.[106] The IR spectra of the sample vacuum treated at 400 °C after the adsorption of C_5H_{12} contained absorption bands from weakly adsorbed olefins, and after the adsorption of a $C_5H_{12} + O_2$ mixture they contained the bands from adsorbed anhydride. The intensity of the absorption band from the anhydride increases with time, and bands associated with more highly oxidised substances are produced. By using a TAP reactor it was shown that at 427 °C pentane is converted into furan (reaction time 0.2 s), which reacts further to give maleic anhydride (0.3 s) and phthalic anhydride (0.5 s). On the basis of these observations the following reaction scheme was proposed:

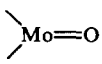
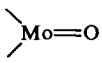
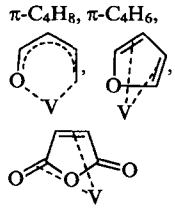
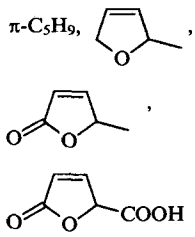


The formation of methylmaleic anhydride in the initial stages of the reaction, which confirms the proposed scheme, was observed. All the substances specified in this scheme are on the surface in an adsorbed state. A competition then takes place between the addition of atomic oxygen, which leads to the formation of maleic anhydride, and the elimination of an H atom, with formation of phthalic anhydride. To form phthalic anhydride we also require the presence on the surface of another adsorbed molecule of an unsaturated C_5 hydrocarbon. By using the TAP reactor in a study of the oxidation mechanism of butane on $(VO)_2P_2O_7$ (see Ref. 108) it was shown that this catalyst has a unique ability to retain absorbed oxygen and to transmit it effectively to a hydrocarbon. We observe the conversion of $(VO)_2P_2O_7$ into amorphous $VOPO_4$,

$$^{18}O_2 + 2\,(VO)_2P_2O_7 \rightleftharpoons 4\,VOPO_4,$$

which involves the transfer of four oxygen atoms in a single step.

Table 5. Intermediate compounds in the partial oxidation of alkanes.

Reaction, catalyst	Intermediate complex	Reliability	Ref.
Oxidative condensation of methane on BaO/MgO	O_2^{2-}	H	90–92
Oxidation of methane to CH_2O on MoO_3		M	93
Oxidation of methane to CH_2O on Mo–Si–O		L	94, 95
Oxidation of methane to CO + H_2 on Mo	C(ads), H(ads)	L	97
Reaction of CH_4 + CO_2 on Rh/Al_2O_3, Rh/TiO_2	C(ads), H(ads), CH_x(ads)	L	98
Vapour conversion of methane on Ni/NaY	$HCOO^-$	L	99
Oxidation of ethane on Pd/TiO_2	CH_3CO-Ti, CH_3CHO(ads), C_2H_4(ads),	L	102
Oxidation of butane to maleic anhydride on V_2O_5/TiO_2	π-C_4H_8, π-C_4H_6, 	M	103, 104
Oxidation of pentane to maleic anhydride on $(VO)_2P_2O_7$	π-C_5H_9, 	H	106–108

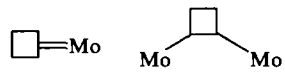
Data on the intermediate compounds which contribute to the partial oxidation of alkanes are shown in Table 5.

The oxidation reactions of alkanes can be classified into two groups: high-temperature reactions (500–600 °C, gas-phase conversion of methane and other alkanes, oxidation of alkanes to synthesis gas, and possibly also extensive oxidation), which take place by a complete dissociation mechanism with formation of H_{ads}, O_{ads}, and C_{ads}, and low-temperature reactions (oxidative dehydrogenation with formation of oxygen compounds), involving various large surface complexes. Among all the partial oxidation processes the oxidation of butane to maleic anhydride has been studied in most detail. In this stage the formation of intermediate complexes has been established with a high level of reliability.

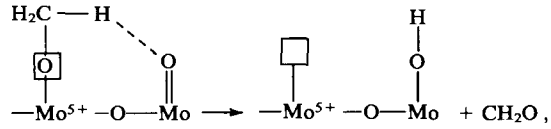
VIII. Oxidation of alcohols

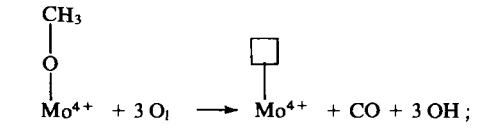
The mechanism of the oxidation of alcohols has been studied on various oxides: MoO_3,[109,110] Cr_2O_3,[111,112] TiO_2,[112] and ZnO.[113] Alkoxides, formates, and other forms resembling the complexes observed in the dehydrogenation of alcohols (see Ref. 1) were found on the surface.

The oxidation of methanol on MoO_3 at 170–440 °C was studied by in situ FTIR spectroscopy in the transition regime.[109,110] According to these data the CH_3OH is adsorbed on vacancies of two types:



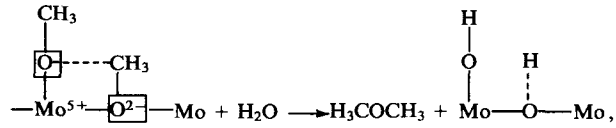
The products CH_2O and CO are formed on vacancies of the first type:

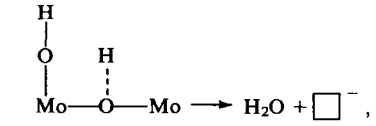


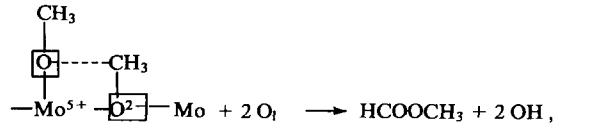


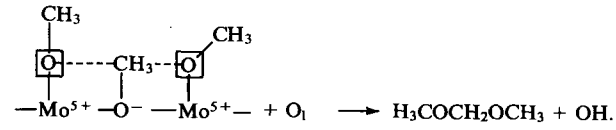
O_l is lattice oxygen.

On the vacancies of the second type the following reactions take place:









In the stationary state the MoO_3 surface is slightly reduced, and the rate-limiting step is provided by reoxidation, i.e. the filling of vacancies with oxygen.

On Cr_2O_3 the reaction was studied by in situ FTIR spectroscopy; the kinetics of the formation of the products H_2O, CO_2, and CH_2O were monitored at the same time.[112]

However, the quantity of adsorbed substances was not compared with the composition of products in the gas phase. The mechanism of the reaction is

$$CH_3OH + O^{2-} \longrightarrow CH_3O^- + OH^-,$$

$$CH_3OH + OH^- \longrightarrow CH_3O^- + H_2O,$$

$$CH_3O^- + O^{2-} \longrightarrow CH_2O + OH^- + 2e,$$

$$CH_2O + 2O^{2-} \longrightarrow HCOO^- + OH^- + 2e,$$

$$2HCOO^- \longrightarrow H_2 + 2CO_2 + 2e,$$

$$HCOO^- + OH^- \longrightarrow H_2O + CO + O^{2-},$$

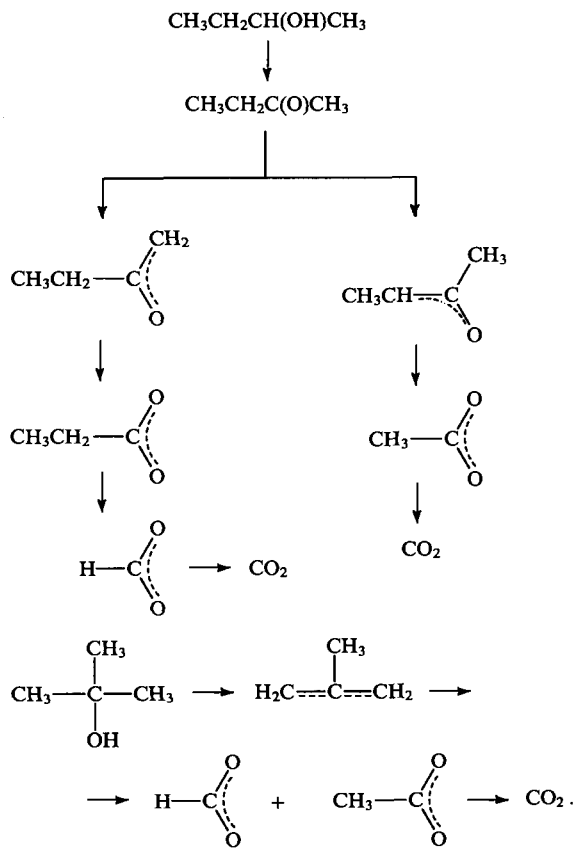
$$O_2 + 4e \longrightarrow 2O^{2-},$$

$$2OH^- \longrightarrow H_2O + O^{2-}.$$

Thus the oxidation of methanol on Cr_2O_3 takes place by the series of reactions [111]

$$CH_3O \longrightarrow CH_3O(ads) \longrightarrow HCOO(ads) \longrightarrow CO, CO_2.$$

After the oxidation of *sec*-butanol and *tert*-butanol on ZnO at 80–150 °C formates and carboxylates were detected by IR spectroscopy.[113] The same bands were found in the IR spectra after the oxidation of butan-2-one. It follows that the first step in the reaction is the conversion of butan-2-ol into butan-2-one. This is followed by the reactions



An interesting study (by in situ EXAFS spectroscopy in conjunction with UV-VIS and IR spectroscopy) of the oxidation of ethanol to acetaldehyde on dimeric Mo complexes supported on SiO_2 has been reported.[114] The EXAFS spectra were measured at 70 °C (or in some cases at −195 °C). The cooling time from the reaction temperature (150 °C) was relatively long (up to 1 h). The following oxidation–reduction mechanism was proposed on the basis of these results:

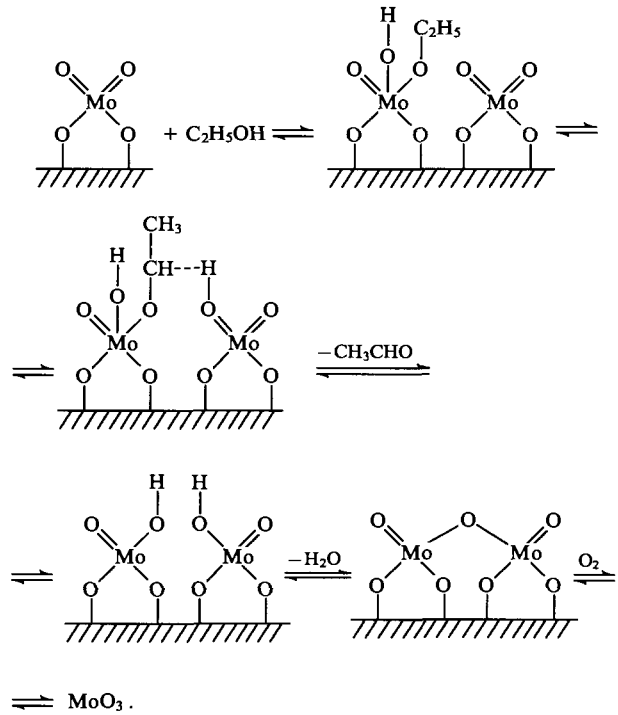


Table 6. Intermediate compounds in the oxidation of alcohols.

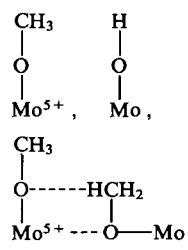
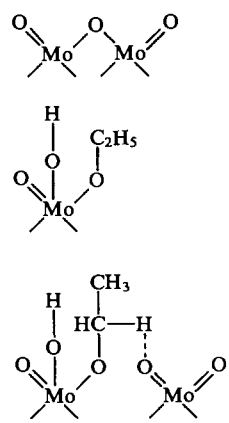
Reaction, catalyst	Intermediate complex	Reliability	Ref.
Oxidation of methanol on MoO_3		H	109, 110
Oxidation of methanol on Cr_2O_3	CH_3O^-, OH^-, $HCOO^-$	M	111, 112
Oxidation of *sec*-butanol and *tert*-butanol on ZnO	$HCOO^-$, $RCOO^-$, $R^{\cdot}$	L	113
Oxidation of ethanol to acetaldehyde on Mo/SiO_2		L	114

Table 6 gives a summary of the data on the intermediate compounds which take part in the oxidation of alcohols.

The formation of alkoxides and carbides during the oxidation of alcohols on oxide surfaces can be taken to be established to a relatively high degree of reliability. However, their influence on the kinetics of the reaction is still uncertain.

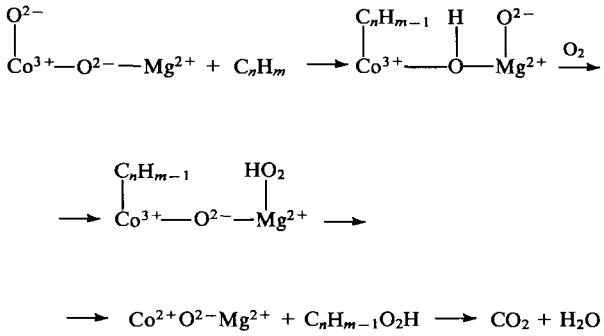
IX. Extensive oxidation of organic compounds

We have already discussed several processes which contribute to the oxidation of organic compounds and ultimately lead to the formation of CO and CO_2. It is generally thought that extensive oxidation takes place through surface carboxylates and carbonates. The formation of carboxylate structures of the $HCOO^-$ type (in some cases destructively oxidised as a C–C bond) by the interaction between hydrocarbons and surface oxygen was first reported by Kuznetsov et al.[115] However, real kinetic data on the contribution of these forms to the catalysis are still scarce.

The oxidation of CH_4, C_2H_6, and C_2H_4 on CeO_2 at 20–400 °C was studied by in situ EPR and FTIR spectroscopy methods.[116] At 200 °C the surface contains $HCOO^-$, which is converted into carbonate at 300 °C. The initiation of extensive oxidation is independent of the oxygen pressure, but it is affected by the pretreatment of the CeO_2 catalyst. The O_2^- ion is inert up to 300 °C: evidently, the O_2^{2-} ion reacts with hydrocarbons in this temperature range. In the IR spectra obtained under the conditions of oxidation of C_2H_4 and C_3H_6 at 100–300 °C on $Bi_2O_3-MoO_3$ bands from strongly bound complexes leading to the deep oxidation products were observed[48] in addition to the bands corresponding to π-allyl. On Ag/Al_2O_3 and Tl_2O_3/Al_2O_3 the precursors of the deep oxidation products were found to be surface carbonates.[48]

In the oxidation of ethane on Pd/Al_2O_3 absorption bands due to adsorbed acetates and acetaldehyde were seen in the IR spectra.[117] On Pd/SiO_2 or on pure Al_2O_3 these surface compounds are not formed: their formation requires the presence of both Pd and Al_2O_3. Probably the compounds are formed on the Pd and then migrate to the Al_2O_3 by the spillover mechanism. Under these conditions ethane is not adsorbed.

Acetates, formates, and benzoates were observed in the oxidation of C_3H_6 and $C_6H_5CH_3$ on 5% CoO–MgO.[118] The formation of O_2^- was also noted. According to these workers[118] the reaction may follow the scheme

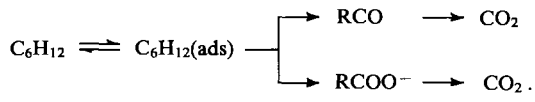


$$\longrightarrow Co^{2+}O^{2-}Mg^{2+} + C_nH_{m-1}O_2H \longrightarrow CO_2 + H_2O\,.$$

The hydroperoxide $C_nH_{m-1}O_2R$ (for example, All–OOH) can decompose into $CH_3CHO + H_2CO$ and then be oxidised to carboxylates and finally to CO_2. We note that a similar mechanism was proposed earlier[119] for the oxidation of C_3H_6 on CoO–MgO. The oxidation of isobutene on V_2O_5/TiO_2 was studied by FTIR spectroscopy.[120] At low V_2O_5 concentrations dimerisation takes place, and at high concentrations the isobutene undergoes extensive oxidation. In the former case π-complexes of iso-C_4H_8 are observed on the surface, in the latter we find alkoxides and carboxylates. As reported,[120] acid centres of the Brønsted type and the lattice oxygen give rise to the extensive oxidation.

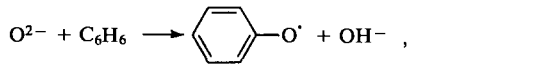
In the oxidation of butene on Mg–Fe–O and Zn–Fe–O[121] the strongly adsorbed C_4H_8 σ-complex is retained on the surface up to 500 °C, but in the presence of O_2 it is retained only up to 200 °C, i.e. up to the temperature at which CO_2 appears in the gas phase. It is suggested that the σ-complex interacts with O_2 to give the $HCOO^-$ form, which is an intermediate in the extensive oxidation reaction of C_4H_8 to CO_2. On $MgO-Al_2O_3$, $ZnO-Al_2O_3$, and Al_2O_3 the σ-complex is not oxidised to $HCOO^-$, and these catalysts do not show any activity in the extensive oxidation process. The interaction of a series of hydrocarbons (C_3H_6, C_4H_6, and C_6H_6) with oxides was studied by FTIR spectroscopy.[122] On SiO_2 only physisorbed molecules were observed. On γ-Al_2O_3 at 300 °C bicarbonates and acetates were formed from C_3H_6, whereas on γ-Fe_2O_3 carbonates were formed at room temperature, and at 150 °C formates and acetates were formed from C_3H_6, carboxylates from C_4H_6, and an oxidised product from C_6H_6. On TiO_2 bicarbonate was observed at room temperature, and at 150 °C acetone, aldol (from C_3H_6), and carboxylates (from C_4H_6) were observed. These substances may be the precursors of the extensive oxidation products.

The kinetics of the extensive oxidation of cyclohexane on NaX and KY zeolites were studied in our laboratory[123–126] in conjunction with in situ measurements of the IR spectra. The reaction can follow two paths:



The rate of the catalytic reaction is proportional to the overall concentration of the two complexes, but the carbonyl complexes decompose faster than the carboxylates (acetates and formates). Thermal desorption data confirm that the carbonyl complexes decompose at temperatures 50–100 K lower than the carboxylates, and therefore transformations through the carbonyl compounds are the main reaction path of the extensive oxidation. Self-oscillations were observed[123,125] in the oxidation of cyclohexane on KY zeolite, and oscillatory changes synchronous with those of the reaction rate were noted in the intensity of the IR bands from adsorbed carbonyl compounds. It was assumed that the carbonyl group is bound to a peroxide group.

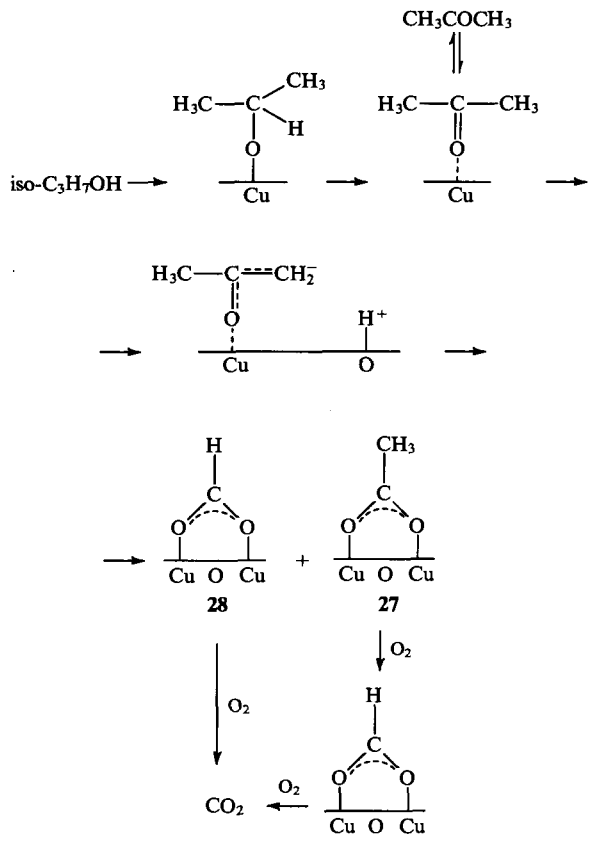
The oxidation of benzene (and also of toluene and *o*-xylene) was studied on supported vanadium oxide catalysts by the EPR method.[127] The reaction



leads to the formation of free-radical products which are ultimately oxidised to CO_2.

The mechanisms of the oxidation of alcohols on oxides have already been discussed above. Here we shall only deal briefly with some studies specially aimed at the mechanism of the extensive oxidation of alcohols. According to spectroscopic data,[128] in the oxidation of isopropanol on CuO at 20–80 °C the resulting isopropylates interact with oxygen from the gas phase. The lattice oxygen reacts in a similar way only at 120–150 °C. The formation of CO_2 is accompanied by the disappearance of the carboxylates. The kinetics of the disappearance of the carboxylates during the treatment of the surface in the iso-$C_3H_7OH + O_2$ reaction mixture at 100–200 °C were studied by in situ IR spectroscopy.

Under these conditions the concentration of isopropylates decreases, but that of formates goes through a maximum:



Under stationary conditions the concentration of formates on the surface is constant, and the time needed to establish the steady state is shorter than the time needed for the chromatographic analysis. Thus we have two extensive oxidation regimes: in the low-temperature regime the reaction proceeds through weakly bonded forms (type **27**) and through more strongly bonded forms (type **28**).

The oxidation of ethanol, n-propanol, isopropanol, n-butanol, isobutanol, and *tert*-butanol on Sn–Mo–O at 125–200 °C was studied by in situ IR spectroscopy. When the alcohol was removed from the reaction mixture the intensity of the IR bands corresponding to alcoholates and alcohols bound to the surface by a hydrogen bond and to aldehydes and acids rapidly fell to zero. The other bands remained in the IR spectrum for a much longer time. These bands are mostly due to condensation products containing carbonate and anhydride fragments. In the oxidation of butyric anhydride the same compounds are formed as in the oxidation of n-butanol, but the oxidation of the acids does not give oxidative condensation products (OCP). Under stationary conditions (in contrast to the initial period) absorption bands due to adsorbed alcohols and alcoholates are not observed. The following formal scheme has been proposed[129] for the reaction:

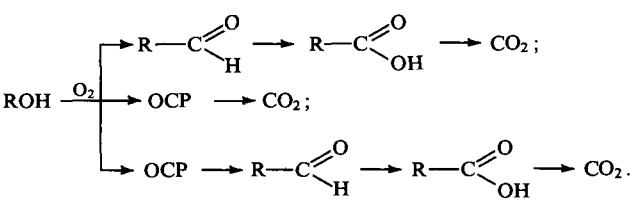
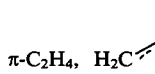
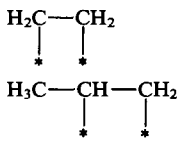
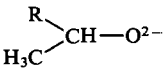
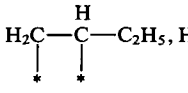
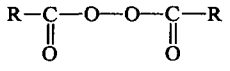
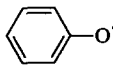
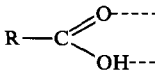
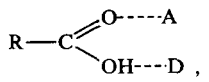


Table 7. Intermediate compounds in the deep oxidation reactions of organic compounds.

Reaction, catalyst	Intermediate complex	Reliability	Ref.
Oxidation of CH_4, C_2H_6, C_2H_4 on CeO_2	$HCOO^-$, CO_3^{2-}, O_2^{2-}	M	126
Extensive oxidation of C_2H_4, C_3H_6 on $Bi_2O_3-MoO_3$	π-C_2H_4, 	L	48
Extensive oxidation of C_2H_4, C_3H_6 on Ag/Al_2O_3, Tl_2O_3/Al_2O_3		L	48
Oxidation of ethane on Pd/Al_2O_3	CH_3COO^-, CH_3CHO(ads)	M	117
Oxidation of C_3H_6, $C_6H_5CH_3$ on $CoO-MgO$	CH_3COO^-, $HCOO^-$, $C_6H_5COO^-$, O_2^-	L	118
Extensive oxidation of iso-C_4H_8 on V_2O_5/TiO_2		M	120
Oxidation of C_4H_8 on Mg–Fe–O, Zn–Fe–O		L	121
Oxidation of C_3H_6, C_4H_8, C_6H_6 on oxides	$HCOO^-$, CH_3COO^-, $RCOO^-$, CO_3^{2-}, HCO_3^-	M	122
Oxidation of cyclohexane on NaX, KY zeolites	RCO, $RCOO^-$ 	H	123–126
Oxidation of benzene on V/SiO_2, MgO, ZrO_2	O_2^-, 	M	127
Oxidation of i-C_3H_7OH on CuO	$C_3H_7O^-$, CH_3COO^-, $RCOO^-$, CO_3^{2-}, HCO_3^-	M	128
Oxidation of alcohols on Sn–Mo–O	Oxidative condensation products	M	129
Oxidation of HCOOH and CH_3COOH on Pt/Al_2O_3		L	130
Oxidation of $H_2C=CHCHO$ and CH_3CH_2CHO on Cu_2O	$RCOO^-$, $RCH=CHO^-$, C_xH_y, C_x	L	131

The oxidation of the acids HCOOH and CH_3COOH on Pt/Al_2O_3 also was studied by IR spectroscopy.[130] At low temperatures the complexes



were detected (where A is an electron acceptor and D is an electron donor).

These complexes interact with O_2 at 200–300 °C. Strongly bound acetates and formates do not react with O_2. In the HCOOH complex the C–H bond is broken during the interaction with O_2, and in the CH_3COOH complex the C–C bond is broken.

X-Ray photoelectron spectroscopy and thermal desorption methods were used to study the extensive oxidation of acrolein and propionaldehyde on a $Cu_2O(100)$ surface.[131] The products of this reaction are CO, CO_2, and H_2O. Enolate and carboxylate complexes are observed on the surface, but the latter (in general) do not take part in extensive oxidation, and only a small fraction of the products is formed from the enolate. It is suggested[131] that the main extensive oxidation path includes the deoxygenation of the adsorbate, the dehydration of C_xH_y, and the final burning of the surface carbon by oxygen from the lattice.

A list of data on the intermediate compounds which contribute to the extensive oxidation is given in Table 7.

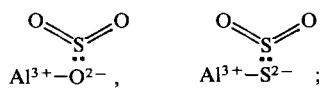
Though surface carbonates and carboxylates are very often observed in the extensive oxidation of organic compounds these complexes do not provide the main path for the formation of CO_2. At low temperatures a different path can be established, involving intermediates which are difficult to identify because of their short lifetimes. They are probably free-radical or peroxidic products. The extensive oxidation takes place by a free-radical mechanism (and in some cases by a heterogeneous–homogeneous mechanism). At high temperatures a complete decomposition of the organic molecule with oxidation of C_{ads} to CO_2 and of H_{ads} to H_2O is more probable.

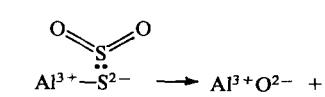
X. Reactions involving sulfur

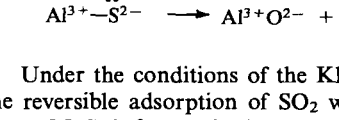
The Klaus reaction $H_2S + SO_2 \rightarrow S_2 + H_2O$ takes place on several oxide catalysts. After the interaction of $H_2S + SO_2$ on Al_2O_3 the IR and UV spectra of the surface compounds were recorded at 20–400 °C.[132] The SH and OH groups are stable up to 150 °C.

$$H_2S + O^{2-}(surf) \longrightarrow H_2O + S^{2-}(surf)$$

At higher temperatures we find the S^{2-} form, which is stable up to 300–400 °C, with bands at 220–260 nm in the UV spectrum. The interaction of $Al^{3+}S^{2-}$ and $Al^{3+}O^{2-}$ with SO_2 at 150 °C produces sulfite–sulfate complexes:







Under the conditions of the Klaus reaction on Sn–Mo–O the reversible adsorption of SO_2 was observed by IR spectroscopy. MoS_2 is formed in the presence of H_2S. If SO_2 is adsorbed first, followed by H_2S, the absorption bands due to adsorbed SO_2 are weakened and the bands at 800–1000 cm^{-1} become stronger. This is because of the formation of S_2 molecules, with the possibility of reoxidation of the catalyst with formation of the Mo=O bond.[133] The IR and UV spectra of the adsorbed substances were recorded also after carrying out the Klaus reaction on the NaX zeolite.[134] The changes in the intensity of the bands were ascribed to the reactions

$$SO_2 + OH^- \longrightarrow HSO_3^-,$$

$$H_2S \longrightarrow HS^- + H^+,$$

$$2\,HSO_3^- + H_2S \longrightarrow S_2O_4^{2-} + S + 2\,H_2O,$$

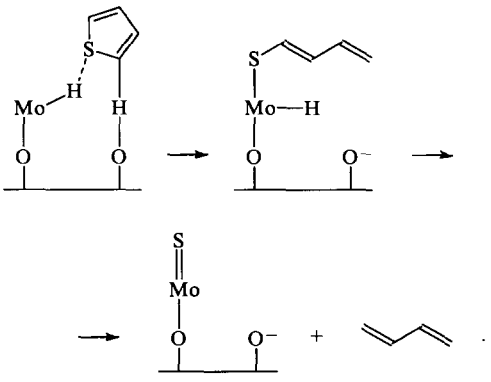
$$2\,HSO_3^- + 2\,HS^- \longrightarrow S_2O_4^{2-} + S_2^{2-} + 2\,H_2O,$$

$$S_2^{2-} + 2\,SO_2 \longrightarrow S_2O_4^{2-} + 2\,S,$$

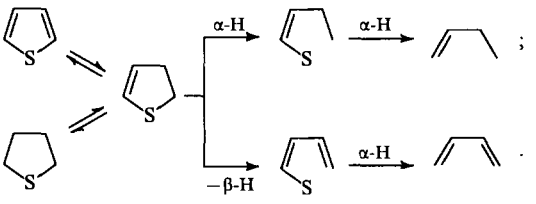
$$SO_2 + H_2O \longrightarrow HSO_3^- + H^+.$$

Polymers of the S_8 type, which behave both as products and as intermediates, were also observed. The same products were found when the oxidiser SO_2 was replaced by oxygen.

The hydrogenation and the hydrodesulfurisation of thiophene on a 10% MoO_3/Al_2O_3 catalyst were studied by IR spectroscopy.[135,136] Thiophene weakly adsorbed on the OH groups was observed, together with carboxylates and thiocarboxylates. These may be the intermediate compounds. Thiophane is not an intermediate compound, and therefore we may assume that breaking of the C–S bond precedes the hydrogenation:



According to thermal desorption data[137,138] the key intermediate in the hydrogenation of thiophene on $Co–Mo–O/Al_2O_3$ is dihydrothiophene, which (depending on the hydrogen pressure and on the temperature) can be converted into thiophene, thiophane, and the reaction products. Butene can be formed from the dihydrothiophene intermediate by the two-stage hydrogenation of the α-carbon with simultaneous breaking of the C–S bonds, whereas β-elimination in the first stage and α-hydrogenation in the second stage give butadiene:

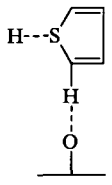
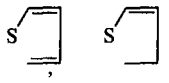


It may be assumed that the hydrogenation–dehydrogenation reactions take place on centres of one type, and the hydrodesulfurisation reactions on centres of another type. The main weakness of the published work[135–138] is the failure to allow for the contribution to the reaction from the sulfur atoms of the sulfide catalyst. It was shown[139] that under the conditions of the reaction on MoS_2/Al_2O_3 a strong exchange of sulfur takes place between H_2S and MoS_2.

The reaction of methanol with H_2S on Al_2O_3 and WO_3/Al_2O_3 was studied by NMR.[140] It follows from the analysis of the NMR spectra taken after the reaction that CH_3O and CH_2S groups are present on the surface. It is suggested that CH_3SH is formed by the interaction of the CH_3O and HS surface groups, and $(CH_3)_2S$ by the interaction of CH_3O and CH_3SH.

The data on the intermediate compounds in reactions involving sulfur are summarised in Table 8.

Table 8. Intermediate compounds in reactions involving sulfur.

Reaction, catalyst	Intermediate complex	Reliability	Ref.
Klaus reaction on Al_2O_3	SH^-, OH^-, H_2S(ads) S^{2-}, SO_3^{2-}, HSO_3^-, SSO_2^-	L	132
Klaus reaction on Sn–Mo–O	SO_2(ads), S_2(ads)	L	133
Klasu reaction on NaX	HSO_3^-, HS^-, S_2^{2-}, $S_2O_4^{2-}$, S_8	M	134
Hydro-desulfurisation of thiophene on MoO_3/Al_2O_3		L	135, 136
Hydro-desulfurisation of thiophene on Co–Mo/Al_2O_3		M	137, 138
Reaction of $CH_3OH + H_2S$ on Al_2O_3, WO_3/Al_2O_3	CH_3O, CH_3S	L	140

XI. Conclusion

In our previous reviews[1,2] an attempt was made to describe the results of studies of the surface complexes formed in heterogeneous catalysis carried out during the past 15 years using modern experimental methods. Our aim was to cover the largest possible number of investigations, but because of the rapid developments in this field of catalysis the task was not easy. Some general conclusions can be drawn from the data which have been assembled.

(1) In spite of our critical assessments of the reliability of the contributions made by various intermediate states there is little doubt that in the great majority of cases the confidence level is not high. The most convincing evidence that an observed surface compound is an intermediate in the reaction is the coincidence of the rates of transformation of the surface complex and of formation of the product. Only few studies adopting this approach have been reported, mainly because of the great experimental difficulties. The most serious of these difficulties is the need for simultaneous measurements of the spectroscopic and the catalytic characteristics of the system. Another difficulty is the need for quantitative spectroscopic measurements. This requires a knowledge of the extinction coefficients or of the scattering coefficients in the surface complexes, and information of this type is scarce. However, we should stress the fact that this approach is being strongly developed at the Institute of Chemical Physics of the Russian Academy of Sciences.

(2) Both the spectroscopic and the kinetic measurements of the consumption of reactants and of the accumulation of products in the gas phase usually have an unacceptably low time resolution. In order to create a complete picture of the mechanism we require faster measurements, at least in the millisecond range (i.e. at the lower limit of the time constants in catalysis). This calls for the development of new methods of measurement. One of the most promising of the new methods is the use of the TAP reactor.

(3) Many different surface compounds are formed when a given reaction is carried out on different catalysts. Even in the case of similar catalytic systems different workers report different surface complexes. This is usually attributed to differences in the reaction mechanism. However, another possible explanation[141] suggests that for a given mechanism the relative rates of the different stages may be different on different catalysts. As a result we may observe different surface complexes on different catalysts. Of course, in order to test this explanation we require detailed information on the intermediate compounds formed in a given reaction on different catalysts.

(4) By analogy with empirical dependences such as the Polanyi–Semenov rule, which describes the relationship between the energy of a bond and the activation energy of the reaction, it has been possible to establish general dependences relating the activation energy of a reaction to the decomposition energy of the intermediate complexes. In some cases, when the structure of the intermediates on the surface is close to the structure of the final products, we observe a lowering of the activation energy. However, data of this type are still too few to provide unambiguous conclusions.

(5) Often spectroscopic studies detect surface compounds which are formed on an active part of the catalyst but then migrate towards an inactive part. A characteristic of these compounds is their lack of sensitivity (or low sensitivity) towards changes in the reaction parameters (temperature, pressure, composition of the components). Typical of this behaviour is the accumulation of surface compounds on a carrier, on one of the phases of a mixed catalyst, or on one of the faces of a simple catalyst by the spillover mechanism. The accumulated surface compound can 'feed' the main reaction when the process conditions are changed. In complex multistage reactions this accumulation can produce the transport of molecules from some active centres towards others, spatially separated from the former.

(6) The data presented in our review show that the mechanisms proposed for heterogeneous catalytic reactions, though plausible, are largely conjectural. Obviously, this state of affairs is due to the almost total absence of reliable information on the intermediate compounds. Therefore we may finally conclude that further progress in our understanding of heterogeneous catalysis calls for a systematic study of intermediates.

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Approaches to the total synthesis of sesquiterpenoids of the guaiane series

B T Zhuzbaev, S M Adekenov, V V Veselovskii

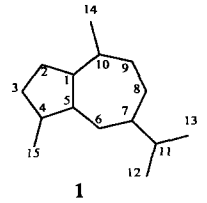
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Abstract. The approaches to the synthesis of guaiane sesquiterpenoids are considered. Attention is concentrated on the most general methods for the construction of their hydroazulene carbon skeleton. The bibliography includes 91 references.

I. Introduction

The guaiane series sesquiterpenoids **1**, which are widely distributed in nature,[1–4] are interesting objects to chemists engaged in synthesis. The development of research into their synthesis has also been stimulated by the discovery of many-sided biological activity in numerous representatives of compounds of this class.[4–6]



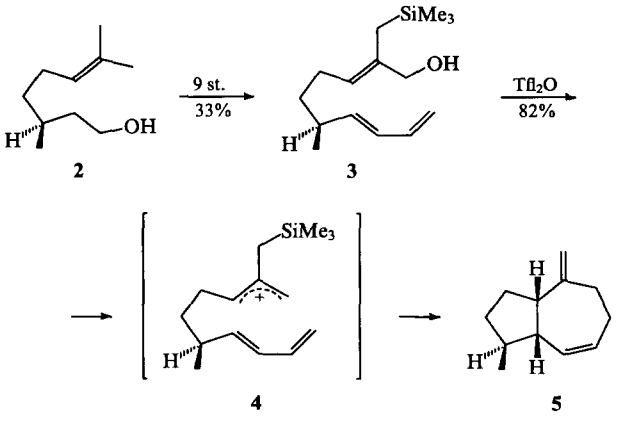
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The present review includes data obtained on the synthesis of guaiane sesquiterpenoids (GS) mainly during the last 10–15 years as well as earlier studies which have not been adequately described in review articles[7–12] and a monograph.[13] Virtually all the known methods of synthesis of GS can be divided into three groups: (1) skeletal isomerisation of mono-, bi-, and tri-cyclic precursors; (2) pentacondensation of derivatives of cycloheptane; (3) the construction of the hydroazulene skeleton from suitably functionalised cyclopentanes. Two novel methods, based on the intramolecular cationoid [4 + 3]- and [3 + 2]-cycloadditions, remain outside the limits of this classification.

B T Zhuzbaev, S M Adekenov Laboratory of the Chemistry of Natural Products, Institute of Organic Synthesis and Coal Chemistry, National Academy of Sciences of the Republic of Kazakhstan, ul. 40 let Kazakhstana 1, 470061 Karaganda, Kazakhstan.
Tel. (7-321) 251 22 41.
V V Veselovskii Laboratory of Polyunsaturated Compounds, Zelinskii Institute of Organic Chemistry, Russian Academy of Sciences, Leninskii prosp. 47, 117913 Moscow, Russian Federation.
Fax (7-095) 135 53 28. Tel. (7-095) 135 88 54.

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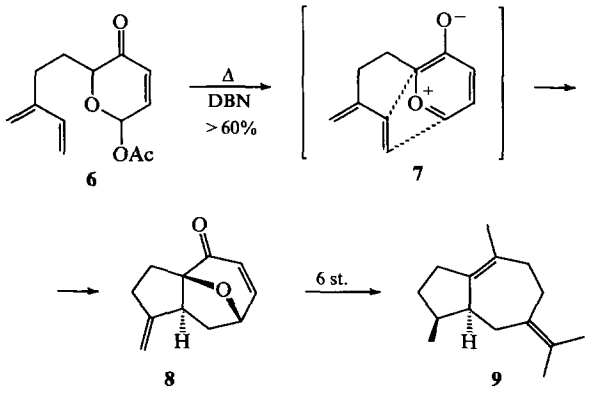
According to the first of these,[14,15] the hydroazulene **5** is formed from the intermediate **4**, generated from the allyl alcohol **3**—a product of the nine-stage (9 st.) transformation of (*S*)-citronellol **2**. In view of the high stereoselectivity of the formation of the hydroazulene **5**, the use of this procedure may prove exceptionally effective for the construction of the molecules of *cis*-joined GS.[15]



2 **3** **4** **5**

Tfl = trifluoromethanesulfonyl.

In the second method, the key stage of the synthesis of (±)-β-bulnesene **9**[16,17] is the stereospecific conversion of the dihydropyranone **6** into the *trans*-joined hydroazulone **8**, probably via the pyrylium intermediate **7**.



6 **7** **8** **9**

DBN = 1,5-diazabicyclo[4.3.0]non-5-ene.

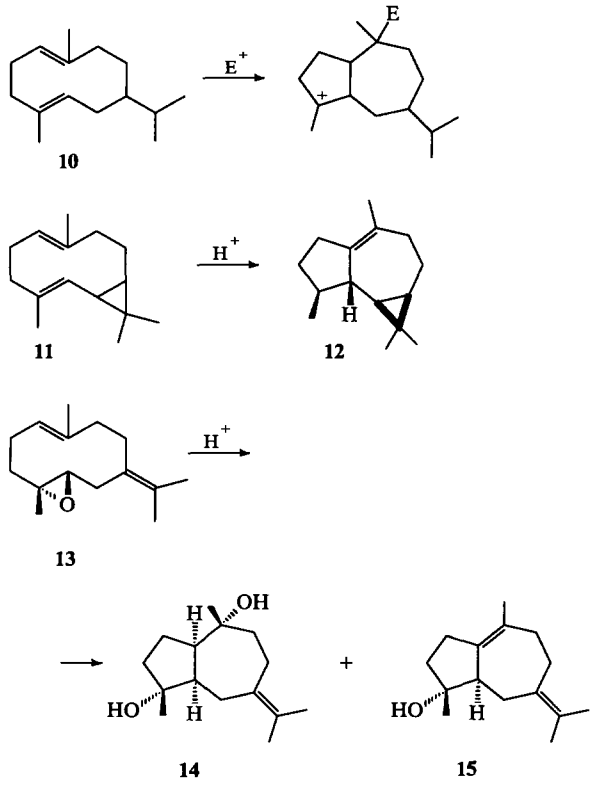
II. Synthesis of guaiane sesquiterpenoids by the skeletal isomerisation of mono-, bi-, and tri-cyclic precursors

This approach is used at present fairly widely. It proved particularly effective in the partial synthesis of guaianolides from germacrane and eudesmane sesquiterpene lactones.

1. Transformation of cyclodecane derivatives resembling biogenesis

According to Hendrickson,[18] the key stage in the biogenesis of GS is the anti-Markovnikov electrophilic cyclisation(EC) of their germacrane precursors of type **10** (Scheme 1).

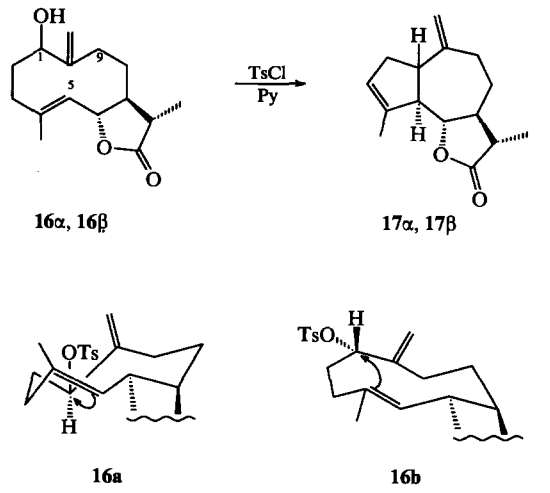
Scheme 1



This hypothesis stimulated a vigorous search for equivalent models. The result of such search has led to the development of a large number of biogenesis-like schemes for the synthesis of GS.[12,19] One of the early examples of the use of this approach is based on the acid-initiated conversion of bicyclogermacradiene **11** into a mixture of tricyclic products with a significant predominance of guaiane **12**.[20] Another example of the anti-Markovnikov electrocyclisation in the series of germacranes is the transformation of the epoxide **13** into a mixture of the diol **14** and the alcohol **15**.[21]

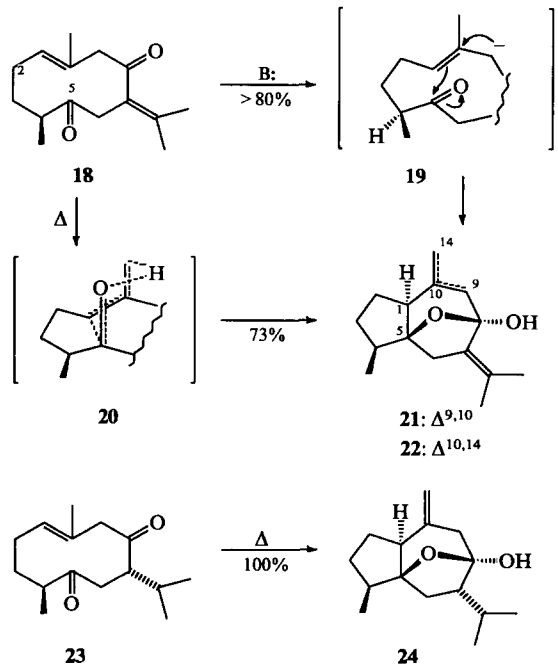
Analysis of the stereochemical results of such transformations permits the conclusion that the biomimetic reaction, proceeding via a concerted mechanism, is subject to conformational control.[12] This is confirmed, for example, by the results of the solvolytic electrocyclisation of gallicin **16β**[22] and of its C(1)-epimer **16α**,[23] which proceeds readily under the conditions of the tosylation of the secondary alcohols indicated (Scheme 2). The product of the cyclisation of gallicin **16β** is then the *cis*-joined guaianolide **17α**, the stereospecificity of the formation of which is evidently due to the preferred conformation **16a** of the initial allyl alcohol (and of its tosylate) with the equatorial orientation of the leaving group and with the disposition of the C(1), C(4), and C(5) centres in close proximity in space. The solvolysis of the epimer **16α**, leading to *trans*-**17β**, is treated taking into account the fact that the conformer **16b** is preferred.

Scheme 2



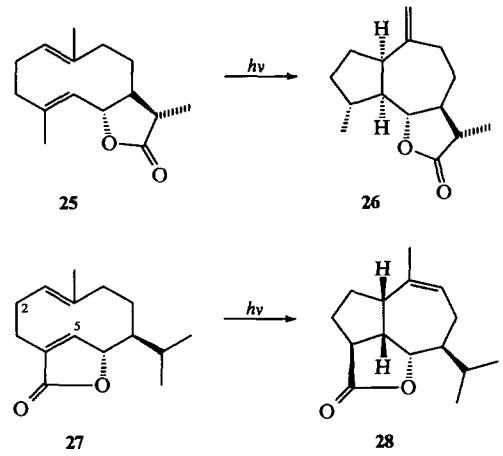
Rigid stereochemical control is also characteristic of the thermal or base-catalysed cyclisation of $\Delta^{1,10}$-5-ketogermacranes — the probable biogenetic precursors of the *trans*-joined 5-hydroxyguaianes.[12,24,25] Thus, on treatment with K_2CO_3 in methanol or with basic Al_2O_3 in benzene, the dehydrocurdione **18** is smoothly converted into the curcumenol **21**, evidently via a stage involving the formation of the allyl carbanion **19** (Scheme 3).[24] Its regioisomer **22** has been obtained in a high yield from the dehydrocurdione **18** under the conditions of the thermal reaction proceeding in accordance with a mechanism of the ene type via the probable transition state **20**. The thermolysis of the curdione **23** leads similarly to the curcumol **24** also without epimerisation of the centre adjoining the carbonyl group.[25]

Scheme 3

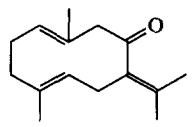


Individual examples of the stereospecific photocyclisation of compounds of the germacrane series to GS have been described. In particular, it has been shown that the sole product of the photolysis of dihydrocostunolide **25** is the *cis*-joined guaianolide **26**.[26] The irradiation of the germacranolide **27** leads similarly to the tricyclic lactone **28** (Scheme 4).[27]

Scheme 4



There are at present no reliable methods for the oxidative transformation of the functionalised germacrane skeleton into the guaiane skeleton. In a study recently undertaken for this purpose,[28] it has been shown that treatment of the germacratrienone **29**

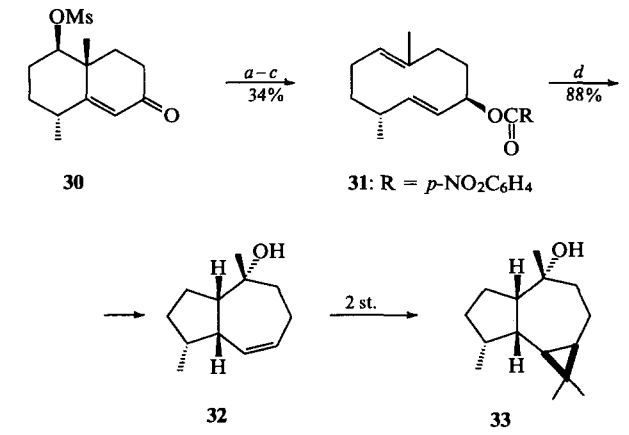


29

with a solution of $Pb(OAc)_4$ in acetic acid results in the formation of a complex mixture of substances containing predominantly unsaturated *cis*-guaiane ketoacetates.

It is noteworthy that the syntheses of GS considered above, based on the transformation of germacranes which are difficult to obtain, are hardly of preparative value. The approach, developed by Marshall,[29] by virtue of which the type **31** cyclodecadienes, which are related to germacranes, become obtainable from decalin derivatives **30**, is of definite interest. For example, the Grob fragmentation of the methanesulfonate **30**, initiated by a strong base, readily affords the trisnorderivative of germacrane, the solvolysis of which in the form of the nitrobenzoate **31** leads stereospecifically to the hydroazulenol **32**, which is subsequently converted into (±)-globulol **33**.[30]

Scheme 5

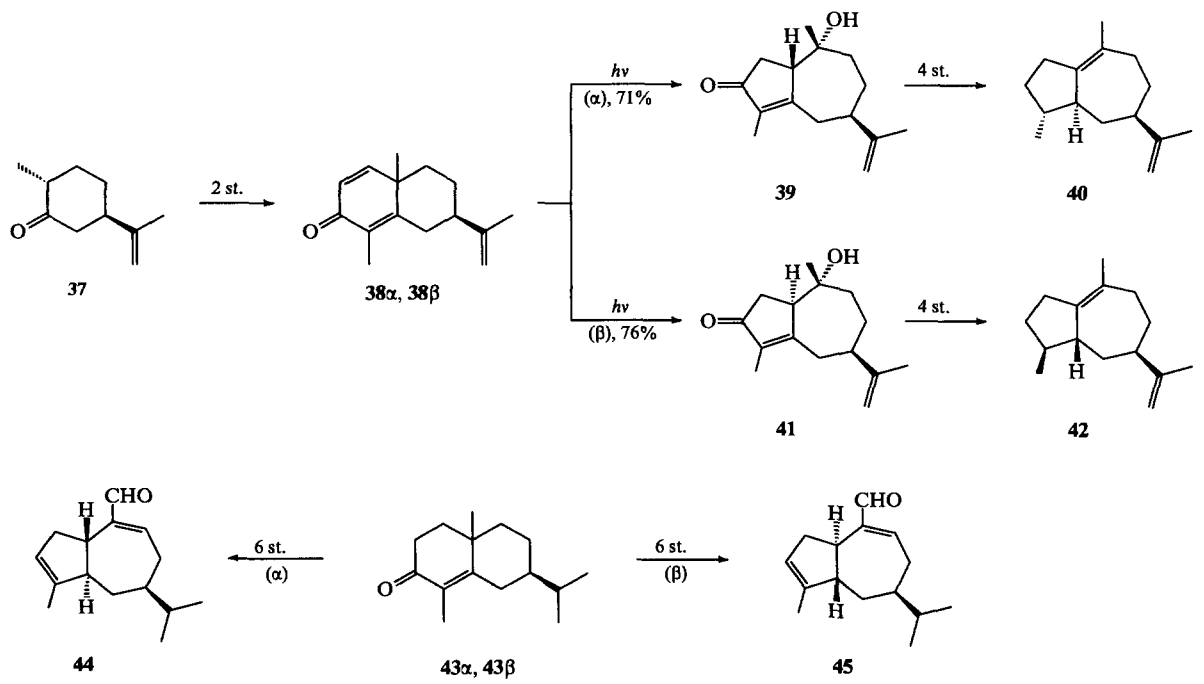


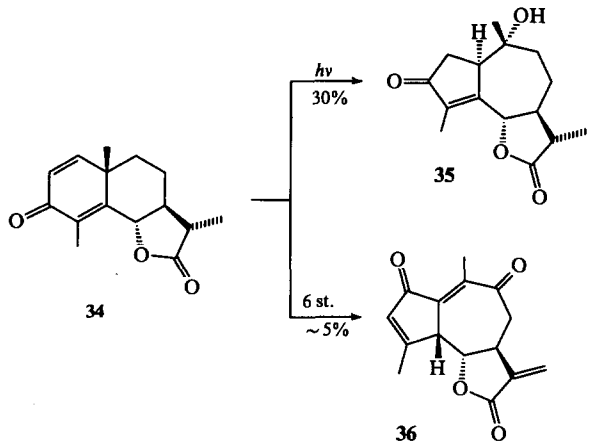
(*a*) BH_3; (*b*) NaOMe–MeOH; (*c*) p-$NO_2C_6H_4COCl$; (*d*) $NaHCO_3$, H_2O–$C_4H_8O_2$.

2. Skeletal rearrangements of derivatives of bicycloalkenes

The skeletal rearrangements of bicycloalkenes as a method for the construction of GS molecules has been studied mainly in relation to decalin derivatives, among which sesquiterpenes of the eudesmane series occupy an important place. One of the first examples of the application of this approach is the photoisomerisation of α-santonin **34** and some of its C(8)-derivatives to the corresponding type **35** guaianolides observed by Barton.[31,32] The latter are used subsequently in the partial synthesis of many natural products.[33] The stereospecific nature of the rearrangement, noted also for the photolysis of cross-conjugated tetrahydronaphthalenes related to compound **34**,[34–38] makes it possible to regard this procedure as a reliable means of obtaining the hydroazulene precursors of GS and some of their natural representatives. For example, the guaianolide **36** has been synthesised in this way from α-santonin **34**.[39] Data are available concerning the use of a series of derivatives of α-santonin **34** for the synthesis of (−)-estafiatin.[40]

Scheme 6

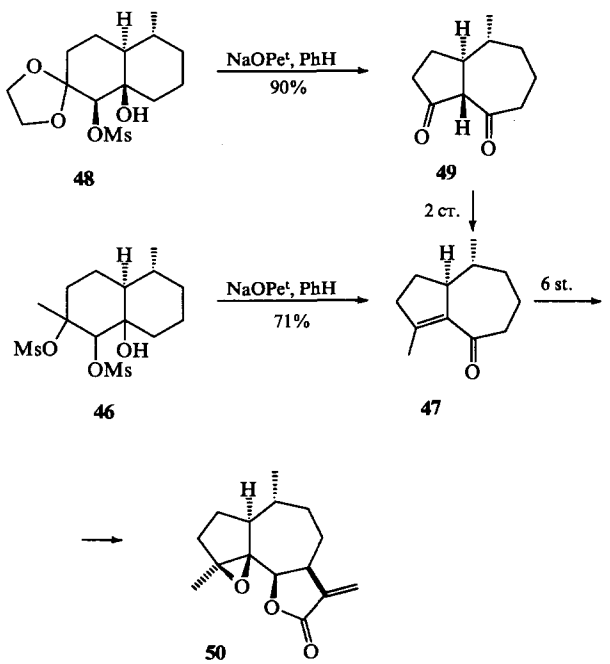




The methodology described above proved effective also in the syntheses of the bulnesenes **40** and **42** (Scheme 6), the key stage of which is the photolysis of the α- and β-dienones **38**, leading to the epimeric guaianes **39** and **41** respectively.[41,42] [The α- and β-dienones are obtained in their turn from (+)-dihydrocarvone **37** by Robinson's method.]

The dihydro-analogues of guaianes **39** and **41**, synthesised by the same procedure from the enones **43**, have been used in the synthesis of the corresponding stereoisomeric aldehydes **44** and **45** with the *trans*-joined hydroazulene skeleton.[43]

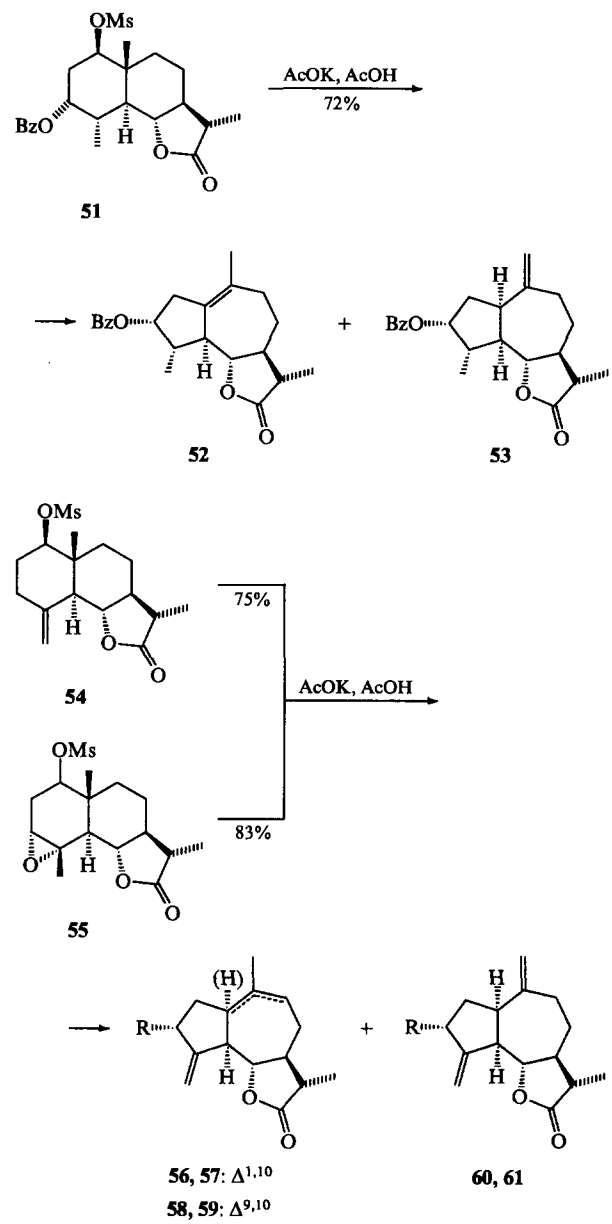
An alternative procedure, ensuring the stereospecific formation of the hydroazulene precursors of GS from perhydronaphthalenes, uses the solvolytic rearrangement of suitably functionalised derivatives. For example, a scheme for the total synthesis of the guaianolide **50** is based on a pinacol type rearrangement of the sum of the diastereoisomeric methanesulfonates **46**, leading to the hydroazulenone **47**. The latter can also be obtained from the diketone **49** — the product of the solvolysis of the methanesulfonate **48**.[44,45]



Pe^t = *tert*-pentyl (Translator).

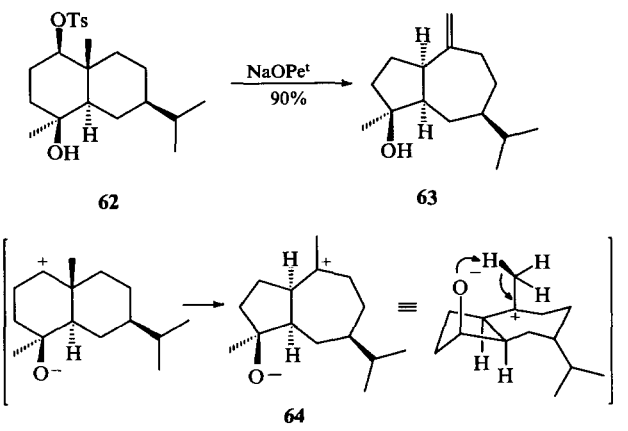
The synthesis of diverse representatives of guaianolides from α-santonin **34** similarly involves the use of the skeletal isomerisation of the α-santonin derivatives **51**, **54**, and **55**.[46-50] It was found that the solvolysis of these methanesulfonates by potassium acetate in acetic acid leads to mixtures of the corresponding regioisomeric hydroazulenes *endo*-**52**, **56**–**59**, and *exo*-**53**, **60**, **61** in comparable proportions (Scheme 7).

Scheme 7

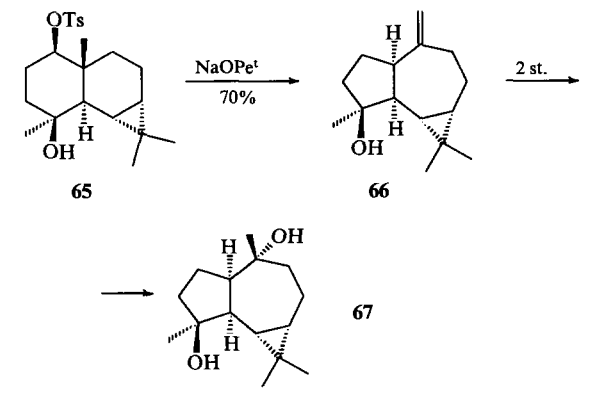


The observation by de Groot and coworkers[51-53] that the *tert*-pentyloxide-initiated skeletal rearrangement of type **62** tosylates leads to a virtually quantitative yield of *exo*-methylene products, in particular to (±)-epi-nardol **63** (Scheme 8), is of special interest in this connection.

Scheme 8

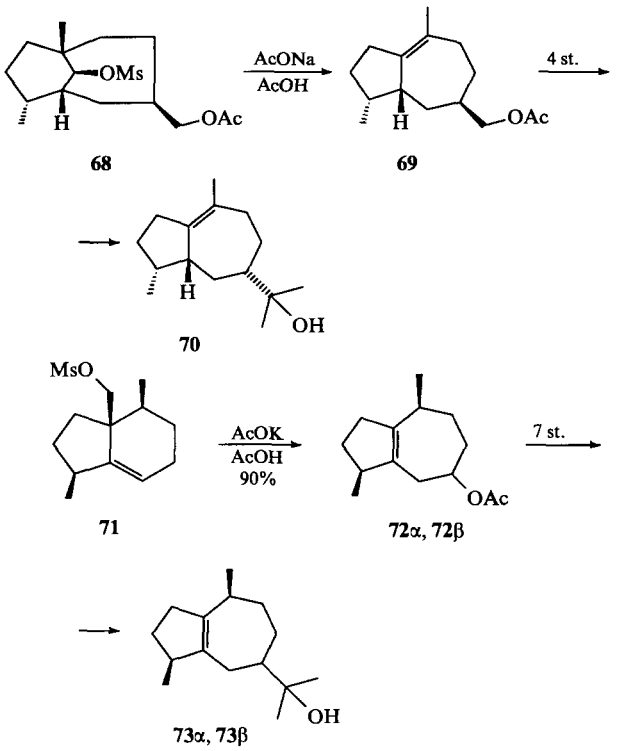


The significant increase in the regioselectivity of the reaction in this case can be accounted for by the presence in compound **62** of an axial hydroxy-group at the C(4) atom, its deprotonation and the involvement of the resulting alkoxide ion in the intramolecular elimination of a proton from the carbonium ion **64**, which leads to the alkene **63**.



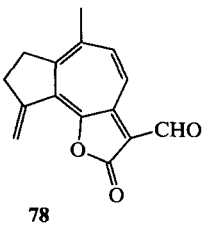
The isomerisation of the tricyclic tosylate **65** [53] leads similarly to the exclusive formation of the guaiane **66** — the key compound in the total synthesis of the natural diol **67**.

Thus the skeletal isomerisation of decalins is used fairly widely in the synthesis of hydroazulenoids. The use for this purpose of the skeletal rearrangement of other bicycloalkanes is so far restricted to only isolated examples (see also Heathcock and coworkers [8,9]). For example, the solvolysis of the bicyclic methanesulfonate **68** leads to smooth formation of the hydroazulenoid **69** from which (±)-bulnesol **70** was subsequently obtained. [54] In the scheme for the total synthesis of the guaiol **73β** and its epimer **73α**, the solvolytic isomerisation of the bicyclo[4.3.0]nonane derivative **71** to a mixture of the epimeric acetates **72** was employed as the key stage. [55]



Another novel method of synthesis of bulnesol **70** is based on the ability, observed by Sakai and coworkers, [56] of type **74** δ-diketones to undergo a rearrangement with ring expansion leading to cycloheptane derivatives under the conditions of the $F_3B.OEt_2$-initiated formation of an ethylene ketal. This reaction of the diketone **74** evidently includes the formation of the intermediate aldol **75** and the ethylene ketal of the β-hydroxyketone **76** and the cleavage of the latter to the hydroazulene **77** on treatment with a Lewis acid (Scheme 9).

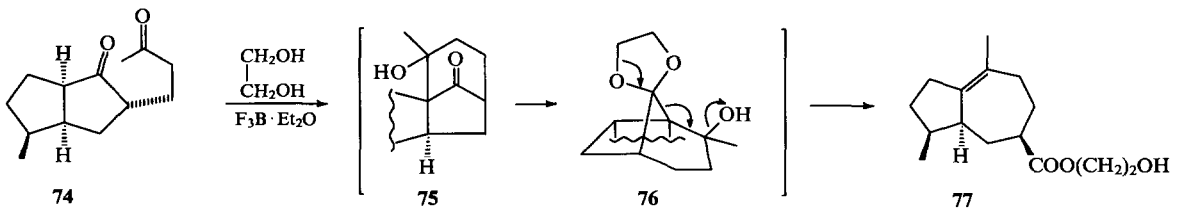
Mention must also be made of the recently developed scheme for the synthesis of the guaiane phytoalexin lettucenin A **78**, [57] in which use is made of the known ability of the type **79** dibromomethylcyclohexadienones to be converted into substituted tropones on treatment with $HSnBu_3$ (in the presence of a source of radicals).



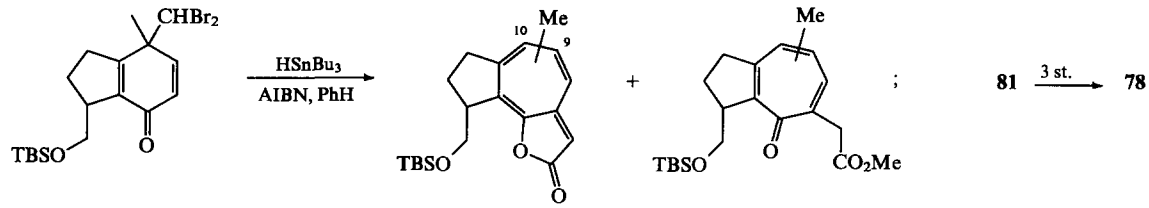
In the case of the hexadienones **79**, this reaction leads to a mixture of products **80–83** (Scheme 10) with compound **81** predominating. The latter was converted into the guaianolide **78** in three simple stages.

Thus the use of the skeletal isomerisation of bicycloalkanes is a fairly universal strategy applicable to the synthesis of a wide variety of representatives of GS.

Scheme 9



Scheme 10

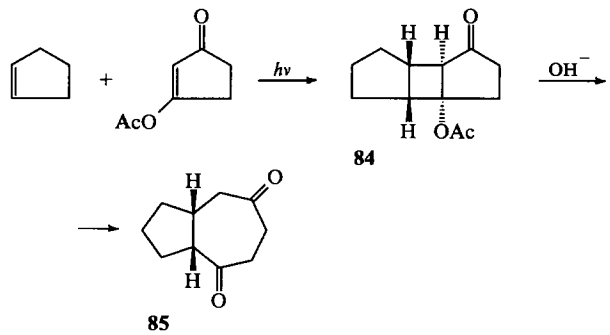


79 80: 9-Me 81: 10-Me 82: 9-Me 83: 10-Me

TBS = Bu^tMe_2Si.

3. Skeletal isomerisation of tricyclodecanes

The skeletal isomerisation of functionalised tricyclodecanes, involving the degradation of their cyclobutane fragment, serves as an effective method of synthesis of GS. The likely usefulness of this approach was first demonstrated by de Mayo and co-workers [58] in relation to the two-stage synthesis of the diketone **85** involving the retroaldo type of cleavage of the photoadduct of cyclopentene and cyclopentadione enol acetate.

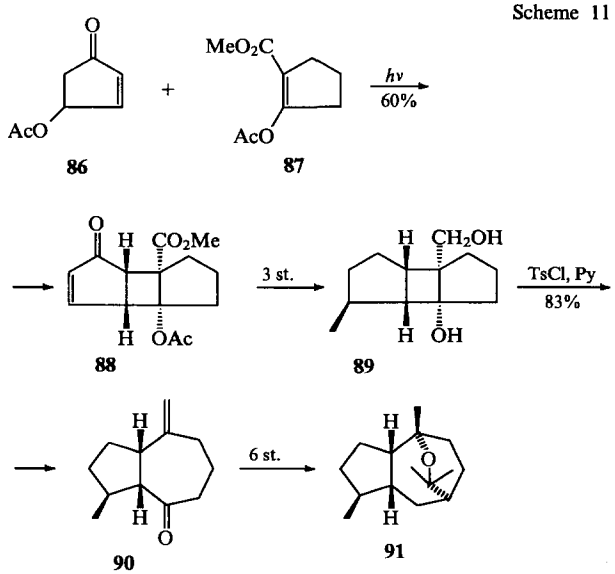


84 85

An evident advantage of this approach is the availability of compounds of type **84**, which have been synthesised by the [2 + 2]-cycloaddition of simple initial materials.

Thus the photochemical [2 + 2]-cycloaddition of substituted cyclopentenes **86** and **87**, leading predominantly to the cyclic adduct **88**, has been used in the total synthesis of (±)-5-epikessane **91** [59] in order to construct the carbon skeleton of the key tricyclodecane **89**. Next the enone **88** was converted in three stages, including the Michael methylation which proved stereospecific in this instance, into the diol **89**. The latter was smoothly cleaved under the conditions of the solvolysis into the hydroazulenone **90** — the precursor of (±)-5-epikessane **91** (Scheme 11).

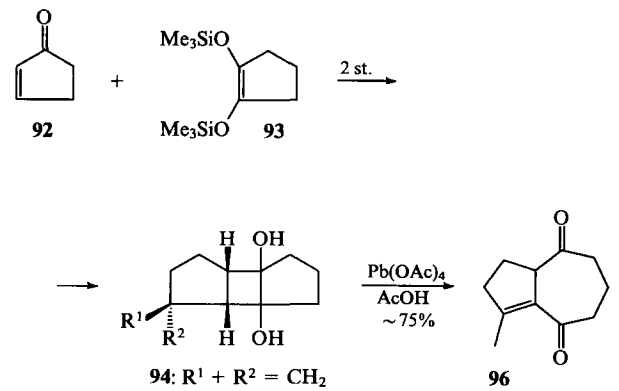
Scheme 11



86 87 88 89 90 91

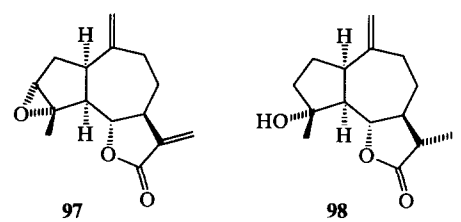
The tricyclic diol **94** and the triol **95** were obtained similarly from the cyclopentene derivatives **92** and **93**. The oxidative degradation of the diol and triol, accompanied in the case of the triol **95** by the degradation of the tertiary alcohol, affords smoothly the diketone **96** (Scheme 12).

Scheme 12



92 93 94: $R^1 + R^2 = CH_2$ 95: R^1 = Me; R^2 = OH 96

The diketone was then used in the synthesis of (±)-estafiatin **97** and (±)-compressanolide **98**. [60-62]

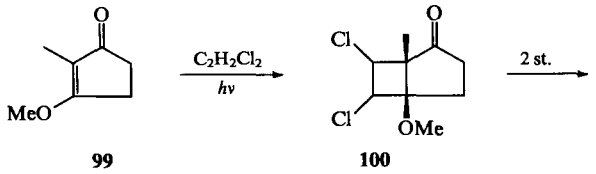


97 98

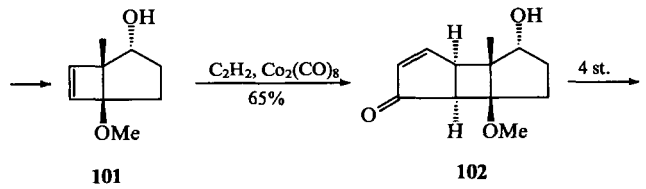
An alternative method of synthesis of the type **84** tricyclodecane compound has been used successfully in the synthesis of a GS precursor — the hydroazulenone **104**. [63] Thus the key stage in the synthesis of the hydroazulenone **104** is the formation of the tricyclic enone **102** under the conditions of the Pauson–Khand reaction of ethyne with the bicycloheptene **101**, which is formed in its turn from the photoadduct **100** of the methoxycyclopentenone **99** and *trans*-1,2-dichloroethene.

Yet another variation of this approach is the use of intramolecular [2 + 2]-cycloaddition in order to construct tricyclic precursors of hydroazulenoids. It was first demonstrated by Pattenden and coworkers [64] in relation to the photolysis of the enol acetate **105**.

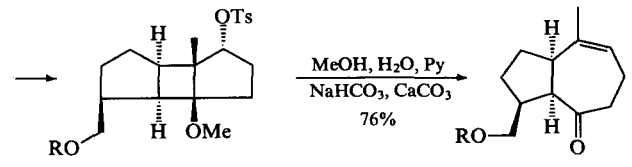
The effectiveness of this scheme in the synthesis of the hydroazulene **108** proved, however, to be low in view of the low regioselectivity of the photocyclisation of the enol acetate **105**, leading to a mixture of the isomeric tricycloalkanes **106** and **107** in proportions of approximately 3:2, and only the minor component **107** gives rise to the target diketone **108** on retroaldol cleavage.



99 100

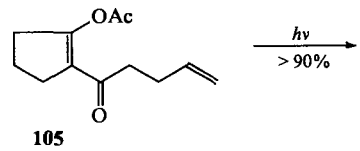


101 102

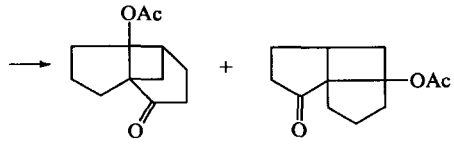


103 104

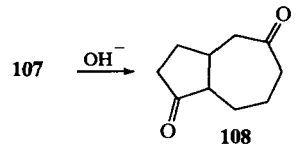
R = $SiPh_2Bu^t$.



105



106 107

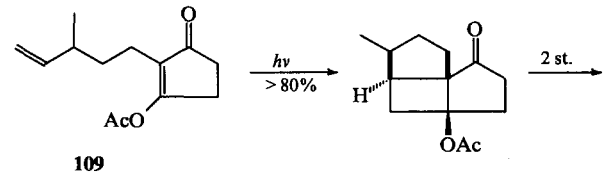


108

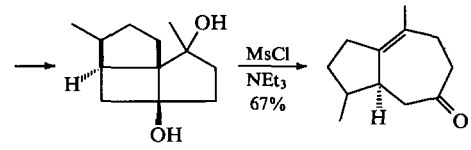
The photochemical [2 + 2]-cycloaddition of the enol acetate **109** takes place regiospecifically and leads to the sum of the epimeric tricyclodecanes **110** in a yield exceeding 80%.[65] The latter are then converted into the diols **111**, which are smoothly converted under the conditions of the solvolysis into a mixture of the epimeric hydroazulenones **112** in proportions of approximately 3:1. The conversion of the ketones **112** into the corresponding alkenes afforded the epimeric (±)-β-bulnesenes **9**.

An interesting development of this methodology arose in a recent study by Korean chemists,[66] who synthesised a series of hydroazulenones (compounds **116**, **120**, and **124**) from the readily available silyl vinyl ethers **113**, **117**, and **121**. The thermal [2 + 2]-cycloaddition of the latter to the dichloroketene generated in situ leads regio- and stereo-specifically to the tricyclic dichloro-derivatives **114**, **118**, and **122**. The reduction of the latter with Bu^n_3SnH in the presence of azobisisobutyronitrile (AIBN) leads to the tricyclodecanes **115**, **119**, and **123**, which are cleaved almost quantitatively under the conditions of mild desilylation by F^-, affording the diketones **116**, **120**, and **124** respectively.

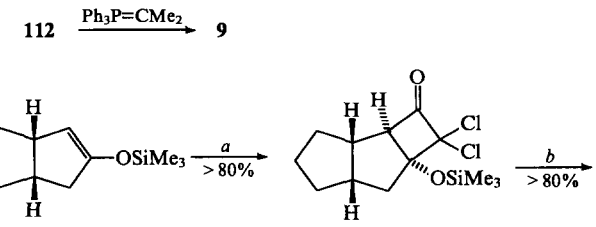
Thus an attractive feature of this approach is the possibility of its use from readily available starting materials, the choice of the key tricyclic structure ensuring the necessary functionalisation of the hydroazulene precursor of GS formed on its isomerisation.



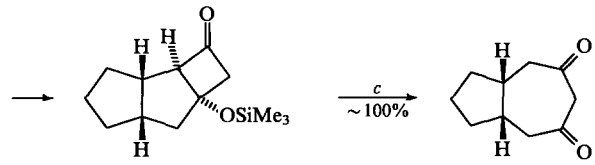
109 110α, 110β



111α, 111β 112α, 112β

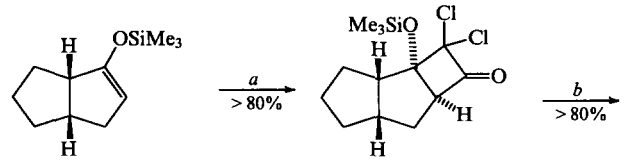


113 114

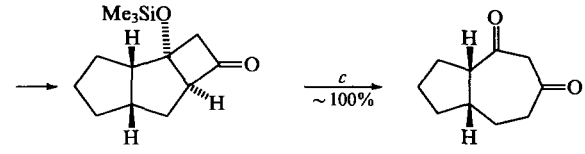


115 116

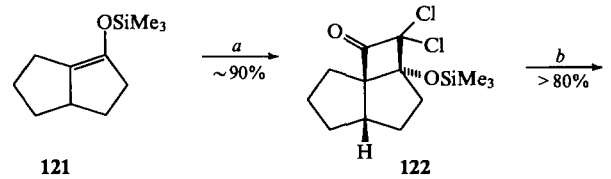
(*a*) Cl_3CCOCl, Zn; (*b*) Bu^n_3SnH, AIBN; (*c*) Bu^n_4NF.



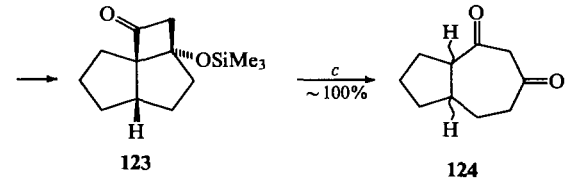
117 118



119 120



121 122



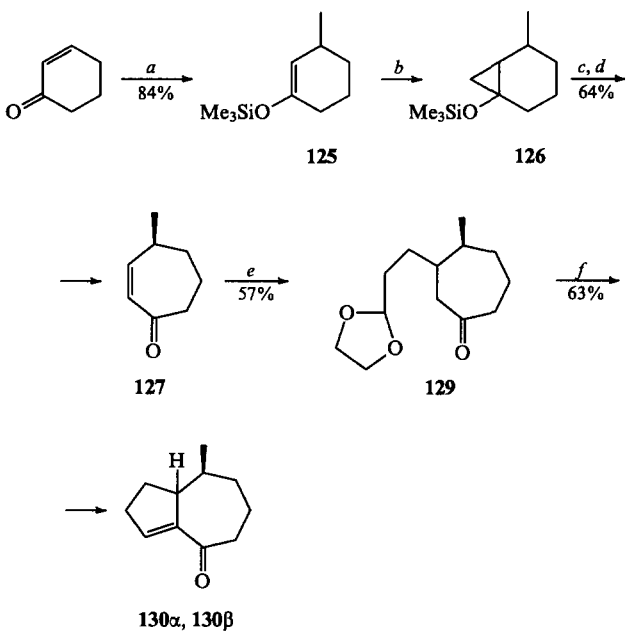
123 124

(*a*) Cl_3CCOCl, Zn; (*b*) Bu^n_3SnH, AIBN; (*c*) Bu^n_4NF.

III. Pentacondensation of cycloheptane derivatives

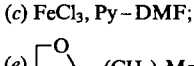
The strategy in the synthesis of GS based on the construction of their hydroazulene skeleton by the pentacondensation of cycloheptane derivatives was first employed as late as 1982.[67] Its subsequent development arose from effective methods being devised for the synthesis of suitably functionalised cycloheptane precursors. Thus Heathcock et al.[67] synthesised the cycloheptenone **127** from the cyclohexenone, which was converted, via the silyl vinyl ether **125** stage, into the bicyclic compound **126**. The latter underwent skeletal isomerisation to the cycloheptenone **127** (Scheme 13). The CuI-catalysed Michael coupling of the enone **127** and the Grignard reagent **128** takes place stereoselectively and leads to a mixture of the isomeric ethylene ketals **129** (*trans*:*cis* ≈ 4:1). Under the conditions of mild hydrolysis and as a result of the accompanying intramolecular crotonic condensation, the latter are smoothly converted into the epimeric hydroazulenes **130** in the same proportions.

Scheme 13



(*a*) Me_2CuLi, then Me_3SiCl, Et_3N; (*b*) CH_2I_2, Zn(Cu);

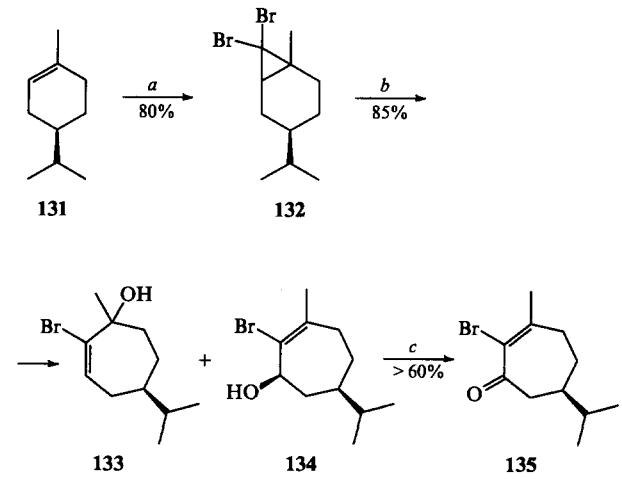
(*c*) $FeCl_3$, Py–DMF; (*d*) NaOAc, MeOH;

(*e*)  (**128**), CuI, THF; (*f*) 5% HCl, EtOH.

This methodology may acquire special interest in connection with the recent studies by Brocksom et al.,[68] who used the industrially available (+)-menthene **131** in order to synthesise the bicycloheptane **132**. The oxidation of the regioisomeric alcohols **133** and **134**, formed on skeletal rearrangement of compound **132** catalysed by Ag^+ ions, affords smoothly the chiral cycloheptenone **135** as the sole product.

In a recently published study,[69] the cycloheptenones **142** and **143**, related to the ethylene ketals **129**, were obtained by isomerisation under solvolytic conditions of the bicyclo[3.2.0]-heptane derivatives **140** and **141** respectively (Scheme 14).

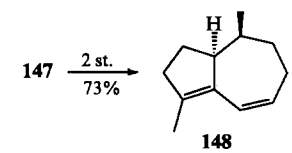
The latter proved to be obtainable by means of the thermal [2 + 2]-cycloaddition of dichloroketene to the silyl vinyl ether **136**.[70] The dehalogenation of the resulting bicycloheptanone **137** by Bu^n_3SnH in the presence of AIBN and the coupling of the resulting ketone **138** with the corresponding organomagnesium reagents **128** and **139** leads to compound **140** and **141**. The hydrogenation of the alkenes **142** and **143** over a rhodium catalyst, accompanied by the partial reduction of the ketones **129**



(*a*) $CHBr_3$, $C_{16}H_{34}Me_3N^+Br^-$; (*b*) $AgNO_3$, Me_2CO-H_2O (9:1);

(*c*) $C_5H_5N^+H\,ClCrO_3^-$, CH_2Cl_2.

and **146** to the alcohols **144** and **145**, and then cyclisation of the latter led ultimately to the hydroazulenone **130α** described above and the azulenone **147** — the key compound in the synthesis of (±)-clavukerin A **148**.

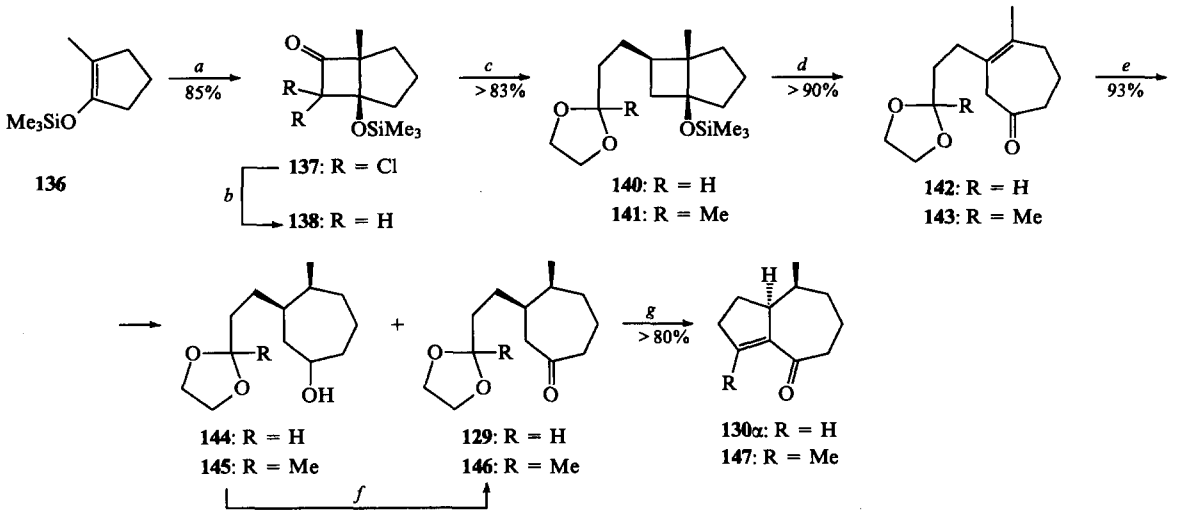


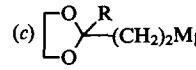
Mori and coworkers[71] developed a novel scheme for the total synthesis of the guaiane **159**. Compound **152**, a cycloheptene precursor of compound **149**, was obtained in 14% yield from alkylglutaric acid **149** via the intermediate bisdiazodiketone **151**, which cyclises to the enedione **152** in the presence of copper acetylacetonate (Scheme 15). The product of the hydrogenation of compound **152** — the cycloheptanedione **153** — was then converted into the monoketal **154**, the regio- and stereo-selective alkylation of which by the bromo-derivative **155** and subsequent ozonolysis of the resulting alkene **156** led ultimately to the diketone **157**. On treatment with a base, the latter cyclises smoothly to the hydroazulenone **158**, the eight-stage transformation of which afforded the target product (±)-**159**.

The γ-diketone **167**, structurally related to the diketone **157** and employed recently[72] in the total synthesis of (±)-gnididione **168**, was synthesised from methylglutaric acid anhydride **160** (Scheme 16). The ketodiester **162** was obtained by coupling compound **160** with the dilithium derivative **161**. It was subsequently converted into the hydrazone **163**, which underwent smoothly the Dieckmann condensation with formation of the bicyclic compound **164**. The alkylation by the bromo-derivative **166** of the ketone **165**, obtained from compound **164**, required the use of a double excess of the deprotonating agent and afforded the required diketone **167** as the sole product, which exists in the enolic form.

Yet another aspect of the approach under consideration, the development of which appears especially attractive, involves the use of the industrially available 2,4,6-cycloheptatrienone (tropone) as the starting material for the synthesis of GS. This methodology was first applied by Rigby and coworkers[73–75] in the total syntheses of (±)-estafiatin **97**, (±)-dehydrocostus-lactone **169**, and (±)-grosshemin **170**, which are discussed in detail in two reviews.[11,13]

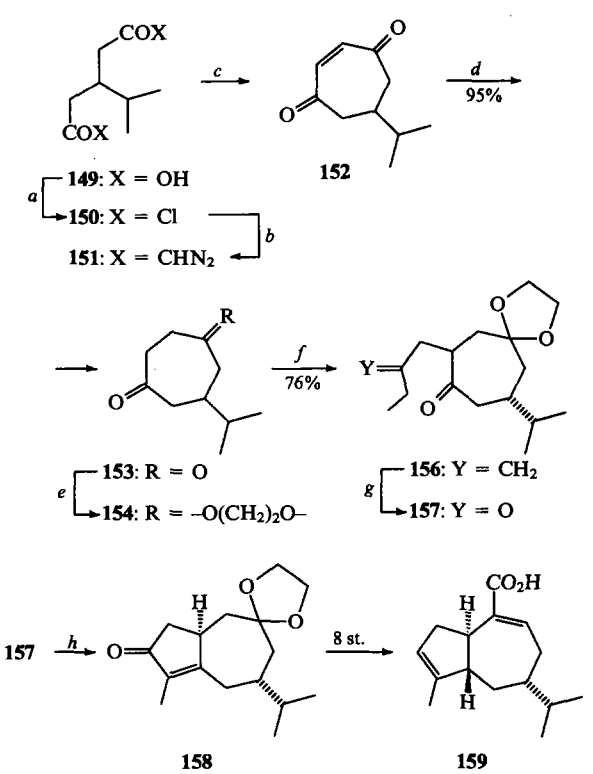
Scheme 14



(*a*) Cl_3CCOCl, Zn; (*b*) Bu^n_3SnH, AIBN; (*c*)  (**128**: R = H, **139**: R = Me), THF

(*d*) MsCl, Et_3N, CH_2Cl_2; (*e*) H_2, Rh/Al_2O_3, EtOAc; (*f*) $(C_5H_5NH)_2Cr_2O_7$, CH_2Cl_2; (*g*) 5% HCl, EtOH.

Scheme 15

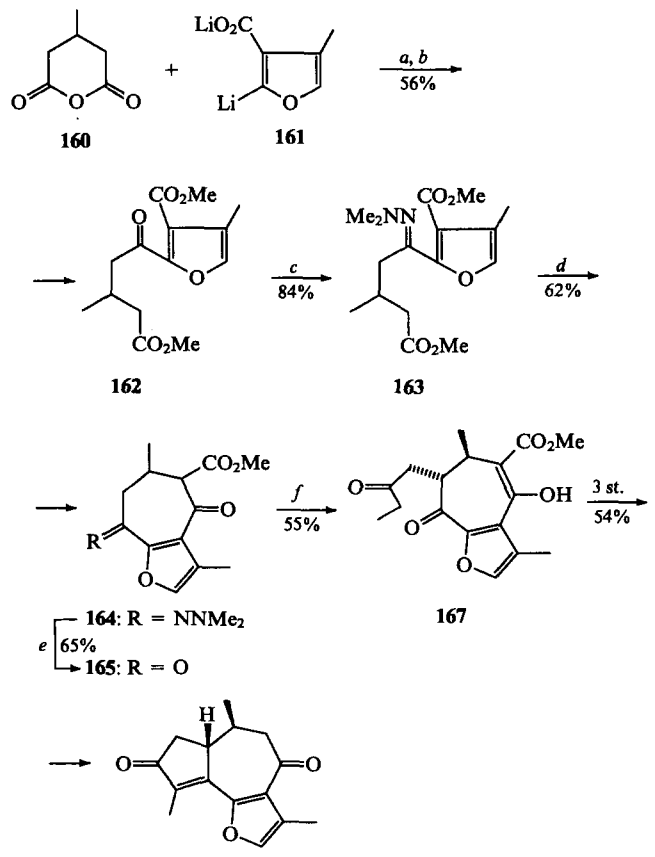


(*a*) PCl_5; (*b*) $CH_2N_2-Et_2O$; (*c*) $Cu(acac)_2$, PhH; (*d*) H_2, Pd/C, EtOH;

(*e*) TsOH,  , PhH; (*f*) $LiNPr^i_2$, THF, $EtCCH_2Br$ (**155**),
CH_2

(*g*) O_3, MeOH, Me_2S; (*h*) NaOH, $H_2O-EtOH$.

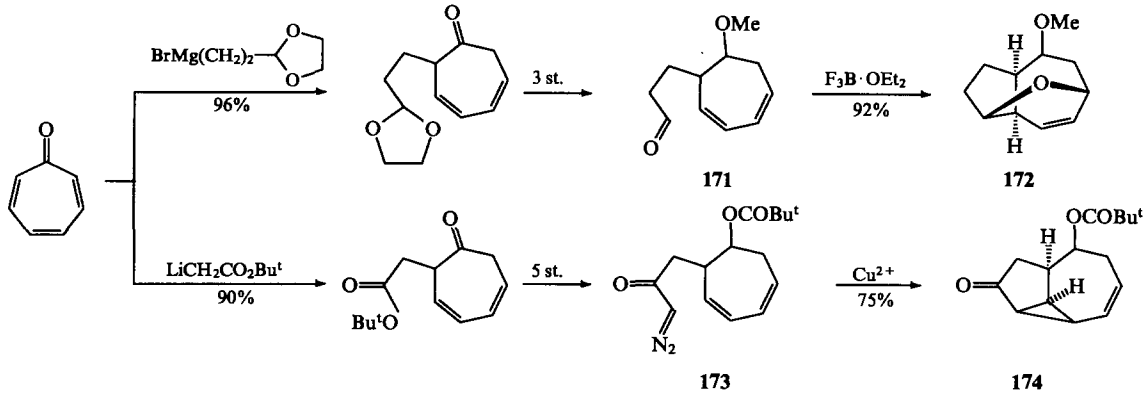
Scheme 16

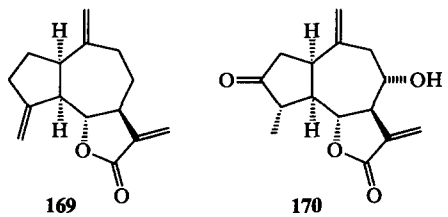


(*a*) THF; (*b*) AcCl, MeOH; (*c*) Me_2NNH_2, AcOH–EtOH;
(*d*) $NaN(SiMe_3)_2$, Et_2O; (*e*) MeI, EtOH;
(*f*) $LiN(Pr^i_2)$, $EtCOCH_2Br$ (**166**), THF.

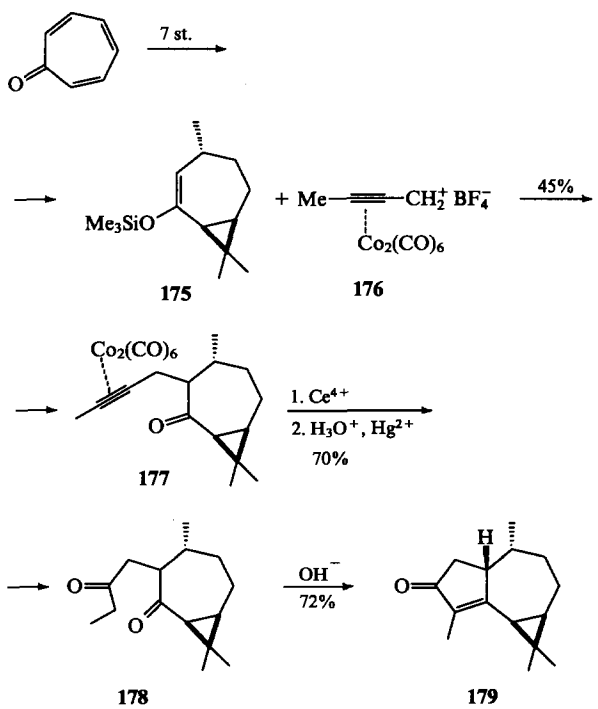
The principal stages of the syntheses of these compounds are presented in Scheme 17. Thus the hydroazulene precursor of the guaianolides **97** and **169** — the epoxide **172** — was obtained as a result of the $F_3B.OEt_2$-catalysed cyclisation of the aldehyde **171**.[73] The known ability of tropone to interact with organometallic reagents via the 1,8-addition mechanism is used in its turn to synthesise the aldehyde **171**. The tricyclic compound **174**, which is of key importance in the synthesis of grosshemin **170**, was obtained similarly. It is a product of the $Cu/CuSO_4$-catalysed cyclisation of the diazoketone **173**.[74]

Scheme 17





Yet another synthetic scheme, based on the 11-stage transformation of tropone into (±)-cyclocolorenone **179**,[76] involves the condensation of the silyl ether **175** with the cationoid complex **176**. The resulting diastereoisomeric adducts **177** were converted into a mixture of epimeric γ-diketones **178** (*cis*: *trans* ≈ 8:1) by successive demetallation and hydration in the presence of Hg^{2+}. The dominant component, compound *cis*-**178**, was isolated chromatographically and was smoothly cyclised to the target product **179** by treatment with a base.

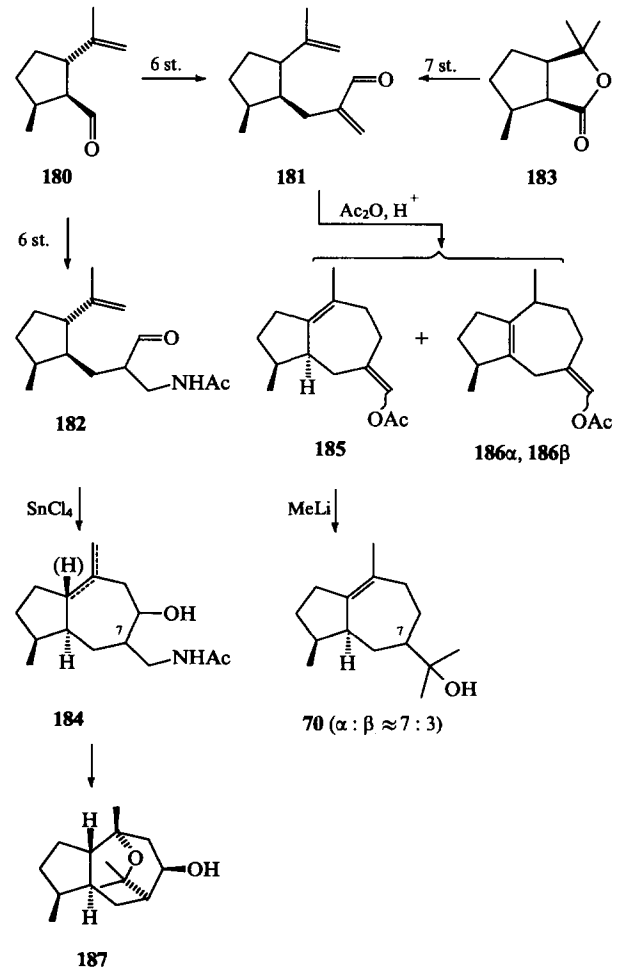


Thus examples of the application of this strategy in the synthesis of GS considered in this section demonstrate the possibility of its successful use to obtain diverse natural products from readily available starting materials.

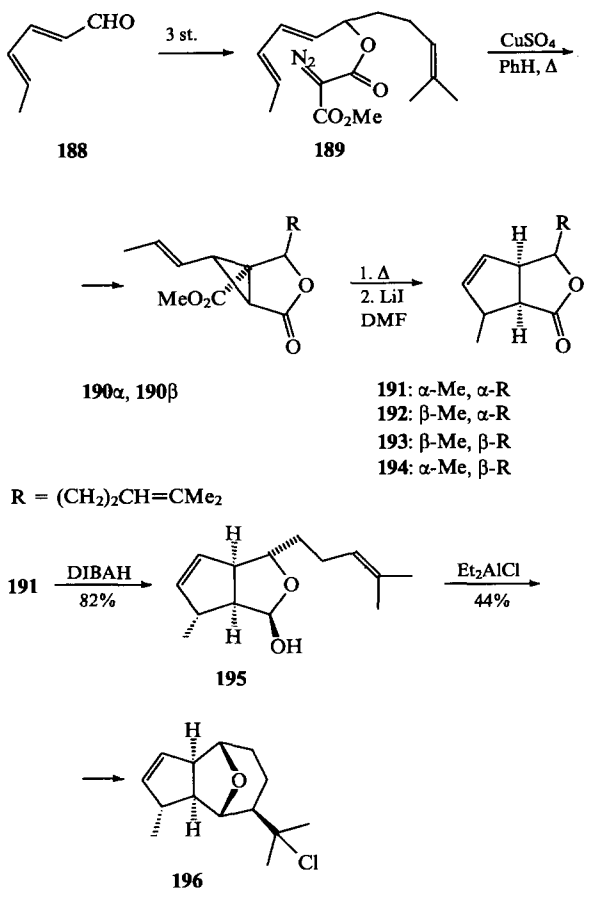
IV. Heptacondensation of cyclopentane derivatives

In contrast to the approach described in the previous section, the present one involves the construction of the hydroazulene skeleton of the GS by the closure to a seven-membered ring of the side chains of suitably functionalised cyclopentane precursors. For example, Andersen and coworkers, who were the first to apply this strategy in the total synthesis of certain natural guaianes,[77–79] used the unsaturated aldehydes **182** and *trans*- and *cis*-**181** as the cyclopentane precursors. The aldehydes **182** and *trans*-**181** were synthesised from the product **180** of the photocyclisation of citral, while compound *cis*-**181** was obtained from the lactone **183**. The principal results of these investigations, which have been analysed in a review,[9] are illustrated by Scheme 18.

Scheme 18



Scheme 19



In particular, the regioselectivity of the electrocyclisation of the unsaturated aldehyde *trans*-**181** proved to be low, which significantly reduced the overall effectiveness of the synthesis of (±)-bulnesols **70**. The latter were obtained as a result of the further transformation of the hydroazulene precursor **185**, which predominates in the **185**:**186**α ≈ 2:1 mixture.[77] The unsaturated aldehyde *cis*-**181** is cyclised similarly, affording the sum of the regioisomers **185** and **186**β (~3:1).[78] The intramolecular version of the Prins reaction also leads to a mixture of the regio- and stereo-isomeric hydroazulenoids **184** in the case of the aldehyde **182**. *exo*-Methylene 7α-epimers, employed subsequently in the synthesis of (±)-kessanol **187**, were isolated chromatographically and their overall yield was ~40%.[79]

In order to develop further this methodology, Hudlicky et al.[80] investigated the possibility of obtaining the guaiane structures from the bicyclic hemiacetal **195** synthesised from a suitably substituted diazoketone **189** (Scheme 19). The diazoketone **189**, prepared from sorbaldehyde **188**, cyclises smoothly in the presence of Cu^{2+} ions with formation of the epimeric cyclopropanolides **190** (α:β ≈ 2:1), which can be readily separated chromatographically. Each of them undergoes subsequent thermolysis and demethoxycarbonylation, which results in the formation of **191**:**192** ≈ 2:1 and **193**:**194** ≈ 3:1 mixtures of the stereoisomeric cyclopentanolides. The possibility of using lactones of this type as the precursors of GS has been demonstrated in relation to the lactone **191**, which was isolated chromatographically in a pure state. It was reduced by diisobutylaluminium hydride (DIBAH) to the hemiacetal **195**, which cyclises stereospecifically to the hydroazulenoid **195** on treatment with Et_2AlCl.

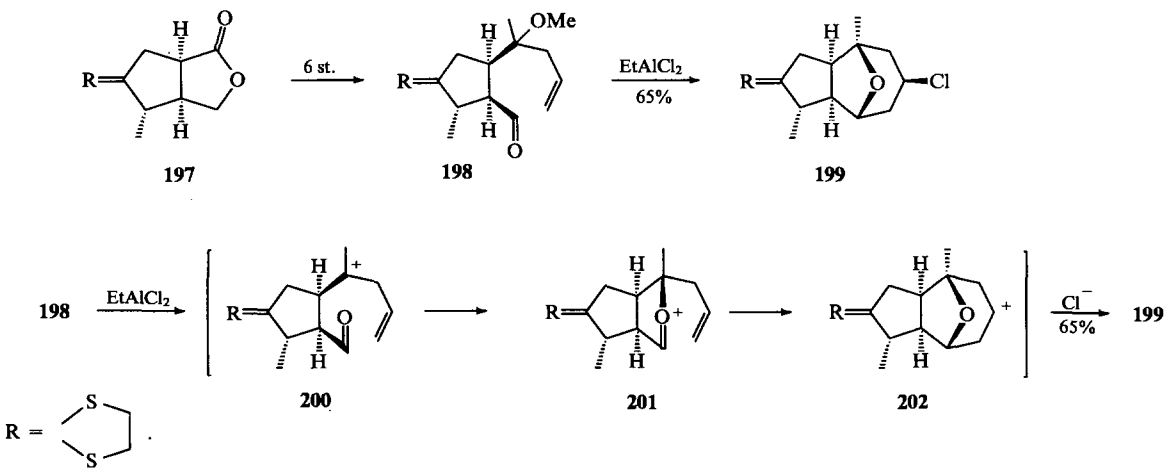
The intramolecular Prins reaction of the unsaturated aldehyde **198**, obtained from the chiral cyclopentanolide **197**,[81] was recently used similarly[82] in the enantioselective synthesis of the hydroazulenoid **199**, homochiral with respect to grosshemin **170** (Scheme 20). The formation of the enantiomerically pure hydroazulenoid **199** as the only product of the cyclisation of the mixture of the diastereoisomers of compound **198** can be explained by their initial cleavage on treatment with $EtAlCl_2$ and by the stabilisation of the cation **200**, arising as a result of such cleavage, in the form of the oxonium ion **201**. The electrophilic attack by the latter on the multiple bond in the side chain of the same molecule and the interaction of the resulting carbonium ion **202** with the excess $EtAlCl_2$ lead ultimately to the chloro-derivative **199** in ~65% yield.

Two variants of the heptacondensation of substituted cyclopentanes have been achieved using the *trans*-ketoester **203**, obtainable from methylheptenone, as the monocyclic precursor of the GS.[83] Thus the cyclopentanone **203** was initially converted into the ethylene ketal, the reduction of which by DIBAH affords smoothly the aldehyde **204** (Scheme 21).[84]

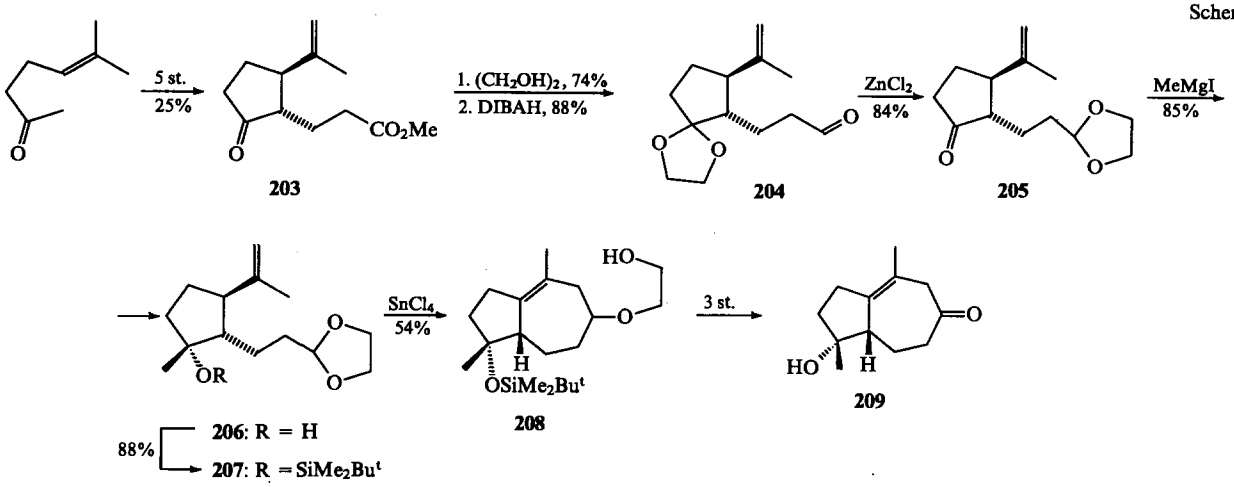
The attempt to cyclise the latter under the conditions of the Lewis acid-catalysed Prins reaction unexpectedly led to the product of intramolecular transketalisation — the ketone **205**, which was subsequently converted into the silyl ether **207** in two stages, including the reaction with MeMgI, which proved to be highly stereoselective. Treatment of the silyl ether with $SnCl_4$ leads to the bicyclic product **208**, the conversion of which into the hydroazulenone **209** is carried out in three stages.

A shorter route to the formation of guaiane structures from the ketoester **203** proved possible[85,86] via the Dieckmann intramolecular cyclisation of the sulfonecarboxylate **212** (Scheme 22). The latter was obtained from the ketoester **203** in three stages via the chloroderivative **210** and the sulfone **212**. Treatment of the sulfonecarboxylate **212** with sodium *N*,*N*'-bistrimethylsilylamide in benzene leads stereospecifically to the hydroazulenone

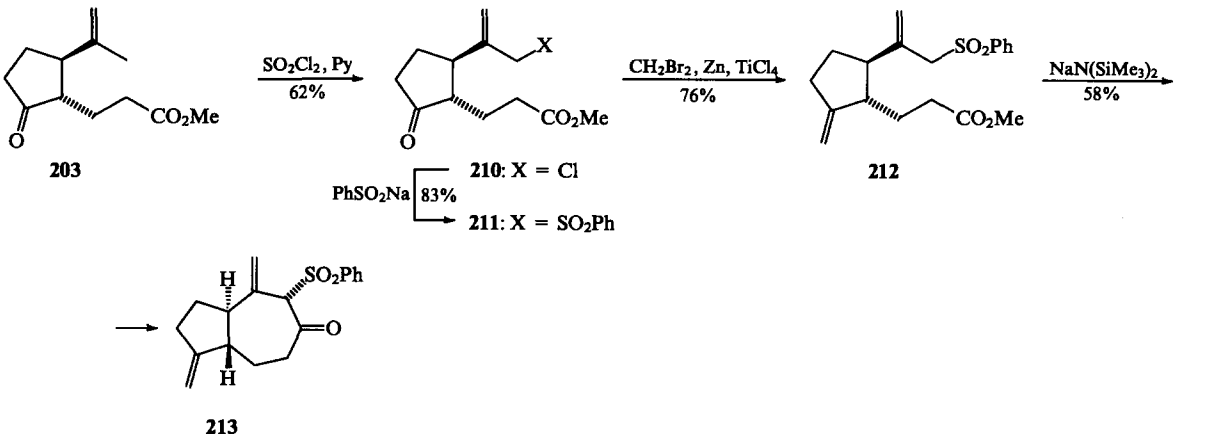
Scheme 20



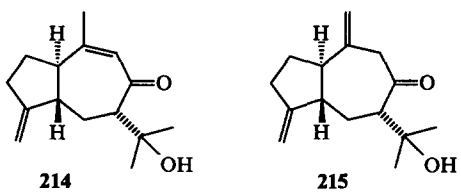
Scheme 21



Scheme 22



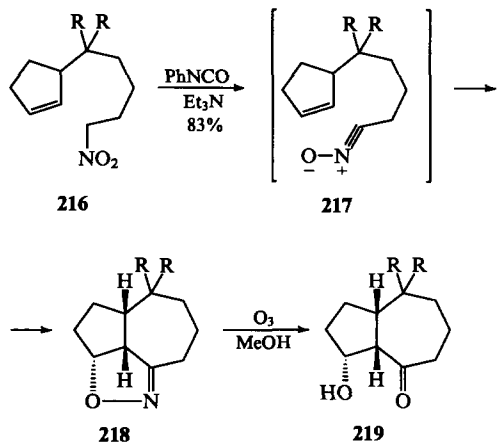
213, which was used further in the synthesis of the ketoalcohols 214 and 215 having the guaiane skeleton.



Among other known methods for the heptacondensation of substituted cyclopentanes, a novel procedure, employed in the synthesis of the hydroazulenone **219** and involving the intramolecular [3 + 2]-cycloaddition of the nitrile oxide **217** generated in situ from the nitroalkene **216**, may be of definite interest for the synthesis of the hydroazulene precursors of GS.[87]

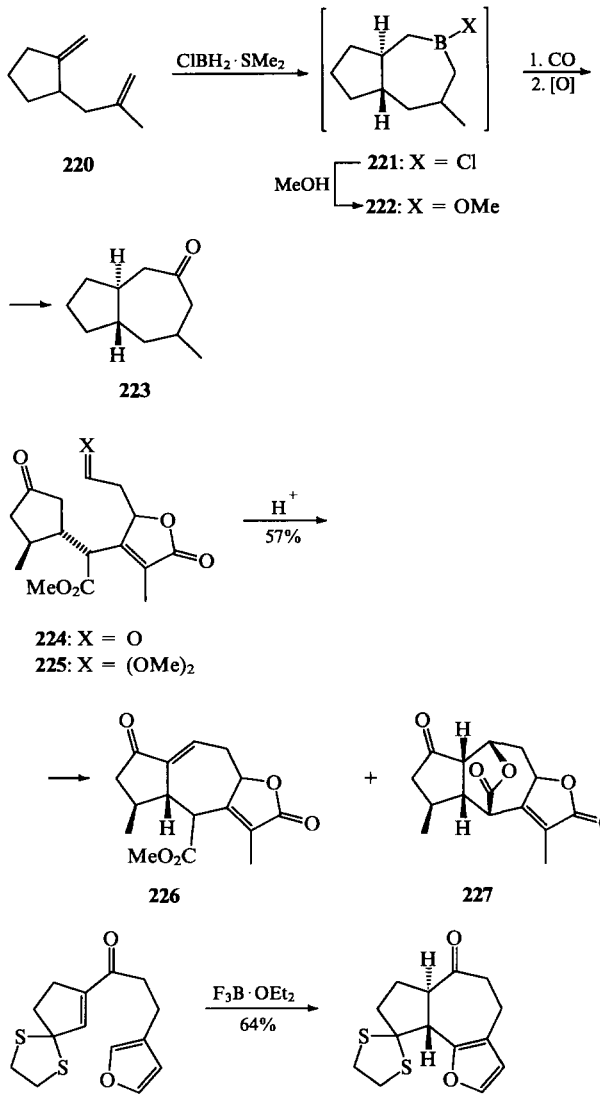
Yet another variant of a nontraditional attainment of the same aim has been recently demonstrated by Stevenson and Bryson.[88] The hydroboration of the diene **220** by $ClBH_2.SMe_2$ leads to the smooth formation of the boracyclane **221**, the conversion of which into the hydroazulenone **223** has been achieved by means of standard carbonylation.

The scheme for the total synthesis of guaianolides proposed by Winterfeldt and coworkers,[89] in which the stage involving the cleavage of the acetal **225** to the aldehyde **224** by CF_3COOH is accompanied by the formation of the diastereoisomeric enones **226** and an insignificant amount of the transesterification product **227**, is based on the intramolecular crotonic type condensation of the ketoaldehyde **224**.



R = CO_2Me

It is noteworthy that the heptacondensation of substituted cyclopentanones, carrying in the side chain a lactone ring already formed or its synthetic equivalent, is regarded nowadays[89–91] as a promising approach to the construction of the tricyclic skeleton of guaianolides and related furanoterpenoids. One of the variants of the application of this strategy consists, for example, in the electrocyclisation of the cyclopentane derivative **228**, terminated by a furan substituent, which affords the furanohydroazulenone **229** as the only product.[90]

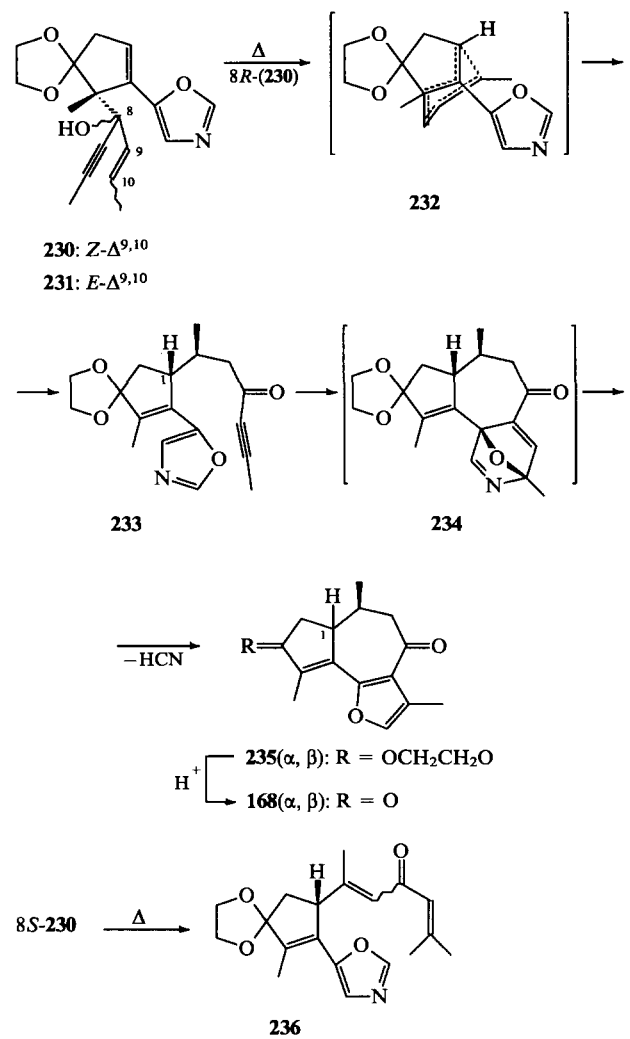


220 223 226 227 228 229

The recently published study[91] on the total synthesis of (±)-gnididione **168**, the key stage of which is the intramolecular [4 + 2]-cycloaddition of the oxazole **233** — the product of the oxy-Cope rearrangement of the tertiary alcohol **230**, is of interest in this connection (Scheme 23). It was found that the formation of the chair-shaped transition state **232**, leading to the secohydroazulenoid **233**, is favoured by the (*R*)-configuration of the C(8) centre of the carbinol **230**. In the case of the thermolysis of the (*S*)-carbinol **230**, the preferential formation of the dienone **236** is observed. The dienone arises as a result of the involvement of the ethyne fragment of the molecule of compound **230** in the rearrangement. Under more severe conditions, the transformation of the carbinol **230** is not limited to the formation of the oxazole **233**, which is converted as a result of the thermal [4 + 2]-cycloaddition into the unstable cyclic adduct **234**, cleaved subsequently to give the target furanoterpenoid in the form of its ethylene ketal **235β**. It is noteworthy that the relative configuration of the substituents at the C(1) atom of the ketal **235** is controlled by the (*Z*)-geometry of the butenyl residue of the initial alcohol **230**. It was found that, when the carbinol **231** with a transoid $\Delta^{9,10}$ bond is used, the above sequence of reactions makes it possible to obtain the C(1)-epimer of gnididione **168β** — the hydroazulenoid **168α**.

* * *

Scheme 23



In conclusion one should note that the search for the specific syntheses of sesquiisoprenoids of the guaiane series makes a significant contribution to the development of the fundamental and methodological aspects of modern organic chemistry. In addition, further studies in this field are of current interest, because they make it possible to discover reliable sources of these terpenoids, which are difficult to obtain from natural raw materials, as well as their analogues, including compounds which are of definite interest for medicine and agriculture.

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Direct synthesis of coordination compounds from zerovalent metals and organic ligands

A D Garnovskii, B I Kharisov, G Gojon-Zorrilla, D A Garnovskii

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Abstract. Data on the direct synthesis of coordination compounds from zerovalent metals and organic ligands are surveyed and described systematically. The preparation of metal complexes in the gas and liquid phases is considered. It is shown that the direct syntheses are single-stage processes and make it possible to obtain all types of coordination compounds — molecular and π-complexes, metal chelates, and dinuclear and polynuclear structures. Problems of competitive reactions in the course of the direct synthesis of complexes of ambident ligand systems are discussed. The bibliography includes 289 references.

I. Introduction

A wide variety of methods are used nowadays to synthesise coordination compounds.[1-5] Metal complexes are obtained mainly by the direct interaction of the components (the ligands and a source of the complex-forming metal),[1-7] as a result of ligand[6-8] and metal[6] exchange, and under the conditions of template synthesis,[7-10] which includes also the method of nascent reagents.† In the reactions listed above, the source of the metal is either its salts or carbonyls.‡ At the same time, it has long been known that coordination compounds may be obtained as a result of direct synthesis from zerovalent metals. The possibility of employing compact metals for the synthesis of coordination compounds was first demonstrated by Gerdes[11] and Chugaev,[12] who obtained metal complexes during electrolysis. Methods for the synthesis of complex compounds under the conditions of gas-phase reactions,[13-15] oxidative dissolution of zerovalent metals in nonaqueous media,[16,17] and in the solid phase[18,19] were developed subsequently. These methods became the basis of a new field in synthetic chemistry — the direct synthesis of coordination compounds and organometallic compounds from zerovalent metals. Particular aspects of this problem have been described in a series of reviews.[13-17,20-25] and monographs.[4,26-28] However, on the whole the direct synthesis of metal complexes has not been dealt with in the review and monograph publications on coordination chemistry.[2-5]

The aim of the authors of the present review was therefore to survey the current data on the direct synthesis of coordination compounds from zerovalent metals and organic ligands. Attention was concentrated on the types of ligand systems and the complexes formed during these reactions.

In describing the data, we adhered to the classification of coordination compounds put forward in a previous review.[29] According to this classification, metal complexes are divided into molecular complexes, chelate complexes, π-complexes and polynuclear structures. Such a classification does not conflict with the subdivision of the complexes employed in modern coordination chemistry (see, for example, Kostromina et al.[5]).

In describing the problems of the direct synthesis of coordination compounds from zerovalent metals and organic ligands, we decided to employ individual postulates and references from earlier reviews[13-15] and monographs.[26]

† The formation of ligands under the conditions of formation of a complex from the components on a metal matrix.

‡ The modification of the complexes is widely carried out in the template syntheses.[7-10]

A D Garnovskii, D A Garnovskii Department of Coordination Chemistry, Institute of Physical and Organic Chemistry, Rostov State University, prosp. Stachki 194/3, 344104, Rostov-on-Don, Russian Federation. Fax (7-863) 228 56 67
B I Kharisov Department of Radiochemistry, Faculty of Chemistry, Lomonosov Moscow State University, Leninskie gory, 119899 Moscow. Russian Federation. Fax (7-095) 932 88 46.
G Gojon-Zorrilla Universidad Autonoma de Neuvo Leon, Departamento de Quimica Organica, Apartado 1864, Monterrey, Neuvo Leone, 64 000 Mexico. Fax (52-83)72 3309 Tel. (52-83)76 5375

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II. Gas-phase synthesis

1. Methods, conditions, apparatus, and reagents

Coordination compounds are obtained in the gas phase in a vacuum apparatus via the direct interaction of the vapour-phase atomic metals and ligands.[14,15,20,21,26,30-36] However, these reactions are restricted by the stability of the complexes in a high-temperature medium: they are frequently accompanied by the decomposition of the coordination compounds and reactions of the ligand systems (see, for example, Domrachev and Zinov'ev's review[15]). For this reason, greatest effectiveness is attained in gas-phase synthesis when metal and ligand vapours are condensed at low temperatures (cryosynthesis).[13-15,25,26,30,31] The range of working temperatures is usually from 10 to 273 K although in isolated instances both high (295 – 325 K)[37-39] and low (~4 K)[40] temperatures have been used.

Cryosynthetic reactions have been considered in reviews[25,41] and in a monograph.[42] It has been emphasised[41] that cryosynthesis involving gaseous metals is an irreversible process, since extremely high supersaturations of the vapour phase with respect to the metal are employed in it. The metal vapour obtained at high temperatures (2000–2500 K) is transported in vacuo as a stream of atoms which react at low temperatures with the condensed ligand phase.

The mechanism of the co-condensation of atomic metals with ligand systems has been considered in relation to the direct synthesis and decomposition of dibenzenechromium.[15] It was shown that the reactions occurring with formation of dibenzenechromium from gaseous chromium and solid, liquid, or gaseous benzene at 77, 298, and 1000 K respectively are thermodynamically allowed. The elementary steps in the synthesis–decomposition reactions of diarene complexes have been considered in two publications.[43,44]

The apparatus for the direct synthesis of metal complexes in the gas phase is on the whole simple in design, since it comprises the usual high vaccum systems.[15,45,46] Different versions of the apparatus differ as regards different solutions of the problem of the evaporation of the metal and of the supply of the ligand to the reaction chamber.

The technology of the vaporisation of metals has been developed quite satisfactorily. This process is achieved mainly by four methods:[15] (1) from a resistively heated evaporator; (2) as a result of the induction heating of the container with the metal; (3) by electron bombardment; (4) by exposing the metal specimen to a laser beam. The advantages and disadvantages of each of the above methods of preparation of metal vapours and the procedures for the supply of ligands to the reaction chamber and for the isolation of the coordination compounds formed in the direct syntheses have been considered.[15] The vaporisation methods indicated make it possible to obtain virtually all the metals of the Periodic System,[13–15,26] including refractory metals (chromium, molybdenum, and tungsten),[14,15,30,31,34,47–50] in the vapour phase.

Organic systems, mainly unsaturated, aromatic, and heteroaromatic compounds and their derivatives, are used as the ligands in the gas-phase synthesis. Taking into account the maximum possible number of electrons which a ligand of the unsaturated hydrocarbon type can give up to the metal, it is useful to differentiate among such ligands monoalkenes,[14,15,26,37–40] dialkenes,[14,15,26,30,51–54] and cyclic dienes[13–15,26,51,55–57] and trienes.[57] Ethyne and its derivatives are also used as ligand systems.[14,15,20,26,37,53,54] Aromatic hydrocarbons, especially benzene and its derivatives,[14,15,47–49,58–62] as well as heteroaromatic ligand systems such as thiophene[26] and pyridine[15,17,26,30,63] are most widely used among the ligands for the gas-phase synthesis of coordination compounds.

Apart from the compounds listed above, oxygen-containing organic derivatives are used as ligands—ethers,[26] ketones (especially acetone),[53,64] β-diketones,[15,35,36] organic acids,[15] and their anhydrides[15] and chlorides.[14]

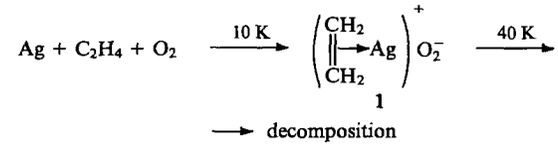
Two types of reactions occurring in the gas phase with formation of metal complexes have been differentiated[15]—reactions involving the addition of metal atoms and reactions involving the insertion of metal atoms in a C–X bond (X = H or a halogen).[15] The first embrace a wide range of the ligands listed above and comprise reactions leading mainly to the formation of π-complexes. Reactions of the second type are accompanied by the formation of organometallic compounds with metal–carbon σ-bonds.[15,25,26,31,32,65]

2. Coordination compounds

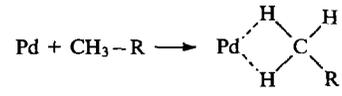
a. Gas-phase synthesis of π-complexes

The metal complex compounds obtained by gas-phase synthesis comprise mainly two types: π-complexes and metal chelates.

The simplest π-complexes have been synthesised by the reaction of metal vapours with alkenes (monoalkenes). The co-condensation of silver and ethene vapours in the presence of oxygen at 10 K leads to an unstable ethenesilver complex **1**, which decomposes on heating to 40 K.[26]

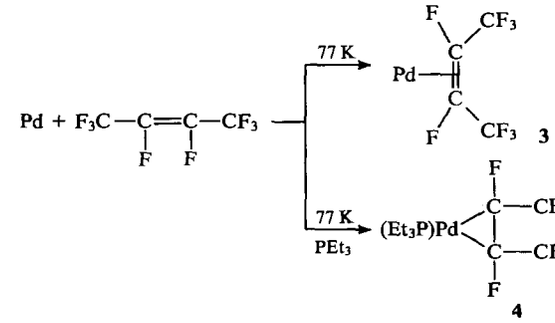


The ethene complexes of copper (argon, 295 and 325 K, pressure 50–600 Torr),[37] nickel (helium),[40] and palladium (helium, 300 ± 5 K, 0.5–0.8 Torr)[38] have been described. The kinetics of the gas-phase reactions of neutral transition metal atoms with alkenes have been investigated in relation to interactions of yttrium, molybdenum, zirconium, and niobium with ethene, propene, butene, and isobutene.[39] The effective rate constants for the above reactions have been found (helium, 300 K, 0.5–0.8 Torr) and it has been shown that under these conditions yttrium, zirconium, and niobium react rapidly with the above alkenes, while molybdenum reacts slowly.[39] Kinetic data indicating the interaction of monoalkenes with 3*d* and 4*d* metals have been published.[38,40,53] Thus the syntheses of scandium, titanium, vanadium, and nickel complexes of alkenes have been reported.[38] The same communications give the effective rate constants for the interaction of nickel and palladium with ethene, propene, and but-1-ene at a pressure of 0.5–0.8 Torr in helium. The formation of stable adducts of palladium with alkanes, to which the structure of the donor–acceptor π-complexes **2** has been attributed, is especially emphasised. These complexes do not fit within the framework of the ideas concerning the usual π-complexes.

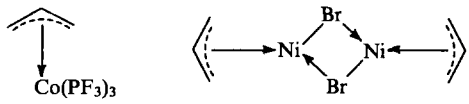


2

The interaction of ethene with iron results in the formation of 1 : 1 adducts,[53] while its interaction with copper affords 1 : 2 adduces.[37] The copper complex has been characterised thermodynamically. It is noteworthy that there are no X-ray diffraction data in the literature for the metal complexes with alkenes obtained by gas-phase synthesis. Therefore the ideas developed by Caroll et al.[39] and the schematic donor–acceptor model of the metal–alkene bond put forward by them are useful for the understanding of the mode of coordination of the metal in the alkene complexes. The σ-interaction makes a significant contribution to this bond. The interactions, not only with alkenes but also with their halo-derivatives, lead to π-complexes. Thus a reaction in which the coordination compound **3** is formed from perfluorobutene has been described in a monograph.[26] The same process in the presence of triethylphosphine leads to the σ-complex **4**.[14,15] However, the structures of complexes **3** and **4** cannot be regarded as rigorously demonstrated.

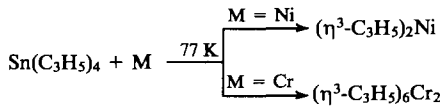


Gas-phase reactions of alkenes and haloalkenes with metals, accompanied by the formation of π-allyl complexes, are known. In particular, the interaction (at 77 K) of propene with atomic cobalt in the presence of phosphorus trifluoride results in the formation of the π-allyl complex **5**.[26,30] The reaction of bromopropene with atomic nickel at 77 and 298 K leads to the bisallyl derivative **6**.[26]



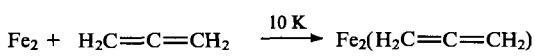
5 **6**

Organometallic compounds can serve as sources of the allyl ligand, which is indicated by the formation reactions of the π-allyl complexes of nickel and chromium.[15,26]

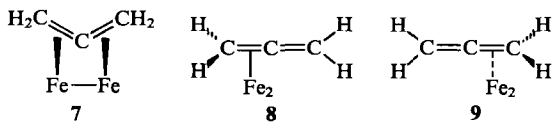


Acyclic diene hydrocarbons form in the gas phase a series of π-complexes in which the unsaturated ligands function predominantly as η^4-donor molecules.[14,15,17,26,30,51-53,66] The main bulk of these complexes have been synthesised from buta-1,3-diene, for which five types of coordination compounds have been differentiated. These have the compositions with metal : diene ratios of 1 : 1, 1 : 2, and 1 : 3 and also metal : diene : another ligand (L) = 1 : 1 : L_n and 1 : 2 : L_n, where L = CO, PF_3, or PR_3. According to Mitchell and Hackett's data,[53] the 1 : 1 complexes are formed in the reaction of buta-1,3-diene with iron at room temperature and a pressure of 100 Torr, while the 1 : 1 : L_n complexes are produced in the reaction of the above diene and trimethyl phosphite.[15] For cobalt and iron, there is a possibility of the formation of 1 : 2 coordination compounds.[15,26] The commonest type of the 1 : 2 : L_n complexes includes those of iron,[14,15,51] cobalt,[15,66] chromium,[14,67] and ruthenium.[52] In particular, ruthenium forms the stable adducts $Ru(\eta^4\text{-}C_4H_6)_2L$, where L = PF_3, CO, and Bu^tNC.[52] The 1 : 3 complexes (M = Mo, W)[15,66] have been characterised by X-ray diffraction. These data indicate equal distances between the molybdenum and tungsten atoms and all the carbon atoms of the butadiene ligand.

The photochemical cryosynthesis of iron complexes with allene in solid argon (10 K) takes place in an unusual manner.[54] The formation of dinuclear iron π-complexes in this process has been detected by Fourier IR spectroscopy.[54]

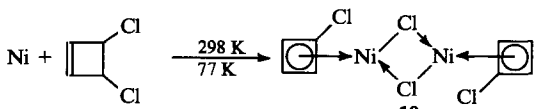


A structure described by formulae **7**–**9** has been proposed for these π-complexes.



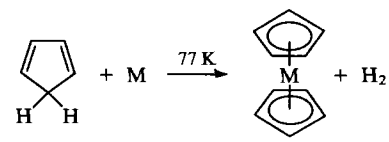
7 **8** **9**

The complexes of cycloalkenes occupy an important place among the coordination compounds synthesised in the gas phase from atomic metals.[14,15,26,50,55,57] The cyclobutadiene complexes are represented by compound **10**, which has been obtained as a result of the following reaction:[26]



10

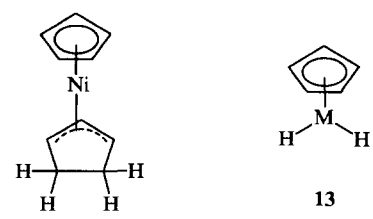
The greatest number of η^5-coordinated complexes having the general formula **11** have been synthesised from cyclopentadiene and its substituted derivatives.[14,15,20,50,55,57,68] During the reaction, the hydrogen atoms are substituted by the metal and the ligand system is aromatised.



11

M = Co, Fe, Cr, Mo, W.

When atomic nickel is introduced into the process under consideration, the cyclopentadienyl ligand rings undergo intramolecular dehydrogenation-hydrogenation, the product of which is complex **12**.

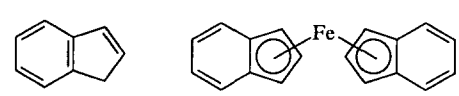


12 **13**

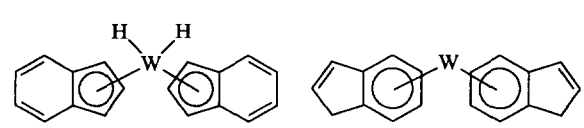
M = Cr, Mo, W.

When cyclopentadiene interacts with atomic chromium, molybdenum, or tungsten, the monocyclopentadienylmetal hydride complexes **13** are formed.[14]

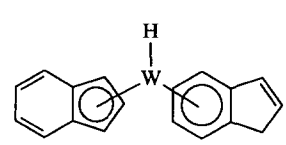
The reactions of indene **14** with iron and tungsten lead to complexes **15**–**18**, a characteristic feature of which is unusual bond isomerism due to the involvement of the cyclopentadienyl and benzene rings in coordination.[26]



14 **15**



16 **17**



18

This interesting phenomenon has been considered in relation to a limited number of systems and its causes are still not clear.

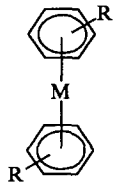
Mixed-ligand carbonylcyclopentadienyl $[C_5H_5M(CO)_2]$, cyclopentadienylpentamethylcyclopentadienyl $(C_5H_5MC_5Me_5)$, and cyclopentadienylethyne $[C_5H_5M(C_2H_2)_2]$ complexes of rhodium and iridium are known.[56]

The π-complexes of cyclohexa-1,3-diene (CHD) and cycloocta-1,3- and 1,5-dienes (COD) have been obtained by gas-phase synthesis with participation of atomic metals.[15,26,57] The complexes formed in these reactions have the compositions MLL'_n, ML_2, ML_2L', where L = diene, L' = H, CO, PF_3, PR_3, $Ph_2PCH_2CH_2PPh_2$, or BuNC, and M = Fe, Cr, or Mn.

The complex $Mn(\eta^4\text{-}1,3\text{-}CHD)_2CO$ has been obtained by condensing atomic manganese with cyclohexa-1,3-diene at 77 K and subsequent heating of the condensate to 293 K.[57] Its structure was demonstrated by X-ray diffraction and is therefore not open to doubt.[57] The manganese complexes of cycloocta-1,3-diene $Mn(\eta^5\text{-}C_8H_{11})(CO)_3$ and $Mn(\eta^3\text{-}C_8H_{13})(CO)_4$, in which the ligand system has undergone dehydrogenation-hydrogenation, have been synthesised under the same conditions.[57] The cocondensation reactions of cycloocta-1,3-diene and cycloocta-1,5-diene with metals have been considered in detail in a review[15] and in a monograph.[26] (New publications concerning ligands of this type have not appeared.) Among the results quoted in the above review,[15] the fact that cycloocta-1,3-diene isomerises, on formation of a complex with chromium, to the 1,5-diene ligand system is of greatest interest. X-Ray diffraction showed that the structure of the complex $C_8H_{11}Cr(PF_3)_3H$ is the same as that of (η^4-cyclooctadienyl)hydridotris(trifluorophosphine)chromium.

There are relatively few data on the gas-phase synthesis of π-complexes of cyclotrienes. However, there are no obstacles to such synthesis being achieved: the complexes $[Mn(\eta^4\text{-}C_7H_8)_2CO]$ and $[Mn(\eta^5\text{-}C_7H_9)(CO)_3]$ have been obtained (cryosynthesis at 77 K) from cycloheptatriene (C_7H_8), although the yield was low (5%–8%).[57]

The use of the aromatic benzene system (formally the hexatriene) system, benzene homologues, and substituted benzene derivatives as the ligands has led to extensive possibilities for the gas-phase synthesis of various arene π-complexes. At the present time, arene π-complexes, the structure of which is described predominantly by formula **19**, have been obtained under the conditions of gas-phase synthesis with virtually all transition metals and a wide variety of aromatic η^6-ligand systems.



19

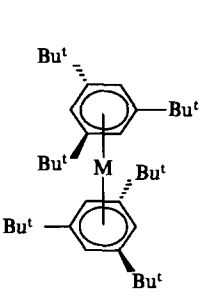
Early publications on the gas-phase synthesis, properties, and structures of type **19** complexes have been surveyed in reviews[13–15,30,47] and in a monograph.[26] Special mention should be made of communication ref. 48 in which 38 diarene sandwich complexes of type **19** (R = F, Cl, CF_3, Alk, OAlk, $NAlk_2$, COOAlk), obtained by the co-condensation of the metal and the ligands at 77 K and a pressure of 5×10^{-4} Torr, have been described. The complexes have been characterised by ^{13}C NMR spectroscopy and their comparative thermal stabilities have been estimated.

A large number of diarenechromium complexes, including those containing fragments coordinatively active in relation to the metal indicated (the phosphorus atom and the C≡C and C≡N bonds) as well as polynuclear aromatic compounds, have been described in a review.[47]

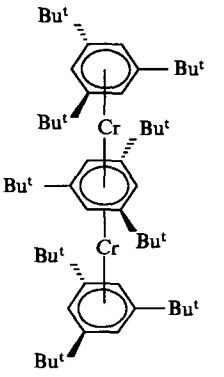
A series of π-complexes containing substituents such as ferrocenyl (yield 1%),[69] PrCO (4%), CH_2Ph (48%), and CH_2CH_2OH (5%) [70] have been obtained.

When the vapours of atomic yttrium, titanium, hafnium, niobium, chromium, molybdenum, and tungsten were heated with 1,3,5-tri-*tert*-butylbenzene, the diarene complexes $M[\eta^6\text{-}C_6H_3Bu^t_3]_2$ **20** were obtained.[59–61] The reactions take place at 77 K and the product yields are 20% (M = W), 30% (M = Cr, Mo), and 40% (M = Y, Ti, Zr, Hf).

In the case of chromium, the triple-decker complex **21** $Cr_2[\eta^6\text{-}C_6H_3Bu^t_3]_2[\mu\text{-}\eta^6 : \eta^6\text{-}C_6H_3Bu^t_3]$ is formed together with the diarene compounds **20** (yield 2%).[61] Reactions of zirconium and hafnium in the presence of carbon monoxide lead to the

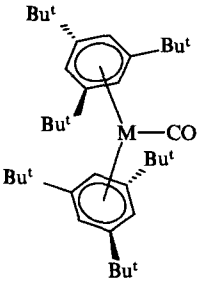


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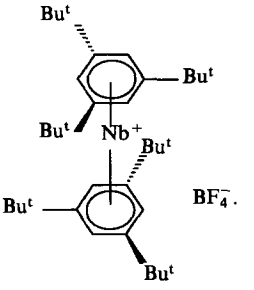


21

stable 18-electron zirconium adduct **22** and the analogous relatively unstable hafnium complex. The reaction of complex **20** (M = Nb) with $AgBF_4$ in toluene is accompanied by the formation of a tetrafluoroborate complex containing the stable 16-electron cation **23**.



22 (M = Zr, Hf)



23

The structures of complexes **20**–**23** have been demonstrated by mass spectrometry and ^1H NMR spectroscopy.[61] The yttrium complex **20** is interesting because it is paramagnetic ($\mu_{ef} = 1.74\ \mu_B$ at room temperature) and gives rise to clear-cut EPR signals in methylcyclohexane solution at 77 K; $g_{\|} = 2.085$ (doublet), $g_{\perp} = 2.005$, and $A = 3.0$ mT for ^{89}Y. X-Ray diffraction studies showed that the complex contains parallel benzene rings and is the first representative of η^6-coordination compounds of zero-valent yttrium.[60]

The chromium complex **19** with a dialkylamino-substituent (R = NMe_2) has been known for more than 20 years[15,48] and its structure has been demonstrated by X-ray diffraction.[71] However, the analogous complex with aniline could not be obtained for a long time. The complex **19** [R = $N(SiMe_3)_2$] has been obtained recently[49] by the co-condensation of chromium with bis(trimethylsilyl)aminobenzene at 77 K. After treatment with tetrabutylammonium fluoride trihydrate in tetrahydrofuran (THF) at 298 K, it affords the dianilinechromium complex **19** (R = NH_2). The reaction described proceeds in accordance with the following scheme:

$$Cr + 2\,PhN(SiMe_3)_2 \xrightarrow[\text{co-condensation}]{77\ K} \longrightarrow \mathbf{19}\,[R = N(SiMe_3)_2] \xrightarrow{Bu_4NF \cdot 3H_2O} \mathbf{19}\,(R = NH_2).$$

Complex **19** (R = NH_2) with $T_m = 501$ K has been characterised by elemental analysis, ^1H and ^{13}C NMR, and mass spectrometry and its reduction potential and Brønsted basicity have been investigated. It is striking that, in the interaction of di(π-aniline)chromium and its π-*N*,*N*-dimethylaniline analogue with HBF_4 in ether, the nitrogen atoms are protonated.

Diarenemetal π-complexes which had not been introduced previously into the reactions of the type considered, in particular those of titanium, have been synthesised.[49,72] Thus complex **19** (M = Ti, R = Et) has been obtained in ~100% yield by the reaction with ethylbenzene at 77 K in vacuo.[72] The study of the properties of η^6-naphthalenechromium complexes showed that a series of coordination compounds having the general formula (η^6-arene)CrL_3, where arene = $C_{10}H_8$, $C_{10}H_7Me$, or $C_{10}H_6Me_2$ and L = CO, PMe_3, $P(OMe)_3$, or PF_3, have been obtained, in addition to di(η^6-naphthalene)chromium(0), on co-condensation of the metal and naphthalene or its methyl derivatives (L) at 193 K. The complexes have been characterised by ^1H NMR. It is emphasised that atomic chromium interacts with 1,4-dimethylnaphthalene stereospecifically, forming predominantly (up to 95%) the isomer in which the metal is bound to the unsubstituted aromatic ring.

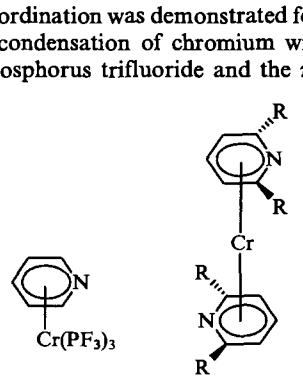
Numerous studies have been devoted to the stabilities, physicochemical properties, and structures of the diarene complexes obtained by gas-phase synthesis (see, for example, Refs 13–15, 26, 30, 49, and 71). The synthesis and decomposition of the diarene complexes have been considered in two investigations.[74,75] The possibility of employing the additivity method to calculate the ΔH for the vapours of the diarene complexes has been demonstrated.[76] Electronic[77,78] and fluorescence[79] spectra of the molybdenum complexes have been obtained and interpreted. The oxidation–reduction properties of the diarene derivatives of zerovalent metals have been investigated.[80]

Apart from the diarene compounds of types **19**, **20**, **22**, and **23**, the monoarene complexes **24** and the cyclopentadienylarene complex **25** have been obtained by gas-phase synthesis.[14,15]



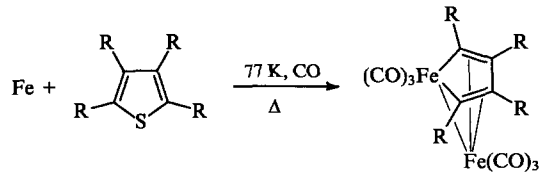
24 (L = PF_3) **25**

Complexes of heteroaromatic systems, obtained by gas-phase synthesis, are represented by the π-complexes of pyridine and its *C*-methyl substituted derivatives. The possibility of the involvement of the heteroaromatic π-system of the pyridine ring in coordination was demonstrated for the first time in relation to the cocondensation of chromium with pyridine in the presence of phosphorus trifluoride and the π-complex **26** was obtained.[30]



The low-temperature interaction of atomic chromium and 2,6-dimethylpyridine led to the sandwich π-complex bis(2,6-dimethylpyridine)chromium **27** (R = Me).[63] Its structure was demonstrated by X-ray diffraction.[81] When trimethylsilylpyridine derivatives were used in the same synthesis, it was possible to obtain di(η^6-pyridine)chromium **27** (R = H).[82] We emphasise that none of the di(η^6-pyridine)metal complexes can be obtained in the usual way.[83,84]

It has been shown in a review[85] that thiophene does not react with zerovalent metals, but a reaction accompanied by the desulfurisation of the heterocycle is known.[26]



This finding indicates a radical rearrangement of the thiophene system during the complex formation reaction. It must be taken into account in the further studies of the gas-phase syntheses of metal complexes with participation of heteroaromatic systems, the π-donor activity of which is not open to doubt.[85–87]

It has been shown in a review[15] that the gas-phase synthesis with participation of zerovalent metals and alkynes leads mainly to the trimerisation of the ligand systems with formation of benzene and its substituted derivatives. This is also confirmed by the data compiled in a monograph.[26] At the same time, a reaction indicating the formation of metal complexes with alkynes is presented in the same communication.

$$Fe + Me_3Si-C\equiv C-SiMe_3 \xrightarrow{77\ K} Fe(Me_3Si-C\equiv C-SiMe_3)$$

The possibility of obtaining the metal complexes of alkynes in atomic syntheses has been confirmed also in subsequent publications.[20,37,53,54,88] When nickel,[88] iron,[53] and copper[37,88] are co-condensed with ethyne at 10 K, the complexes $M(\pi\text{-}C_2H_2)_n$, where $n = 1, 2$, are formed. It is striking that the iron complex with methylethyne having the same composition has been obtained in the reaction of allene with iron at 10 K (argon, irradiation with visible light).[54] The reaction takes place in accordance with the following scheme:

$$Fe + H_2C{=}C{=}CH_2 \xrightarrow{h\nu} Fe(HC\equiv C-CH_3).$$

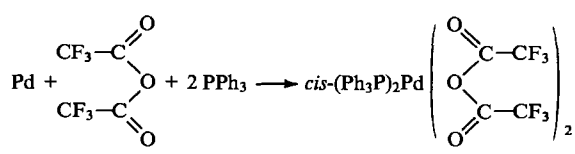
The last compound is converted into the σ-complexes $H-Fe-C\equiv C-CH_3$ and $H_3C-Fe-C\equiv CH$ on irradiation with UV light.[54]

It was shown above that the mixed-ligand complex $C_5H_5Mn(HC\equiv CH)_2$ is formed on interaction of ethyne, cyclopentadiene, and manganese under the conditions of cryosynthesis.[56]

The complexes obtained in gas-phase syntheses from atomic metals and oxygen-containing ligands are represented by a relatively small number of examples. Aromatic alcohols, ethers, ketones, and acids behave as the usual η^6-arene ligands, forming substituted di(η^6-arene)metal complexes of type **19** (R = CH_2CH_2OH,[70] OAlk,[14,15] COAlk,[70] or COOAlk,[15] where Alk = Me or Pr). Alcohols form metal alkoxides in the gas-phase synthesis. Stable complexes giving rise to colloidal systems in nonaqueous solutions with a particle size of ~8 nm have been obtained from acetone and atomic palladium. It has been suggested[64] that the following reaction involving the addition of the metal to the ketone takes place:

$$n\,Pd + x\,Me-\overset{\overset{O}{\|}}{C}-Me \xrightarrow{77\ K} Pd_n\left(Me-\overset{\overset{O}{\|}}{C}-Me\right)_x.$$

However, the structures of the reaction products formed have not been studied in detail. An addition reaction also takes place between palladium and trifluoroacetic acid anhydride in the presence of triphenylphosphine.[15]



At the same time, it is known[14] that the interaction of carboxylic acid chlorides with atomic palladium in the gas phase leads to insertion products of the metal in the C–Hal bond.

An example of such a reaction is presented below:

$$Pd + RCOCl \longrightarrow RCOPdCl$$

$R = CF_3$, C_3F_7.

The data presented in this section indicate the extensive possibilities of gas-phase synthesis in the preparation of diverse metal π-complexes.

b. Gas-phase synthesis of metal chelates

The metal chelates synthesised in the gas phase belong mainly to a single class of complexes — transition and nontransition metal β-diketonates. This is due to the high stability of β-diketones and β-diketonates under the conditions of the gas-phase synthesis.[15,36]

The gas-phase syntheses of metal acetylacetonates having the general formulae $M(acac)_2$ (M = Mn, Fe, Ni, Pd, Cu, Zn, Sn) and $M(acac)_3$ (M = Cr, Fe, Dy, Ho, Er) were described in early communications (see, for example, Domrachev and Zinov'ev[15]). The yields of the complexes obtained by the co-condensation of the vapours of acetylacetone and the atomic metals indicated varied in the range from 10% to 32% under the conditions of cryosynthesis. However, it was later possible to obtain (see, for example, Mazurenko and coworkers[36]) a series of β-diketonates at temperatures in the range 363 – 543 K (M = Co, Ni, Cu, Cr, Fe, Ti, Hf, Zr) in nearly quantitative yields (90% – 100%). It was emphasised[36] that the direct synthesis is the most promising method for the industrial preparation of β-diketonates. The productivity of the apparatus for the synthesis of the complexes increases sharply when the ligands are employed in the form of aerosols, which makes it possible to introduce appreciable amounts of β-diketones into the reaction zone with the simultaneous regulation of their concentration. Among other studies on these lines, mention should be made of the cryosynthesis of coordination compounds containing radionuclides, in particular ^{63}Ni acetylacetonate.[89]

The possibility of using the gas-synthesis for the preparation of various metal chelates is of interest.[90]

Analysis of the data presented in this section indicates extensive possibilities of the gas-phase synthesis for the preparation of π-complexes with alkene and aromatic ligands. At the same time, examples of the employment of heteroaromatic and chelating ligands in such syntheses are extremely limited and so far do not permit conclusions concerning the prospects for the preparation of metal complexes of heterocycles and inner-complex compounds in gas-phase reactions.

III. Liquid-phase synthesis

The syntheses of coordination compounds from zerovalent metals in the liquid phase comprise reactions of three types — direct interaction of the zerovalent metals and ligands, oxidative dissolution of compact metals in nonaqueous media, and electrosynthesis. Such reactions lead to the formation of predominantly molecular adducts and inner complexes as well as individual π-complexes and polynuclear clusters.

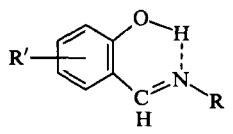
1. Synthesis of complexes by the direct interaction of zerovalent metals and ligands

In contrast to the gas-phase syntheses, this method of direct interaction of metals with ligands does not require special apparatus — the reactions take place under the usual conditions.

The method is used widely for the synthesis of individual types of π-complexes and metal chelates, although it is also possible to obtain other types of coordination compounds. As stated in a review,[17] the method of direct interaction of metals and ligands has been used successfully for the preparation of π-allylpalladium complexes (reaction between bromopropene and palladium at 353 K under a nitrogen atmosphere), the praseodymium complex of cycloocta-1,5-diene (in THF), and cyclopentadienyl derivatives of europium and ytterbium (in liquid ammonia).

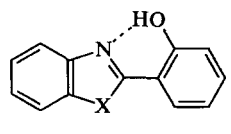
The formation of inner complexes in the syntheses under consideration is difficult mainly due to the chemical inertness of the *d* and *f* metals behaving as complex-forming agents in reactions involving the substitution of hydrogen atoms in the chelating ligands.[3] However, it has been possible to isolate metal chelates in satisfactory yields for individual ligand systems and zerovalent metals. Thus the interaction of acetylacetone with a series of *d* metals (Ti, Mn, Cr, Fe, Co, Ni, Cu, Mo, and Pd) has been investigated and it has been shown that iron forms bis- and tris-acetylacetonates, whereas the remaining metals are passive under an inert atmosphere.

Ligands containing the OH group in the *ortho*-position relative to the C=N group interact extremely effectively with zerovalent metals. Such ligands include salicylaldoxime **28** (R = OH),[17,91] salicylidene-*o*-aminophenol **28** (R = C_6H_4OH-*o*),[92] 2-*o*-hydroxyphenylbenzazoles **29**,[93] 3-hydroxyphenyl-5-R-1,2,4-oxadiazoles **30** (R = Me, Ph, $PhCH_2$),[92,94] 3-*o*-hydroxyphenyl-1,2,4-triazoles **31** (X = NH, NPh), and 3,5-di(*o*-hydroxyphenyl)-oxadiazole **32**.[95]



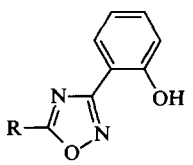
28

R = OH, C_6H_4OH-*o*, Py; R′ = H, OMe



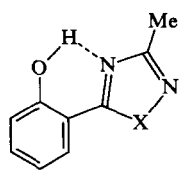
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X = NH, NR′, O, S



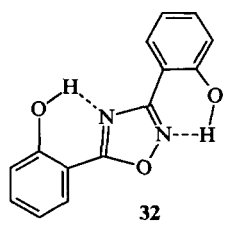
30

R = Me, Ph, CH=CH$_2$



31

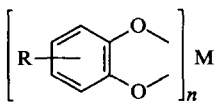
X = NH, NPh



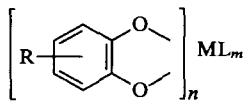
32

The solvents employed in these syntheses were ether, phenol, phenetole, acetylacetone, and dimethylformamide (DMF). The yields of the complexes vary in the range 80% – 100%. The complexes described have the compositions ML_2 [**28**(R = OH) – **31**] and ML [**28**(R = C_6H_4OH-*o*) and **32**] depending on the basicity of the ligands (LH or LH_2). The complexes ML are interesting because they have a dimeric structure (for the ligand **28**) or an oligomeric structure (for the ligand **32**) and are representatives of polynuclear compounds.[29,96,97] The polymeric nature of the complexes from the ligand **32** has been confirmed by magnetochemical[98] and EPR spectroscopic measurements: they indicate the presence in the copper(II) and cobalt(II) complexes considered of exchange-linked ions forming part of the composition of the polymeric coordination structure of the type $LH(ML)_nLH$ ($n = 1, 2, \ldots, \infty$).[95] In the copper complexes investigated, there is an exchange interaction of the antiferromagnetic type with an exchange integral $J \approx -100$ cm^{-1}, whereas in the cobalt coordination polymers ferromagnetic exchange is observed with $J \approx 20 - 30$ cm^{-1}.[95]

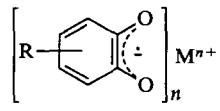
o-Quinones are extremely reactive ligands,[17,99-112] especially those containing *tert*-butyl substituents. Complexes of *o*-benzoquinones, *o*-semiquinones, and catechols of this kind have been obtained. They are radical in nature and play an important role in coordination chemistry.[106-108] In nonaqueous solvents (hexane, dimethoxyethane, toluene, THF, and chloroform), mainly the formation of complexes of types **33**–**36** (R = 3,5- or 3,6-Bu^t_2) has been observed by EPR.



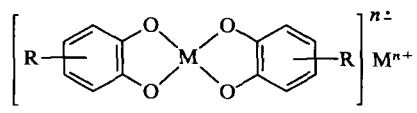
33



34



35



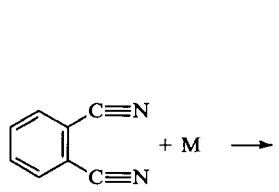
36

The formation of radical *o*-semiquinolates of type **33** has been detected for thallium,[109] indium,[102] zinc,[100,103,110] cadmium,[100,103,110] magnesium,[103] barium,[103] aluminium,[100] gallium,[105] and tin.[99] The adducts **34** are characteristic of copper and silver (L = PPh_3, $m = 2$, $n = 1$)[17] and also of indium (L = phen, m, $n = 1$).[102] Data on the radical-anion salts of types **35** and **36** have been presented in a review[17] and other publications.[99,110] Metal complexes of catechols can be obtained also from tetrahalo-*o*-quinones, for example $Sn(X_4C_6O_2)_2$ (X = Cl, Br).[102]

The data of Ozarowski et al.[103] and Adams et al.[105] are of greatest interest for the study of the properties and structures of type **33** complexes. Magnesium, barium, zinc, and cadmium complexes of 3,5-di-*tert*-butyl-1,2-*o*-benzoquinone (L) and their adducts with pyridine, 2,2′-bipyridyl, and *N,N,N′,N′*-tetramethylethylenediamine(L′), having the compositions ML_2 and $ML_2 \cdot nL'$ ($n = 1, 2$), were isolated preparatively and characterised in the first of these studies. Complexes **33** and their adducts with L′ have been obtained by the reaction of the above zerovalent metals and ligands in toluene; detailed EPR spectroscopic studies confirmed their biradical nature and made it possible to establish the conformations of the biradical ligands. The study of Adams et al.[105] was devoted to the triradical gallium complex of 3,5-di-*tert*-butyl-1,2-*o*-benzoquinone **33** ($n = 3$). This compound was obtained by heating gallium and the ligand in boiling toluene (under an argon atmosphere) and was characterised by X-ray diffraction. The complex has the form of a three-blade propeller with the gallium atom in the centre: the length of the C–C bond between the chelating oxygen atoms is 1.439(12) Å, which indicates the semiquinone nature of the ligands. It is striking that the above value differs little from the length of the same bond (1.433 Å) in the chromium analogue, the structure of which had been characterised previously.[112] The gallium complex **33** ($n = 3$) exhibits ferromagnetic properties; its magnetic moment is 2.95 μ_B at 320 K and 3.58 μ_B at 9 K; it then again decreases and is 3.26 μ_B at 2 K.

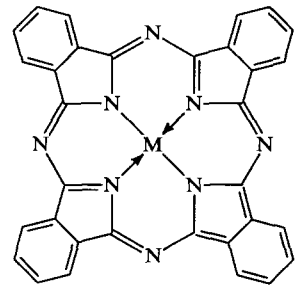
Thus direct evidence for the formation of radical complexes in the reactions of zerovalent metals with *o*-diquinones was obtained in the studies quoted above, methods were developed for the synthesis of these coordination compounds, and the characteristics of their structure and their physicochemical properties were established.

In a number of instances, the interaction of zerovalent metals with the ligand is accompanied by a template reaction, which yields macrocyclic chelates. The template reaction involving the direct synthesis of the macrocyclic phthalocyanine complexes **38** from zerovalent metals and *o*-phthalodinitrile (1,2-dicyanobenzene) **37**, which has long been known, has now become a classical reaction.[9,10,17,113,114]



37

M = Fe, Co, Ni, Cu, Zn, Cd, Sn.



38

The phthalocyanine complexes **38** are formed in high-boiling solvents — α-methyl- and α-chloro-naphthalene, *o*-dichloronitro- and trichloro-benzene, and quinoline. Apart from the ligand **37**, *o*-cyanobenzamide, phthalimide, and diiminoisoindoline have been introduced into this reaction.[17,113]

In conclusion of this section, we may note that molecular complexes are formed on direct interaction of metals and ligands.[17] Such complexes have been obtained, for example, between alcohols and carboxylic acids, on the one hand, and bases (pyridine, bipyridyl, and phenanthroline), on the other.[115-117]

2. Synthesis of complexes on oxidative dissolution of metals

In contrast to the direct synthesis methods considered above, the oxidative dissolution of metals in the liquid phase, accompanied by the formation of coordination compounds, proceeds in the presence of oxidants.[14,16,17,118-153] The simplest mechanism of this reaction may be as follows:[16]

$$M^0 + Ox \xrightarrow[-ne]{mL} L_mM^{n+} + Red + P,$$

where M is the metal, Ox the oxidant, L the complex-forming agent (ligand), Red the reduced form of the oxidant, and P the products of the interaction of the components of the medium.

The halogens were used as the oxidants in the old investigations (see the literature in the review of Gernovskii et al.[17] and also Kurskov[130]). Later, hydrogen halides[17,126,129,132,138,148-150] and halohydrocarbons[118-120,124-127,131,133,137,148,150] began to be employed widely. This change is not fortuitous — the synthesis of coordination compounds with the aid of hydrogen halides and especially halohydrocarbons takes place in donor–acceptor nonaqueous solvents under mild conditions without the use of corrosive media and special apparatus. Apart from the oxidants investigated, the sulfates, perchlorates, bromates, and chromates of certain metals,[17] mercury chloride,[4] and nontraditional oxidants[4,128] — nitrosonium (NO^+X^-), arenediazonium ($ArN_2^+X^-$), and triphenylcarbenium ($Ph_3C^+X^-$, X = BF_4, ClO_4, PF_6) salts — began to be used in individual syntheses.

Ammonium salts are extremely effective reagents in the synthesis of coordination compounds by the oxidative dissolution of metals.[153-171] A simple and readily applicable method of synthesis of metal complexes based on the following reaction has been developed:[153,156,166,169]

$$M^0 + m\,NH_4X + n\,L + \tfrac{1}{2}p\,O_2 \longrightarrow MX_mL_n + m\,NH_3 + p\,H_2O.$$

We may note that metal oxides also enter readily into this reaction.[153,168,169,172-176]

Cobalt,[16,17,119,120,130,155,156,158] nickel,[16,17,120,160,161,164] iron,[16,17,118,120,130,134,145] zinc,[153,159,166,169] and copper[16,17,118,121,123,127,134,135,137,141,142,146,153,159,166,169] are most frequently employed in liquid-phase syntheses. Many studies have been devoted to the dissolution of platinum group metals and the formation in these syntheses of palladium,[16,17,124,129,131,133,134,136,143] platinum,[129,131,133,134] and rhodium[129,131] complexes. Much attention has been devoted to the preparation of gold[132,134,138,148,150] and silver[138,139] complexes in oxidising donor–acceptor media. The preparation of titanium,[119] chromium,[125,134] manganese,[119] cadmium,[163] niobium,[126] tantalum,[126] and europium[128] complexes has been described in individual publications. It has been suggested[117] that lanthanide (Ln) complexes may be formed in the $Ln-PBu_3-CCl_4$ system, but their synthesis has not been described.

Solvents which in the majority of cases are also ligands are represented mainly by compounds with N and O donor atoms such as acetonitrile (AN),[16,17,118,128,129,146] benzonitrile (BN),[130] aliphatic amines (AM),[130,164,166,167,169] pyridine (Py),[16,17,133,178] dimethyl sulfoxide (DMSO),[16,17,118,120,130,138,139,143,146,148–150] dimethylformamide (DMF),[16,17,118,119,124,126,137,146,155,164] formamide (FA), monomethylformamide (MFA), dimethylacetamide (DMA),[121,123,141,145] alcohols,[157,160] and propylene carbonate (PC).[142] Apart from the compounds listed above, azoles,[137] 2,2′-bipyridyl (Bipy),[16,17,121,123,130,142] 1,10-phenanthroline (Phen),[123,131] and adenine[137] function as N donors and urea,[125] pyridine *N*-oxide,[120,133,178] triphenylphosphine oxide,[120,178] dimethylglyoxime,[130,179] and β-diketones[130,151,152,179] function as O donors. Triphenylphosphine has been used as a ligand with a phosphorus donor atom.[130]

The complexes obtained as a result of the oxidative dissolution of zerovalent metals include all types of complexes,[17] but their proportions are very different.

A single example of a π-complex, obtained by the oxidative dissolution of zerovalent copper in the $1,5\text{-COD}-DMF-CCl_4$ system, is known. In the complex $[Cu(COD)Cl]_2$ synthesised, copper is stabilised in the lowest oxidation state (+1) by the soft cyclooctadiene ligand system, which is confirmed by the diamagnetism of the complex considered.[16,179] This result agrees with the familiar postulate that, within the framework of the principle of hard and soft acids and bases (HSAB), soft bases (ligands) stabilise the lowest oxidation states of the complex-forming agents.[180]

There have also been only a few dinuclear and polynuclear complexes synthesised in oxidative systems.[16,17,118,123,141,171,181]

The main bulk of the complexes obtained by the method considered are molecular complexes and metal chelates.

a. Synthesis of molecular complexes

In conformity with the approach proposed in the review of Lavrent'ev and Khidekel',[16] it is possible to differentiate two types of compounds among molecular complexes — neutral and ionic. The former include, for example, adducts having the general formula MX_mL_n, where M = Co,[16,178] Cr,[125] Ni,[16,178] Fe,[118,178] Cu,[16,118,137,146,178] Pd,[131,133,146] Pt,[131] Rh,[131] Zn,[159,166,169] Cd,[163] Au,[132,148,150] Ag,[138] MoO_2,[16] WO_2,[16] and Eu,[128] L = DMSO,[16,17,118,146,148–150] DMF,[16,17,118,137,146] DMA,[16] AN,[16,17,118,128,146] Py,[133,177] Py–O,[133,178] and Ph_3PO,[177] X = Cl, Br, NCS, and BF_4, and *m*, *n* = 1–3. Coordination compounds of the second type are represented by complexes of the following metals: iron complexes[16,17,118] — *cis,trans*-$[Fe^{III}(DMF)_nCl_2].[Fe^{III}Cl_4]$, (*n* = 3, 4), *cis*-$[Fe^{III}(DMSO)_4Cl_2]Cl$, *cis*-$[Fe^{III}(DMSO)_4Cl_2][FeCl_4]$, $[Fe^{III}(DMSO)_5Cl][FeCl_4]_2$, $[Fe^{III}.(DMSO)_5Cl][Fe_2Cl_6O]$, $[Fe^{II}(AN)_6][Fe^{III}Cl_4]_2$, and $[Fe^{II}.(BN)_6][Fe^{III}Cl_4]_2$; copper complexes[146] — $[Cu^{I}(AN)_4]BF_4$, $[Cu^{I}(Me_3S)_3]I_4$, $[Cu^{II}(DMSO)_5](BF_4)_2$, $[Cu^{II}(DMSO)_4(AN)_2].(BF_4)_2$, $[Cu^{II}(DMSO)_4DMF\cdot AN](BF_4)_2$, and $[Cu^{II}(DMSO)_4.AN\cdot H_2O](BF_4)_2$; cobalt complex[16] — $[Co^{II}(DMSO)_6][Co^{II}Cl_4]$; chromium complex[125] — $[NH_2Me_2][CrCl_6]Cl$; palladium complexes — $[NH_4]_2[PdCl_4]$,[129] $[NH_2Me_2]_2[PdBr_4]$,[124] $[NH_2Bz_2]_2.[PdBr_4]$,[124] $[NHMe_3]_2[PdBr_4]$,[133] $[Me_3NOH]_2[PdBr_4]$,[133] $[(PyO)_2H]_2[Pd_2Cl_6]$,[133] and $[PdL_2Br_2][PdBr_4]$ (where L = Ph_3BuP);[131] platinum complexes[129] — $[NH_2Me_2]_2[PtCl_6]$ and $[PtLBr_2][PtBr_4]$; rhodium complexes — $[NH_2Me_2]_4.[RhCl_6]Cl$,[129] $[PyH][RhPy_2Br_4]$, $[Ph_3BuP][Rh(CO)_5Br_4]$,[131] and $[Ph_3BuP][Rh(CO)Br_4(EtOH)]$;[131] titanium complex[126] — $[NH_2Me_2]_4[TiOF_4][TiF_6]\cdot HF\cdot H_2O$; zirconium complex[126] — $[NH_2Me_2]_2[ZrOF_4]\cdot 2HF$; niobium complex[126] — $[NH_2Me_2]_2.[NbOF_5][NH_2Me_2F]\cdot 4HF$; tantalum complex — $[NH_2Me_2].[TaOF_5][NH_2Me_2]\cdot HF$; gold complexes[148,150] — $[Me_3S].[AuBr_4]$, $[Me_3S][AuBr_4(Me_2S)]\cdot H_2O$, $[Me_3SO][AuBr_4]\cdot H_2O$, $[Me_2BuSO][AuBr_4]\cdot H_2O$, $[Me_3S]_2[Au_2Br_8]\cdot 2DMSO\cdot H_2O$, and $[Me_3S][Au_2Br_7(Me_2S)]\cdot 3H_2O$; silver complex[139] — $[Me_2S^{+}CH_2.COR][AgX_2]^{-}$.

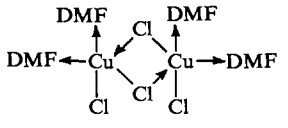
The structures of the dimethyl sulfoxide complexes indicated above have been investigated by X-ray diffraction (see the references in the paper of Lavrentiev et al.[118]).

The above complexes are interesting not only because of their unusual composition but also because in some of them the complex-forming agents are in different oxidation states (for example, in the iron complexes). Another characteristic feature of the complexes obtained in donor–acceptor oxidative systems is the stabilisation in them of uncharacteristic oxidation states of the metals. Thus, together with the usual oxidation states of the metals, in particular +1 and +2 for copper, diamagnetic § Cu(+3) complexes are formed in the $Cu-DMSO-CCl_4-TU$ system (TU = tetramethylthiuram disulfide) according to Shirshova et al.[142]

It is believed[143] that the use of the same system in the case of palladium leads to intermediate univalent palladium complexes. Oxidation of zerovalent gold by hydrogen chloride or bromide in DMSO led to the isolation of univalent and trivalent gold complexes — $[(Me_2S)AuBr]$ and $[(Me_2S)AuBr_3]$.[132,148,150] We emphasise that trivalent copper and gold complexes as well as univalent palladium complexes are encountered comparatively rarely.

It has been emphasised in a review[16] that the complexes considered can contain as ligands both the components of the reaction mixture (solvents, additional ligand systems) and the products of the reactions of these components. This postulate was clearly confirmed when amides[16,118,123,141,179] and sulfoxides[132,144,148–150] were employed as the ligands. Diverse complexes are formed in M^0–amide–Ox systems, the nature of which is determined by the nature of the amide ligand, the metal, and the oxidant. It has been shown in the above review[16] (see the references therein) that complexes with transformed ligand fragments — $[(Me_2NCH)_2CH].[Fe^{III}(DMF)_6][Fe^{III}Cl_4]_4$ and $[MeNH_3]_4[Fe^{II}Cl_6]\cdot H_2O$ — have been isolated from the $DMF-Fe-CCl_4$ system and characterised. The reaction proceeds with dissociation of the bonds in the DMF molecule: N–CH_3, NC–O, and N–CHO.

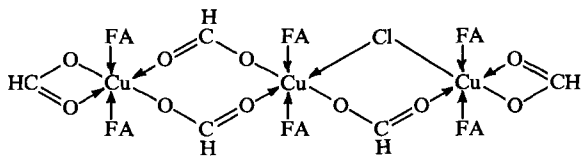
Amides behave similarly in the oxidative system containing copper and CCl_4: apart from the isolation and structural characterisation of complex **39** with the unchanged DMF ligand, complexes with a significantly modified ligand system are formed.



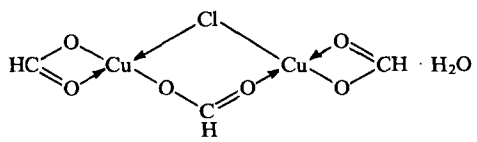
39

§ However, diamagnetism does not constitute incontrovertible proof of the oxidation state of copper, since there are quite a few paramagnetic compounds among trivalent copper complexes.[3] The Cu^{3+} ion has the d^8 electronic configuration, like Ni^{2+}.

For example, formamide (FA) gives rise to three types of complexes in the same system:[141] $[Cu(HCOO)_2(FA)_2]$, $[Cu_3Cl.(HCOO)_5(FA)_6]$, and $[Cu_2Cl(HCOO)_3].H_2O$, while methylformamide[141] gives rise to the tetrameric cluster $[(MeNH_3).Cu(HCOO)_3]_4$. The complex $[Cu(HCOO)_2(FA)_2]$ has also been obtained by dissolving copper in formamide in the presence of atmospheric oxygen and α,α′-bipyridyl.[123] On the basis of X-ray diffraction data, a polymeric structure was attributed to it and it was demonstrated that it belongs to the class of network carboxylates. The copper atom, which occupies the centre of inversion, coordinates the oxygen atoms of two formamide molecules and four formate groups. The coordination polyhedron is a tetragonal bipyramid. In the formate group and in the formamide molecule, the bond lengths are close to the standard values. In the tetrameric compound $[(MeNH_3)Cu(HCOO)_3]_4$, the individual formatocuprate anionic fragments are linked by NH...O hydrogen bonds to the methylammonium cations.[141] The N...O distance is 2.81 Å. The structures of the complexes $[Cu_3Cl(HCOO)_5(FA)_6]$ and $[Cu_2Cl(HCOO)_3]\cdot H_2O$ can be represented by formulae **40** and **41** respectively.



40



41

The formation of copper formate complexes in the Cu–FA(or MFA)–CCl_4 systems has been accounted for by the hydrolysis of formamide and methylformamide under the copper oxidation conditions in the presence of CCl_4.[141]

Analysis of the data presented shows that the compositions of the complexes formed on oxidation of zerovalent copper in the CCl_4–amide system are determined mainly by the nature of the amide ligand: complexes of the type $[Cu_nCl_{2n}(DMF)_m]$ are formed in the case of DMF, whereas FA and MFA hydrolyse and the products of their hydrolysis behave as ligands. Furthermore, the compositions and structures of the complexes formed in the Cu^0–CCl_4–DMF system are influenced by the component ratios:[179] the complex $[CuCl_2(DMF)_2]_2$ was isolated for $[CCl_4]=[DMF] \gg [Cu^0]$, whereas in the case where $[CCl_4] \approx [DMF] \approx [Cu^0]$ the complexes $[Cu_3Cl_6(DMF)_2]$ and $[Cu_4OCl_6(DMF)_6]$ were isolated.

In the DMA–Fe–CCl_4 system, dimethylacetamide gives rise[145] to the complex $[Fe^{II}Fe^{III}_2Cl_8(DMA)_6]$ with an unaltered ligand system. X-Ray diffraction showed that the iron atoms in the crystals of this complex are in typical octahedral and tetrahedral environments in proportions of 1:2. DMA is coordinated via the oxygen atoms. This mode of coordination of the ligand considered follows also from IR spectroscopic data: an appreciable decrease [in the frequency?] of the stretching vibrations of the carbonyl group in the complex (~1600 cm^{-1}) is observed compared with the analogous absorption of free DMA (1655 cm^{-1}). Dimethylformamide undergoes even more prolonged changes in the DMF–Pd–$PhCH_2Br$,[16] DMF–Pt–HCl,[129] and DMF–Rh–HCl[129] systems. Ionic ammonium halide complexes were isolated in all cases—$[Me_2N(PhCH_2)_2][PdBr_4]$, $[H_2NMe_2]_2[PtCl_6]$, and $[H_2NMe_2]_4[RhCl_6]Cl$ respectively. The structures of the complexes described have been demonstrated[129] by X-ray diffraction for the platinum complex and by X-ray diffraction, magnetic susceptibility, and electronic and photoelectron spectroscopic methods for the rhodium complex.

Like DMF, dimethyl sulfoxide forms complexes containing as the ligand system a DMSO molecule[16,17,118,130] and the products of the reaction of this ligand and the oxidant.[132,138,139,143,148–150] As stated above,[16,17,118,130] molecular adducts of DMSO have been obtained in the DMSO–M^0–CCl_4 systems, where M = Fe or Co. In the case of Pd, Au, and Ag, the sulfoxide molecule is deoxygenated and sulfide complexes are formed. The oxidation of palladium in the presence of DMSO and HBr involves the formation of the complex $(Me_2S)PdBr_2$;[16] when CI_4 is used as the oxidant, the complex PdI(MeS).H_2O is obtained.[143] The oxidation of zerovalent gold in the DMSO–RX system (R = H, Bu; X = Cl, Br) is accompanied by the formation of a series of the dimethyl sulfide complexes examined above.[132,148,150] One of the processes occurring in this case is described by the scheme[132]

$$Au^0 + Me_2SO + HBr \xrightarrow[293\ K,\ 72\ h]{} \underset{A}{[(Me_2S)AuBr]} + [(Me_2S)AuBr_3](solution) \xrightarrow{H_2O} \underset{B}{[(Me_2S)AuBr_3]}.$$

The structures of complexes **A** and **B** have been established by X-ray diffraction. It was shown that the crystals of complex **A** contain intermolecular Au...Au chain contacts and intermolecular Au...Br contacts, which build up the square-planar coordination of the gold atoms to a distorted bipyramidal coordination. At the same time, a complex with an unaltered ligand system has been obtained in the DMSO–Au^0–BuBr system—the butyldimethyloxosulfonium salt $[Me_2SO(Bu)].[AuBr_4]$.[148,150] Together with a deoxygenated molecule of the sulfur-containing ligand, the mixed compound $\{[Me_3S]_2[Au_2Br_8].2DMSO\cdot H_2O\}$ contains also DMSO.[148,150]

Silver forms in the same systems the trimethylsulfonium salts $[Me_3S]AgBr_2$ and $[Me_3S]Ag_2X_3$, where X = Br or I.[138] When ketones were added to the reaction mixture, the ionic complexes $[R_2\overset{+}{S}-CH_2COR][AgX_2^-]$ (R = Me, Ph) were synthesised. These are carbonyl-containing sulfonium salts of silver halides. It has been suggested[139] that the above complexes are formed as a result of the condensation of DMSO with the ketones in an acid medium in the presence of silver halides in accordance with the scheme

$$Me_2SO + R'-CH_2COR \xrightarrow[-R'OH]{HAgX_2} [Me_2S^+-CH_2COR][AgX_2^-].$$

The condensation occurred when silver was dissolved in a DMSO–HBr mixture at 333 K for 3 h or after being allowed to stand for two days with subsequent addition of ketones (acetone or acetophenone). Similar complexes, containing iodine as the ligand X, have been obtained in the reaction of $Me_2S.I_2$ with acetone to which AgI and a mixture of hydriodic acid and alcohol had been added or on dissolution of the complex $[Me_3S]Ag_2I_3$ in a DMSO–HI mixture on heating with addition of an alcoholic solution of acetone.[138] The structure of the carbonyl-containing complexes has been demonstrated by X-ray diffraction.

The isostructural compounds with X = Br or I and R = Me contain a chain of the tetrahedral anions $[AgX_4]^-$, in which small differences are observed between the Ag–X bond lengths together with appreciable angular distortions (up to 20°). The structure of the analogous complex with R = Ph and X = Br is made up of the tetrahedral anions $[AgBr_4]^-$ joined together via the common edges of the tetrahedra to give an infinite chain.[139] The proposed mechanisms of the interaction of sulfoxides with

zerovalent transition metals in donor–acceptor media are based on the literature data concerning the chemistry of sulfoxides and the results of studies on the oxidation processes considered.[148–150]

An attempt has been made to describe the mechanism of the oxidative dissolution of metals.[16,17,140,146] It was initially suggested (see the bibliography in the relevant reviews[16,17]) that these processes proceed via the intermediate formation of reactive complexes between the oxidant and the solvent, which possess an enhanced ability to bind the electrons of the metal, facilitating thereby its oxidation. The mechanism of such a process has been tentatively represented as follows:

$$S + A \rightleftharpoons S\cdot A \rightleftharpoons [S^{\delta+}\cdot A^{\delta-}] + M^0 \rightleftharpoons$$
$$\rightleftharpoons M^0[S^{\delta+}\cdot A^{\delta-}] \rightleftharpoons M^+[S\cdot A^-] \rightleftharpoons M^+ + [SA^-] \rightleftharpoons \ldots$$

where S is the solvent and A the oxidant (electron acceptor). The role of the metals and oxygen in the oxidation processes considered has been discussed.[16,17] However, the evidence for the above mechanism is so far inadequate.

The concept of donor–acceptor electron-transport systems (DAETS) is therefore more attractive.[140,146] According to these ideas, dipolar onium compounds, simulating the intermediate products of the DAETS interaction, are formed in oxidising media. The interaction of onium compounds of the type $[Me_2Et\overset{+}{S}=O][BF_4^-]$, $[Me_2N\overset{+}{C}H-OEt][BF_4^-]$, and $[Me_3\overset{+}{S}=O]I^-$ with metallic copper has been investigated to demonstrate the oxidation of metals in nonaqueous media with formation of DAETS.[146] This led to the isolation of a series of complexes containing the metal in the +1 oxidation state—$[Cu^I(AN)_4]\cdot[BF_4]$, $Cu^I[Me_3S^+]_3I_4$, and Cu^IPy—and in the +2 oxidation state—$[Cu^{II}(DMSO)_5][BF_4]_2$, $[Cu^{II}(DMSO)_4(AN)_2][BF_4]_2$, $[Cu^{II}(DMSO)_4\cdot AN\cdot H_2O][BF_4]_2$, and $[Cu^{II}(DMSO)_2\cdot AN\cdot DMF][BF_4]_2$. Mixed-ligand complexes containing DMSO, DMFA, and AN molecules simultaneously have been obtained from a solution of the $[Me_2Et\overset{+}{S}=O][BF_4^-]$–$Cu^0$DMSO DAETS system to which a mixture of DMFA and AN had been added. It is striking that some of the above complexes can be obtained also under the usual conditions involving the oxidative dissolution of copper. The structure of the complex $[Cu^I(AN)_4][BF_4]$ has been established by X-ray diffraction.

The complexes containing DMSO as a ligand are interesting because, as suggested by Epel'baum et al.[146] on the basis of IR spectroscopic data, three types of bonding of the DMSO molecule to divalent copper occur in them—via the oxygen and sulfur atoms and with participation of both donor centres. Since the commonest bonding between Cu^{II} and DMSO involves the coordination of the metal to an oxygen atom,[180] the above results[146] require additional evidence, in particular X-ray diffraction studies of the structures of divalent copper complexes of DMSO.

b. Synthesis of metal chelates

The inner complexes obtained in oxidative donor–acceptor systems in the presence of chelating ligand systems are represented by transition metal acetylacetonates,[16,130,151,179] carboxylates,[152] dimethylglyoximates,[142,143] 8-hydroxyquinolinates,[16,179] and dithiocarbamates.[142,143] The acetylacetonates $Co(acac)_2$ and $Fe(acac)_3$ are formed in the acacH–DMSO–BN oxidative system (where BN = benzonitrile) under a nitrogen atmosphere.[130] Atmospheric oxygen accelerates not only the dissolution of cobalt but also the formation of $Co(acac)_3$. The same complex has been isolated in the presence of triethylamine, which is not coordinated to the metal of the acetylacetonate considered. On the other hand, N donors such as pyridine and α,α′-bipyridyl (L) form with the acetylacetonate the adducts $M(acac)_2\cdot nL$, where M = Co or Fe and $n = 1, 2$. The complex $Cu(acac)_2$, obtained in an oxidative system incorporating a hydrogen halide, has been described.[16,179] The oxidative dissolution of yttrium in systems containing acetylacetone as the main component as well as acetone, ether, dioxane, acetonitrile, pyridine, α,α′-bipyridyl, DMSO, DMF, 2-pyrrolidinone, and acetic acid (AcOH) has been investigated recently.[151] Complexes having the same composition $Y(acac)_3\cdot 2H_2O$ have been isolated from Y–acac–Me_2CO (ether, dioxane, acetonitrile) mixtures. The complexes $Y(acac)_3\cdot H_2O\cdot Py$, $Y(acac)_3\cdot H_2O\cdot\frac{1}{2}Bipy$, $Y(acac)_3\cdot H_2O\cdot DMSO$, $Y(acac)_3\cdot\frac{5}{3}H_2O\cdot\frac{1}{3}DMF$, $Y(acac)_3\cdot\frac{5}{3}H_2O\cdot\frac{1}{3}PC$, and $Y(OAc)_3\cdot 2H_2O$ are formed in the acac–Py (α,α′-Bipy, DMSO, DMFA, PC, and AcOH) systems respectively.

Direct dissolution of zerovalent bismuth and antimony in the presence of an oxidant has been used to obtain the carboxylates of the above metals.[152] The reaction proceeds in accordance with the scheme

$$2M + 6HL + 3[O] \longrightarrow 2ML_3 + 3H_2O.$$

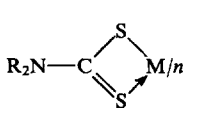
Bismuth formate and acetate (in the presence of atmospheric oxygen or H_2O_2 as oxidants) and antimony acetate and trifluoroacetate (in the presence of nitric acid, acetyl peroxide, or acyl nitrates) have been obtained in this way.

Coordination compounds are readily synthesised in oxidative metal donor–acceptor systems when dimethylglyoxime is used as the ligand.[16,17,130,179,182] Dimethylglyoxime is a classical chelating ligand.[3,12] Inner complexes of the type ML_2, where LH = dimethylglyoxime (DGl) have been obtained from it. However, the use of the method involving the oxidative dissolution of metals makes it possible to obtain not only the complexes ML_2, but also $MX_n(LH)_m$ and $MX_{n-p}(LH)_mL_p$. In addition, the mixed-ligand complexes $MX_n(LH)_m\cdot p$Solv, where Solv = DMSO or DMF, are known. A complex of the first type is formed in the Ni^0–LH–AN–CCl_4 system.[179] Coordination compounds of the second type are represented by the complexes [CuCl.LH] obtained in the Cu^0–LH–EtOH–CCl_4 system;[17,179] compounds of the third type comprise the complexes $[CoX_2(LH)L]$, where X = Cl, Br, or I.[130,179,182] Their formulae have been expressed in the form $H[CoX_2L_2]$. One of the complexes of this type described (X = Cl) is diamagnetic,[179] which indicates that it contains cobalt in the +3 oxidation state.

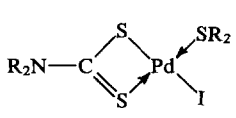
Solvated complexes include a series of compounds, for example $[CuCl_2(LH)_2DMSO]$[179] and $[NiCl_2(LH)_2]_n\cdot DMF$.[17,130] The preparation of complexes with a fully preserved ligand system (LH) is of fundamental importance for the coordination chemistry of chelating ligands incorporating an acid EH group, to which much attention has been devoted recently.[7,183]

Copper[142] and palladium[143] dimethyldithiocarbamates have been synthesised in oxidative systems containing FA, DMF, and DMSO or PC, CI_4, and tetramethylthiuram (or its cation). A series of copper complexes containing apparently both copper(II) and copper(III)—$[CuI(Me_2NCS_2)_2]CHI_3$, $[Cu_2I(Me_2NCS_2)]$, $[Cu_2I_4(Me_2NCS_2)_3]$, $Cu_2SCN(Me_2NCS_2)_2\cdot H_2O$, $[Me_2NH_2]\cdot[CuCO_3(Me_2NCS_2)]\cdot Cu_2S$, and $[Cu_3I_2(Me_2NCS_2)_5]$—and palladium complexes—$PdI[Me_2NCS_2]$, $Pd[Me_2NCS_2][Me_2S]$, and $Pd_3I_3[Me_2NCS_2]_3[Me_2S]$—have been obtained.

The presence of the dimethyldithiocarbamate fragment in the complexes considered has been demonstrated by IR spectroscopy and, in the case of the coordination compounds **42** (M = Cu^{2+}, $n = 2$)¶ and **43**, by X-ray diffraction.[142,143]



42



43

R = Me, Et.

¶ Complex **42** has been obtained on slow sublimation of the compound $[Cu_3I_2(Me_2NCS_2)_5]$ at 473–493 K.

The data presented in this section indicate the possibility, in principle, of synthesising inner complexes by the oxidative dissolution of metals in donor–acceptor media. However, few chelating ligand systems are known for this type of the direct synthesis of metal complexes.[3,6,7,9,10,182]

c. Synthesis of dinuclear and polynuclear complexes

The polynuclear complexes synthesised as a result of the oxidative dissolution of zerovalent metals in donor–acceptor systems are of undoubted interest from the standpoint of the chemistry of dimetallic and polymetallic coordination compounds.[29,97,184–186] The dinuclear and trinuclear copper compounds **39–41** as well as ionic iron, palladium, gold, and silver compounds containing several metal atoms in the molecule may be assigned to complexes of this type.

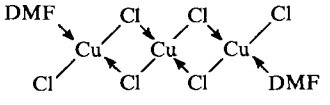
The advantage of direct synthesis is the possibility of the specific preparation of complexes with different contents of metal atoms. Thus, by varying the component ratios in the Cu^0–DMF–CCl_4 system, di-, tri-, and tetra-nuclear cluster structures have been obtained.[181] The reactions are described by the following scheme:

$$Cu^0 + DMFA + CCl_4 \xrightarrow{[DMFA]\approx[CCl_4]\gg[Cu]} [Cu_2Cl_2(DMFA)_4]_4 \quad \mathbf{39}$$

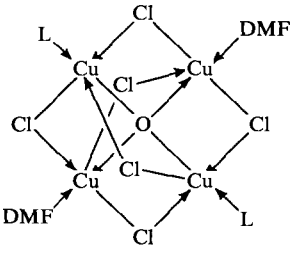
$$Cu^0 + DMFA + CCl_4 \xrightarrow{[DMFA]\approx[CCl_4]\approx[Cu]} [Cu_3Cl_6(DMFA)_2] \quad \mathbf{44}$$

$$Cu^0 + DMFA + CCl_4 \xrightarrow{[Cu]\ll[DMFA]\ll[CCl_4]} [Cu_4OCl_6(DMFA)_2] \quad \mathbf{45}$$

The structures of complexes **39**, **44**, and **45** have been demonstrated by X-ray diffraction.[118,181]



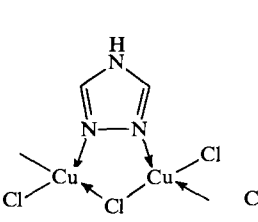
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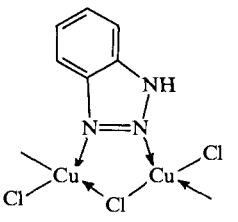
45, L = DMF,[181] Me_2NH[171]

Clusters with the same metal core and a structure similar to that of complex **45** have been described.[171] Their general formula is $Cu_4OCl_6 \cdot n(CH_3)_2NH \cdot m$Solv, where $n=4$, $m=0-2$, and Solv = MeOH or DMSO.

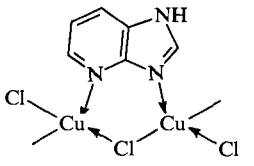
The bimetallic compounds **46–48** with two copper atoms are formed in the Cu^0–DMF–L system, where L represents nitrogen-containing heterocycles: 1,2,4-triazole, benzotriazole, and adenine.[137] We emphasise that the authors[137] attributed an erroneous formula to complex **48**, having included in the coordination the nitrogen atom of the NH-pyrrole fragment, which is known[29,187–190] to lack donor properties almost completely.



46



47



48

However there is no doubt about the bridging function of the triazole ligand in complexes **46** and **47**: this mode of coordination of triazoles and their derivatives has been unambiguously demonstrated by X-ray diffraction (see the bibliography in the review of Garnovskii et al.[190])

In conclusion we may point out that the physicochemical properties and the structures of the coordination compounds described here have been relatively little investigated. This remark applies particularly to the fact that the magnetic properties of dinuclear and polynuclear complexes, many of which (for example, complexes **39–41**, **44**, and **45**) are of undoubted interest as magnetic-exchange clusters, have been scarcely studied at all.

IV. Electrosynthesis of coordination compounds

Electrosynthesis is not only the oldest[11,12] but also one of the easiest preparative methods of synthesis of coordination compounds.[4,17,22–24,27,191–194] Electrosyntheses are carried out using dissolving anodes or cathodes, reactions involving the former type of electrodes being particularly widely used. The essential feature of the electrosyntheses of complexes are described by the simple scheme[22]

$$M^+ + L + e^- \longrightarrow [M...L].$$

If the ligands LH with an acid EH group (E = NR, O, S, Se) participate in the process, the following reactions take place:[17]

$$M \xrightarrow[-ne]{} M^{n+},$$

$$LH \longrightarrow L^- + H^+,$$

$$M^{n+} + nL^- \longrightarrow ML_n.$$

In the last case, the mechanism presupposes the anodic dissolution of the metal with subsequent complex formation.[4,24]

Anode: $nL^- + M \longrightarrow ML_n + ne$,

Cathode: $nHL + ne \longrightarrow nL^- + \frac{1}{2}nH_2$.

Thus the electrochemical reactions do not require the use of oxidants or reductants. This makes them definitely attractive.[4] Other important advantages of the electrosynthesis of coordination compounds over the usual synthetic methods consist in the possibility of regulating them, in the preparation of compounds otherwise difficult to synthesise, and in carrying out the processes under mild conditions with high yields.[17,27] Alcohols, THF,

DMF, DMSO, acetonitrile, pyridine, propylene carbonate, sulfolane, diglyme, and hexamethylphosphoramide (HMDA) are most widely used as solvents in electrosyntheses. All types of coordination compounds can be obtained with the aid of electrosynthesis, but the method is most widely applied at the present time in the synthesis of molecular and inner complexes.

a. Electrosynthesis of molecular complexes

The molecular complexes obtained by electrosynthesis are represented by diverse adducts of organic N, P, and O donors with metal halides (pseudohalides) and organometallic halides.[4,23,24,27,195-199] The former have the general formula $MX_n \cdot pL$ and the latter have the formula $R_mMX_{n-m} \cdot pL$, where M are Group I (Cu, Ag, Au),[27,197] Group II (Zn, Cd),[23,27,199] Group III (Ga, In),[23,27] Group IV (Sn, Pb, Ti, Zr, Hf),[23,24,195] Group V (V),[23] Group VI (Cr),[23,196] Group VII (Mn),[24] and Group VIII (Co, Ni, Pd)[23,27,198] metals, L = acetonitrile, pyridine, bipyridyl, *o*-phenanthroline, ethylenediamine (En), imidazole, PR_3, $R_2PCH_2CH_2PR_2$,[23,27] DMSO, dioxane, or urea,[23,27] R = alkyl or aryl, X = OH,[199] halogen,[23,27] CN,[23] NCO,[197] or ClO_4,[197,198] and m, n, $p = 1-3$.

Under the conditions of electrosynthesis with anodic dissolution of cadmium in acetonitrile solution containing *N*-(hydroxyethyl)salicylideneimine and phenanthroline, the adduct $Cd(OH)_2 \cdot (Phen)_2$ was obtained[199] instead of the azomethine chelate.[200] The structure of this molecular complex was demonstrated by X-ray diffraction: it was an octahedral structure with the CdN_4O_2 coordination unit.[199] Ionic complexes of the cationic[4,23,24,195,197,198] and anionic[23,24,195,196] type can be assigned to the same type of coordination compounds. The cationic complexes are represented by a fairly wide range of compounds[23,27] synthesised by the anodic dissolution of metals in organic solvents containing strong inorganic acids — HBF_4 or $HClO_4$. Ammonium salts of perchloric acid also serve as a source of perchlorate anions (see, for example, McAuliffe and coworkers[197,198]).

A series of cationic complexes with the general formula $[ML_n][BF_4]_m$, where L = acetonitrile or DMSO, $n = 4$, 6, and $m = 2$, 3, have been obtained by the electrolytic dissolution of metals (Zn, Cd, In, Ti, V, Cr, Co, Ni, Fe) in acetonitrile or DMSO solution in the presence of HBF_4.[23,27] The electrochemical dissolution of the copper anode in acetonitrile in the presence of 2,2′-bipyridyl, 2(1*H*)-pyridone, and tetramethylammonium perchlorate leads to isocyanatobis(2,2′-bipyridyl)copper(II) perchlorate $[Cu(C_{10}H_8N_2)_2(NCO)]ClO_4$. According to X-ray diffraction data,[197] the cation of the complex considered is a square pyramid with the isocyanate group at the apex. The latter is coordinated to copper via the nitrogen atom, which is of interest for the consideration of the ambident binding of pseudohalide ions.[180,201] Electrosynthesis with a cobalt anode under the same conditions in the presence of 1,10-phenanthroline promotes the formation of the complex $[Co(CO_3)(Phen)_2] \cdot ClO_4$.[198] According to X-ray diffraction data, the cation of this complex has an octahedral structure as a result of the bidentate binding of the phenanthroline ligand (N,N-coordination) and the carbonate ion (O,O)-coordination.[198]

Among the anionic complexes, compounds of the type $[Et_4N]_m[MBr_4]$, formed during electrosynthesis with participation of zerovalent metals, bromine, and tetraethylammonium bromide in solution in a benzene–methanol mixture, have been described.[23,24] The metals employed were Au, Cd, In, Sn, Ti, Hf, Th, Co, Ni, and Fe. The adducts of metal thiolates with N, P, and S donor ligands may be assigned to molecular complexes.[202-205] Thus electrolysis at a copper anode in acetonitrile solution with Et_4NCl as the supporting electrolyte in the presence of *o*-methylthiophenol and 1,10-phenanthroline leads to the formation of the complex $[Cu(SC_6H_4Me\text{-}o)(Phen)]_2 \cdot AN$, the structure of which has been demonstrated by X-ray diffraction.[203] Under the conditions of galvanostatic electrolysis in acetone or acetonitrile, a series of complexes having the general formula $M(SR)_2L_2$, where M = Co or Ni, R = Ph, 2,3,5,6-F_4C_6H, 3-MeC_6H_4, or 2-$C_{10}H_7$, and L = *o*-Phen or Bipy have been obtained.[204] Magnetochemical measurements {μ_{ef} = 2.70 μ_B for the complex $[Co(SPh)_2(Phen)_2]$ and μ_{ef} = 3.30 μ_B for the nickel analogue} and the compositions of the complexes indicate an octahedral configuration. The occurrence of the latter has been unambiguously demonstrated by X-ray diffraction for the cation of the complex $[Co^{III}(SPh)_2(Phen)_2]ClO_4$.[204] Adducts having the general formula $CuSR \cdot nL$, where R = Ph, *o*-, *m*-, or *p*-MeC_6H_4, or 2,3,5,6-F_4C_6H, L = $Me_2NCH_2CH_2NMe_2$, PhNCS, Bu^tNCS, or PPh_3, and $n = 0.5$, 1.5, 2, have been synthesised[205] by the electrochemical dissolution of copper in acetonitrile solutions of the thiols and the ligands (L).

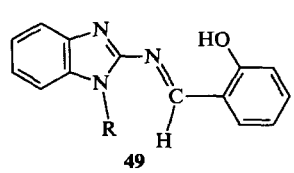
b. Electrosynthesis of π-complexes

Compilations of data on the electrochemical synthesis of transition metal π-complexes have been published.[4,22,24,27] They cover the electrosyntheses of metal complexes of cycloalkenes [for example, the copper complex of cyclooctadiene $Cu(COD)_2ClO_4$,[27] the nickel derivative of cyclooctatetraene Ni(COT),[22] and the bis(η^5-cyclopentadienyl) metal derivatives of type **11** (M = Fe, Mn, Ni,[4,22,27])]. Ferrocene **11** (M = Fe) was first obtained electrochemically by the dissolution of an iron anode in a dimethylformamide solution of cyclopentadienylthallium.[4] The analogous manganese and nickel complexes have been synthesised by the electrolysis of the lithium, sodium, or cadmium salts of cyclopentadiene in solution in THF.[4] However, it was subsequently demonstrated that the metallocene complexes can be obtained directly from cyclopentadiene and its derivatives.[206,207] The electrosynthesis of the type **11** and **15** metallocene complexes from CH acids having the general formula RH, where R = cyclo-C_5H_5, MeC_5H_4, 2,4-$Me_2C_5H_3$, C_5Me_5, indenyl, or fluorenyl, is therefore of special interest.[207] It has been shown that the π-complexes R_2M [207] (R = C_5H_5 or 2,4-$Me_2C_5H_3$ and M = Fe, Ni, Co, or Zn; R = MeC_5H_4 or fluorenyl and M = Fe or Ni; R = indenyl and M = Fe) may be obtained by electrolysis at soluble anodes (M = Fe, Co, Ni, Cu, Zn) and a platinum cathode in solutions in acetonitrile (AN – $MeOCH_2CH_2OMe$ and AN – THF with Bu_4NBr as the supporting electrolyte). In addition, the cyclopentadienyl π-complexes $(C_5H_5)CuPPh_3$, $[Co(C_5H_5)_2]Br$, $[Co(C_5H_5)_2(CoCl_4)]$, and $[Co(C_5H_5)_2(CoBF_4)]$ have been synthesised.

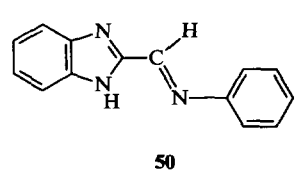
The above examples of electrosynthesis indicate the limited applicability of this method in the preparation of metal π-complexes and this situation has persisted to this day.

c. Electrosynthesis of metal chelates

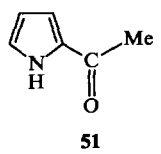
Only individual chelating ligands have been used in the electrosynthesis of inner complexes until quite recently: dimethylglyoxime,[4,12,17,27] β-diketones,[17,23,27] Schiff bases **49** and **50**,[4,17,24,27] azoles,[4,17,27] *o*-hydroxyphenylazoles and benzazoles **29**,[17,27] 2-acetylpyrrole **51**,[23] and 3-hydroxy-4-pyrone **52**.[23]



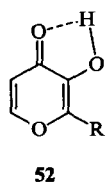
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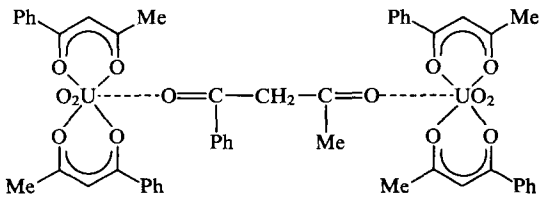


52

Electrosyntheses of inner complexes comprising metallocycles with different numbers of members [ring atoms] and with different ligand environments (N, O, S) have now been achieved.

Among chelates with a six-membered metallocycle, mention should be made of the complexes of β-diketones [36,195,209-211] and azomethines [200,212-223] which have been obtained electrochemically. Thus the electrosynthesis of cadmium,[209] thorium,[195] and dysprosium [210] β-diketonates has been described. The structure of the adduct $Cd(acac)_2$.Phen has been demonstrated by X-ray diffraction.[209] Systematic studies[36] have shown that β-diketonates having the compositions ML_2 (M = Ni), ML_3 (M = Al, In, Co, Fe, Ti, Zr), ML_4 (M = Zr, Hf), ML_2·Solv (M = Ni, Fe), ML_3Cl (M = Ti, Zr), $TiL_2(OMe)_2$, and ZrL_3OMe are formed in satisfactory yields from a wide variety of β-diketones and their fluoro-derivatives under the conditions of electrosynthesis. These chelates have been synthesised from liquid β-diketones or their 15%-20% solutions in methanol, ethanol, acetonitrile, and DMF with LiCl, LiBr, NH_4Cl, or Bu_4NBF_4 as the supporting electrolytes.

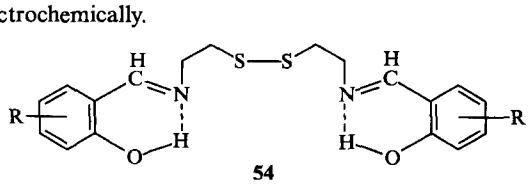
The electrochemical oxidation of uranium leads to chelates of the type UL_4 and UO_2L_2 (LH = β-diketone).[211] Apart from these complexes, the compound $UO_2L_2(HL)_{0.5}$ was isolated and the structure **53** was attributed to it. It was justified by IR spectroscopic data,[211] but in our view this requires more rigorous evidence.



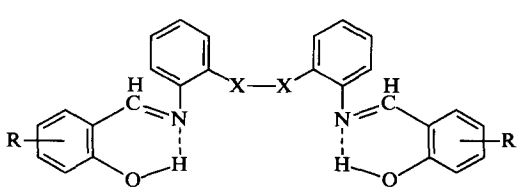
53

The inner complexes of Schiff bases have been obtained by electrosynthesis in an acetonitrile solution of the ligands using a platinum electrode (cathode) and an anode consisting of the complex-forming metal.

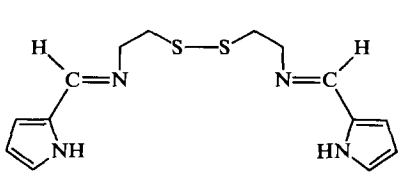
Together with the complexes containing alkyl or aryl substituents at the nitrogen atom of the azomethine group (R = Pr^i, Bu, *p*-MeC_6H_4, *p*-ClC_6H_4, *p*-$O_2NC_6H_4$),[200] a large number of *o*-hydroxyazomethines containing the coordinatively active fragments **28** (R = 2-Py,[212,214] CH_2CH_2Py-2,[213,215] $CH_2CH_2NMe_2$ [213]), **54**,[217] **55** (X = S,[218,220,223] Se [222]), **56**,[216] and **57** [216] at the above nitrogen atom have been synthesised electrochemically.



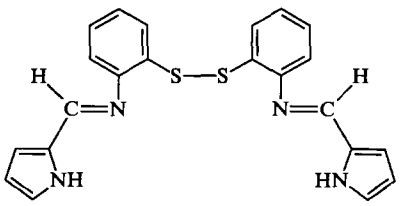
54



55 (X = S, Se)



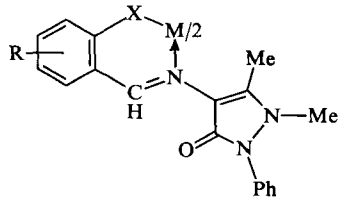
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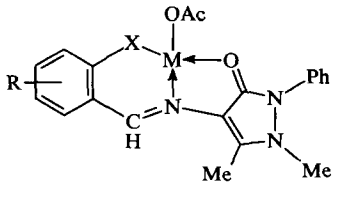
57

Analysis of X-ray diffraction data shows[214] that the nitrogen atom of the pyridine ring in the copper complex of the ligand **28** (R = 2-Py-3-Me, R′ = 5-OMe) is not involved in the coordination, i.e. this formally tridentate ligand system behaves as a bidentate system and the metallocycles MN_2O_2 involving the phenolic oxygen and the azomethine nitrogen are formed in the complexes described. This situation is characteristic of the copper complex obtained from the ligand **28** [R = CH_2CH_2Py, R′ = 4,6-$(OMe)_2$]. The complex has a square-planar structure with a non-coordinated nitrogen atom of the pyridine ring.[213] At the same time, X-ray diffraction data indicate the involvement in the coordination of the pyridine ring in the nickel complex of *N*-(2-pyridylethyl)salicylideneamine **28** (R = CH_2CH_2Py), which leads to the NiN_4O_2 octahedron.[215] The results described are of undoubted value for the understanding of the problem of competitive coordination in a series of formally tridentate ligand systems — different ways of binding the latter depending on the electronic configuration of the metals and the structure of the complexes formed by them.[7,208,224-226]

Azomethines containing an antipyrine fragment at the nitrogen atom can be assigned to the same class of ambident ligand systems.[219] Inner complexes of type **58** (X = O) having the composition ML_2 have been obtained from them by the electrochemical method.[219] Both the involvement[227] and the lack of such involvement of the oxygen atom of the carbonyl group[219,227] in coordination, apart from the phenolic oxygen and the azomethine nitrogen, have been postulated in such inner complexes. In this case, the electrochemical method has the advantage that, when it is employed, complexes **58** with the composition ML_2 alone are formed, whereas under the usual conditions involving the use of the metal acetates coordination compounds of two types were isolated: ML_2 (compounds **58**) and MLAcO (compounds **59**).[227]



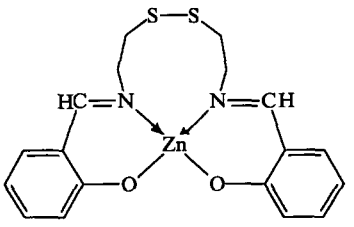
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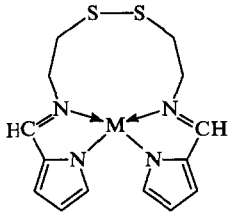
59

The formally hexadentate ligand systems **54**-**57** behave in an unusual manner under the conditions of electrosynthesis. The disulfide structure of the ligand **54** remains unaltered in the complex formation reaction.[217] The structure **60** has been proposed for the complex. The coordination polyhedron is a tetrahedron formed with participation of the phenolic oxygen atoms and azomethine nitrogen atoms.[217]

The complexes ML **61**, obtained from the ligands **56** and **57**, evidently have a similar structure without the involvement of sulfur atoms in the coordination.[216] In the remaining cases, the dissociation of the X–X (X = S, Se) bonds and the formation of a complex with a comparatively rarely encountered N,X- or N,O,X-ligand environment are observed under the conditions of electrolysis.[7,208]

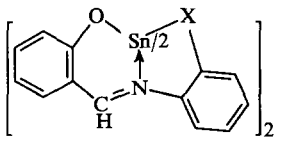


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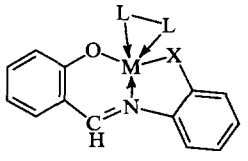


61 (M = Ni, Cu, Zn, Cd)

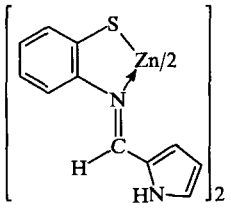
It has been demonstrated by X-ray diffraction that two types of complexes are formed from compound **55**—complexes **62** (X = S,[218] Se[222]) and **63** (M = Zn, L–L = 2,2′-Bipy;[220] M = Co, L–L = *o*-Phen[223]).



62



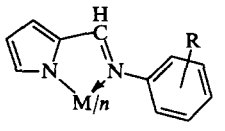
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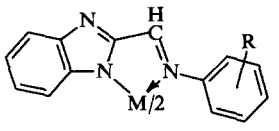
64

The dissociation of the disulfide bond in the ligand **57** (LH_2) results in the formation of the complex $Zn(LH)_2$ **64**, which is, according to X-ray diffraction data, a complex of pyrrolemethylidene-*o*-aminothiophenol, in which the pyrrole fragments are not involved in coordination.[216] The results described expand the possibilities for the synthesis of coordination compounds containing in the coordination units the N and S(Se) donor atoms, in which considerable interest has been shown recently.[7,208,224–227] In this connection, we may note that complexes of type **64**, containing the five-membered coordination units MN_2X_2 (X = S, Se), have been synthesised fairly long ago using metal salts or were obtained by template synthesis.[7,208]

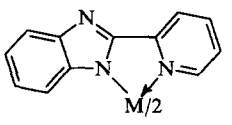
Coordination compounds of another type (compounds **65**–**67**) with the five-membered metallocycle MN_4 have been obtained by electrolysis from azomethines derived from the aldehydes of five-membered nitrogen heterocycles—pyrrole-2-aldehyde[228–237] (complex **65**), benzimidazole-2-aldehyde[4,24] (complex **66**), and 2-(2′-pyridyl)benzimidazole[4,24,27] (complex **67**).



65

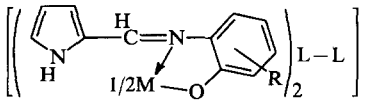


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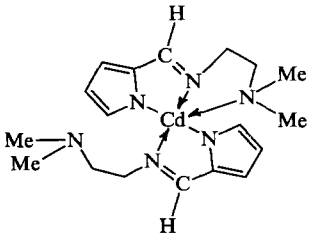
Complexes **65** are classical,[7,208,238–240] but the application of electrosynthesis not only made it possible to expand the range of such compounds but also helped to refine their structures and to elucidate questions concerning the competitive reactions of azole ligand systems with zerovalent metals. X-Ray diffraction data for the pyrrolealdiminates **65**, obtained under the conditions of electrosynthesis (solution in acetonitrile), indicate that the copper complex **65** ($M = Cu^{2+}$, R = *p*-Me, $n = 2$) contains the tetrahedrally distorted metallocycle CuN_4,[229] while the trivalent cobalt chelate **65** ($M = Co^{3+}$, R = *o*-Me, $n = 3$) is an octahedron with the CoN_6 coordination unit.[229] X-Ray diffraction data has shown that an analogous ligand environment MN_6 is characteristic of the adducts of the nickel chelate **65** (M = Ni, R = H, $n = 2$) and the cadmium chelate **65** (M = Cd, R = 2-OMe, $n = 2$) with bipyridyl.[231] Competitive coordination and the formation of three types of structures are characteristic of the ambident ligand systems of the pyrrolealdimine type: with participation of the iminophenol fragment (complex **68**),[232,235,237] with participation of all the nitrogen donor atoms (complex **69**),[233] and with participation of the iminoamine group (complex **70**).[236]



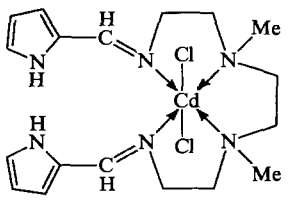
68

R = H, 4-Me, 5-Me, 5-Cl, 3,5-Me_2;

M = Co, Ni, Zn; L–L = acetonitrile, Bipy, *o*-Phen



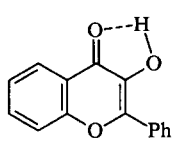
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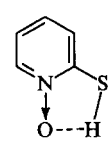
70

We emphasise that the pyrrole fragment in complexes **68** and **70** is not involved in coordination. This may be associated with the electrosynthesis being carried out in solution in acetonitrile and with the presence in the reaction medium of powerful chelating N-donors such as 2,2′-bipyridyl, 1,10-phenanthroline, or a macrocyclic fragment. A definite confirmation of this hypothesis is provided by the finding that, when the electrochemical synthesis is carried out with participation of ligands of the azole series having a lower NH acidity than pyrrole in an alcoholic medium,[241] the *N*-metal-substituted complexes **66** and **67** are formed.[4,24,27,242] A characteristic feature is that *N*-metal substitution is observed in the electrochemical synthesis in methanol (ethanol) and for the azoles themselves.[27,242]

Among other metal chelates with a five-membered metallocycle, one may mention complexes synthesised electrochemically from bidentate oxygen-containing donor ligands **52** (R = Me)[243] and **71**,[244] as well as pyridine-2-thiol *N*-oxide **72**.[245] The presence of five-membered metallocycles of type MO_4 and MO_2S_2 in these complexes has been demonstrated by X-ray diffraction.[243-245]

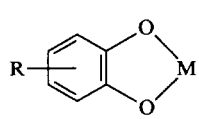


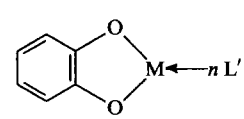
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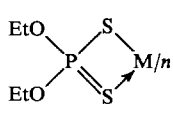
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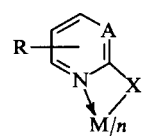
The electrochemically synthesised inner complexes with four-membered chelate units are represented by complexes of catechols (complexes **73**)[246-248] and their adducts with N- and O-bases (complexes **74**),[246-248] dialkylthiocarbamates (complexes **42**),[249] dialkyl phosphorodithioates (complexes **75**).[249] 2-pyridinol [complex **76** (X = O, A = CH)],[250-252] pyridine-2-thiol [complex **76** (X = S, A = CH)], pyrimidine-2-thiol [complex **76** (X = S, A = N)],[255-258] and their molecular adducts with azines and bisazines (complexes **77**).[256-258]

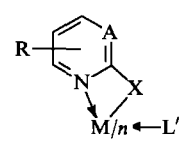




73 (R = H, cyclo-C_4H_4, 3,4,5,6-Br_4) **74**





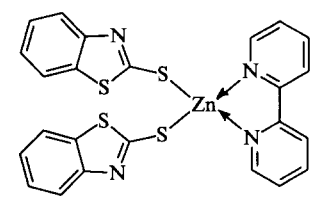


75 **76** **77**

A = CH, N; X = O, S

Complexes **73** and **74**, having the compositions ML and ML·*n*L′ respectively (M = Zn,[246] Cd,[246] Sn;[247] LH_2 = catechols; L′ = Bipy, Phen, Py, DMSO; *n* = 1, 2), have been obtained in acetone with the above metals as the anode. In the case of the indium anode, the complex [In(LH)], in which only one of the two phenolic hydrogen atoms of 1,2-dihydroxybenzene is substituted by the metal, is formed under the same conditions.[248] The electrosyntheses of the complexes of dialkyldithiocarbamates [complexes **42** (R = Me, Et)] and diethyl phosphorodithioates (complexes **75**) have been carried in solution in acetonitrile with silver, zinc, cadmium, indium, thallium, cobalt, nickel and iron anodes.[249] When 1,10-phenanthroline (L′) was added to the reaction mixture, the adducts ML_n·Phen (M = Ga, V, Mn, Co, Fe) were obtained. The complexes were characterised by elemental analysis, the results of which indicated[249] the formation of the inner complexes ML_2 **42** and **75** (*n* = 2), ML **42** (M = Ag, Tl; *n* = 1) and **75** (M = Cu, Tl, Ga; *n* = 1), and ML_3 **42** (M = Fe, In, Tl; *n* = 3) and **75** (M = Co; *n* = 3). The ^{31}P NMR spectra of compound **75** were also obtained. Metal chelates of divalent iron, copper,[250] zinc and cadmium,[251] and cobalt and nickel[252] have been obtained from 2-pyridinone under the conditions of electrosynthesis and isolated. In our view, the results of magnetochemical measurements for complexes **76** and **77** (X = O, A = CH) are of greatest interest. In particular, the values of μ_{ef} for the copper complexes $[CuL_2]\cdot 3H_2O$ and $[CuL_2\cdot Phen]\cdot 3H_2O$ are 1.5 and 2.4 μ_B respectively[250] and may be associated with exchange interactions of the antiferromagnetic and ferromagnetic types.[98]

The heteroarene-2-one and heteroarene-2-thione ligands are known to form several types of complexes.[253,255,256,258,259] X-Ray diffraction data have shown that structures in which the MN_2S_2 metallocycle is a fragment are characteristic of the adducts of pyridine-2-thiol [complexes **77** (A = CH, X = S: M = Ni,[253] L′ = Bipy, R = H, *n* = 2; M = Zn,[254] L′ = Phen, R = H, *n* = 2)] and pyrimidine-2-thiol [complexes **77** (A = N, X = S: M = Ni,[255] L′ = Bipy, R = H, *n* = 2; M = Cd,[256] L′ = Phen, R = H, *n* = 2; M = Zn,[257] L′ = Py, R = 4,6-Me_2, *n* = 2; M = Ni, Cd,[258] L′=Bipy, Phen, *n* = 1)]. The metallocycle is formed via the endocyclic nitrogen atom of the pyridine type and the thiol sulfur atom. The adduct-forming ligand (L′) lead to octahedral (Bipy, Phen)[253-256,258] or trigonal bipyramidal (Py)[257] configurations. On the basis of magnetochemical data, an octahedral structure has been attributed to the adduct of the nickel complex of benzothiazole-2-thione with 2,2′-bipyridyl (μ_{ef} = 3.4 μ_B) and 1,10-phenantholine (μ_{ef} = 2.9 μ_B).[259] However, the magnetic criterion can hardly be used for an unambiguous choice between octahedral and a tetrahedral coordination. The occurrence of the latter for the adducts of benzothiazole-2-thiolates is entirely probable when account is taken of the results of X-ray diffraction studies on the tetrahedral complex **78**.[259]



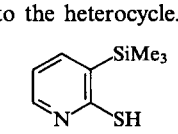
78

The structure of compound **78** is interesting also because it does not involve the formation of a four-membered metallocycle of type MN_2S_2 characteristic of all the complexes of 2-azinols and azine-2-thiols described above.

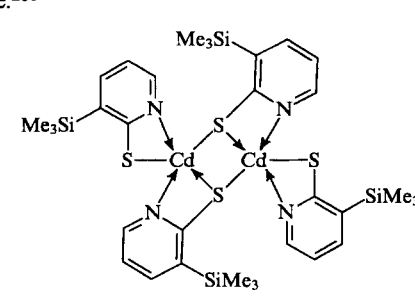
b. Electrosynthesis of bimetallic and polymetallic complexes

The few existing examples of the electrosynthesis of polymetallic complexes show that this method is promising.

A cadmium complex CdL_2 has been obtained under the conditions of the electrolysis (acetonitrile, Et_4NClO_4) of pyridine-2-thiol **79** with a trimethylsilyl substituent attached to the heterocycle.[260]



79



80

According to X-ray diffraction data and in contrast to the inner complexes **76–78**, this compound has the dimeric structure $[CdL_2]_2$ **80**, in which the cadmium atoms involved in a trigonal bipyramidal coordination are linked by sulfide bridges.[260] One cannot rule out the possibility that the nickel and zinc complexes of pyridine-2-thiol **79** have similar structures.[260] The tetranuclear complex $[Cu_4(\mu\text{-}C_5H_{11}S)_4(Ph_2PCH_2PPh_2)_2]$ has been synthesised by the reaction of copper with pentyl sulfide and bis-(diphenylphosphino)methane under the conditions of electrolysis (acetonitrile, Et_4NClO_4).[261] According to X-ray diffraction data, a new type of eight-membered cyclic structure Cu_4S_4, in which the copper atoms are linked by sulfide bridges, is formed in this complex.[261]

Complexes $[Et_3NH]^+[M_4(SPh)_{10}]^-$ with the tetranuclear anions, where M = Zn or Cd, have been obtained by direct electrochemical synthesis with participation of zinc (or cadmium), thiophenol, and triethylamine in acetonitrile with Et_4NClO_4 as the supporting electrolyte.[262] A bicyclic structure with terminal coordination of zinc and with the bridging SPh fragments is produced in the anion with M = Zn.[262] X-Ray diffraction studies have shown that the electrochemical synthesis makes it possible to create two types of hexanuclear cluster structures on the basis of 4,6-dimethylpyrimidine-2-thione: for Cu_6L_6, an octahedral cluster with six Cu atoms, each of which is trigonally coordinated to one N atom and two S atoms of three different ligands,[263] and for Cd_6L_6 a cyclic system with six cadmium atoms linked by sulfide bridges.[258] Since the electrosyntheses of both clusters considered were carried out under the same conditions (acetonitrile, Et_4NClO_4), one may postulate that the decisive factor in the creation of the structures indicated is the ability of the complex forming species (Cu^+, Cd^{2+}) to form different polyhedra.

The possibility of obtaining clusters from the complexes synthesised electrochemically is of undoubted interest. Thus the octanuclear cluster $[Cu_8(SC_5H_{11})_4(S_2CSC_5H_{11})_{11}]$ has been synthesised from the univalent copper complex of pentyl sulfide obtained under the conditions of electrosynthesis in acetonitrile using a copper anode[203] and carbon disulfide.[264] The interaction of the electrochemically synthesised adduct of the cadmium complex of pyrimidine-2-thione with 1,10-phenanthroline [complex **77** (M = Cd, A = N, L′ = Phen, R = H, n = 2)] and divalent copper hexafluoroacetylacetonate (F_6acac) in acetonitrile leads to the tetraheteronuclear complex $[Cu_2(Phen).(\mu^3\text{-}L)_2Cd_2(F_6acac)_2]\cdot 2AN$,[265] where L = the trianion of 1,3,5-tris(trifluoromethyl)cyclohexane-1,3,5-triol.

V. Other methods for the direct synthesis of coordination compounds

Special mention should be made of the synthesis of complexes from zerovalent metals in a melt[10,17,113] and under the conditions of boundary friction of the metals (tribochemical reactions).[17–19,266–279] These methods were segregated in a separate section because syntheses in the melt and tribochemical reactions may be regarded as solid-phase processes accompanied by transition to the liquid phase or (and this cannot be ruled out) may be regarded as processes occurring in a plasma.

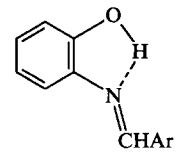
Virtually all the complexes obtained by these methods are inner complexes. Copper, nickel, cobalt, and zinc react exceptionally vigorously with fused salicylidene-*o*-aminophenol **28** (R = C_6H_4OH-*o*, R′ = H), *o*-hydroxyphenyl-1,2,4-oxadiazoles **30**, and 8-hydroxyquinoline.[17] The yields of the inner complexes in these syntheses are fairly high (up to 60%–70%). Benzoylacetone and acetoxime react with copper in the fused state, but the reactions are slow and afford low yields of the metal chelates. Macrocyclic complexes, for example metal-phthalocyanines **38**, have been synthesised in a melt of a mixture of solid reagents (the metal, *o*-phthalodinitrile or phthalimide, as well as certain other derivatives).[10]

The tribochemical method of synthesis of coordination compounds is based on the preparation of inner complexes under the conditions of boundary friction in a reactor which is a modification of the end-face friction machine.[17–19] The friction couple is made from the complex-forming metal (M^1 = specimen) and its alloy (M^2 = counterbody). The tribochemical reactions are described as follows:[19]

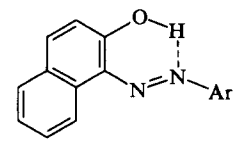
$$M^1 + n\,LH \xrightarrow[\text{friction}]{M^1/M^2} M^1L_n + \tfrac{1}{2}nH_2\,.$$

A scheme has been proposed for the formation of complexes under the conditions of boundary friction via chemisorption processes in which an electron is transferred from the metal atom to the ligand and the adsorbed molecules are rearranged in conformity with the geometry of the complex.[17–19] Another important factor governing the successful tribosynthesis of coordination compounds is the appearance in the region of the friction contact of zones with local temperatures in excess of 1273 K. This leads to the formation of a triboplasma in the microvolumes in which the complex formation reactions take place.[19,267]

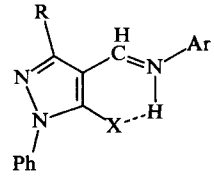
Ideas concerning tribocoordination and the influence of external conditions on the latter have been developed in a number of studies.[19,272,274,277–279] It has been established that a necessary condition for tribocoordination is the presence of acid HX groups (X = NR, O, S) in the molecules of the organic compounds used as ligands.[19] By virtue of their presence, the tribosynthesis of inner complexes has been achieved with participation of salicylideneaniline and its derivatives **28**,[17–19,267,273,276] arylidene-*o*-aminophenols **81**,[17–19] arylazonaphthols **82**,[17–19,266] azomethines **83**,[17–19] and azo-derivatives of the pyrazole series **84**.[17–19]



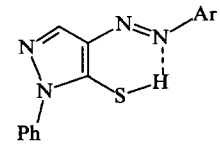
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82

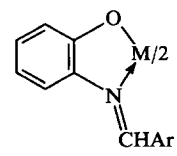


83 (X = S, Se)

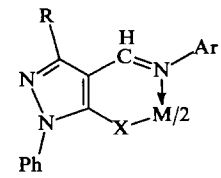


84

Among the complexes obtained from the ligand systems **81–84**, the arylidene-*o*-aminophenoxides **85**, which are formed readily under the conditions of tribosynthesis, require special consideration.[17–19] Under the usual conditions, they are obtained from metal salts with fairly considerable difficulty owing to the hydrolysis of the azomethine linkage.[7,280]



85



86

The successful tribosynthesis of the metal chelates **86** from the ligands **83**, in which a constant interest has been shown in connection with the detailed characteristics of their

stereochemistry and stereodynamics, may be noted.[7,208,281] Inner complexes of other classes of ligand systems have also been obtained under the conditions of boundary friction. Thus the tribosyntheses of metal β-diketonate chelates, in particular the complexes of 3,3,3-trifluoro-1-thienoylacetone, have been described.[270,275]

The tribochemical method has definite advantages, since it makes it possible to obtain complexes over a wide temperature range in polar and nonpolar media. At the same time, the low yields of the final products (see, for example, Kuzharov et al.[18]) are its significant disadvantage. Because of this, the prospects for the application of the tribochemical method in modern synthetic coordination chemistry are obscure.

Definite advances have been made using ultrasound for the synthesis of complexes from zerovalent metals.[282–284] The inner complexes of 3*d* transition metals with salicylideneanilines of type **28** have been obtained with the aid of ultrasound.[282–284] However, much work still remains to be done on the improvement of this type of activation of zerovalent metals before a preparative method of synthesis of coordination compounds can be created on its basis.

VI. Conclusion

In assessing the data presented in the present review from the standpoint of modern coordination chemistry,[3–5,7,29,281] the following features must be emphasised.

First, the direct synthesis from zerovalent metals makes it possible to obtain all types of coordination compounds. In this connection, the gas-phase reactions are carried out mainly in order to obtain π-complexes, while the liquid-phase synthesis is designed predominantly for the preparation of molecular adducts and metal chelates.

Second, diverse organic ligand systems, forming molecular complexes, π-complexes, metal chelates, and clusters may participate in the direct synthesis. This factor permits the specific synthesis of complexes with a specified geometry and a specified location of their coordinate bond (see, for example, Refs 153, 169, 216, 229–238, 253–258, and 263).

Third, under the conditions of the direct synthesis of coordination compounds, it is possible to employ the metals of virtually all the Groups of the Periodic System and to regulate the oxidation states of the complex-forming metals by selecting the ligands. The preparation by this method of gold, silver, and lanthanide complexes is especially promising. Definite progress in regulating the oxidation states of the metals may be attained by means of a correct selection of ligand systems taking into account the principle of hard and soft acids and bases,[180,285,286] namely low oxidation states of the metals should be stabilised by soft bases (P, As, S, and Se donors), while high oxidation states should be stabilised by hard bases (N and O donors).

Fourth, despite the wide-scale employment of direct synthesis for the preparation of metal complexes, individual methods require improvement in order to bring them up to preparative application (gas-phase synthesis and tribosynthesis). For the application of certain methods, it is desirable to expand the range of ligand systems: chelating ligands in the gas-phase synthesis and compounds forming π-complexes and cluster structures in the liquid-phase synthesis.

Extensive possibilities for the study of the products of the direct synthesis arise from the use of ion-cyclotron resonance.[287,288]

All the features described above demonstrate the likely usefulness of the direct synthesis of metal complexes and give rise to the hope for the extensive employment of this method in coordination chemistry. This is also indicated by a review[289] devoted to the electrosynthesis of coordination compounds.

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Theoretical foundations of the use of the transcritical state in extraction, separation, and concentration processes. Pathways of transcritical superextraction

V G Yurkin

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Abstract. The physicochemical foundations of known fluid supercritical extraction processes and of essentially new transcritical extraction processes in liquid–liquid systems, and in ultramicroheterogeneous systems with a subtransitional dispersed phase in micellar and liquid-crystalline transitions, are discussed via a unified approach based on conclusions of the modern fluctuation theory of phase transitions. It is shown that regions of enhanced selectivity of the phase redistribution exist on the path to the critical point both under supercritical and under subcritical conditions, and that a subcritical selectivity maximum is possible only if the system contains a region in which the classical theory of critical phenomena is applicable. In the selective extraction into both the subcritical and the supercritical phases a weak, universal (physical) selectivity may be accompanied and complemented by stronger specific chemical effects leading to selective complex formation. It is shown that the chemical reaction in the homogeneous phase can be treated as a first-order phase transition close to a second-order phase transition, and accordingly we observe a universal physical superextraction into this phase. The bibliography includes 79 references.

I. Introduction

Distillation and extraction processes depend on changes in the state of a fluid (gaseous or liquid) heterogeneous system along the equilibrium curve on a phase diagram caused by macrointeractions in the system. Distillation and extraction processes are usually carried out far from the critical point (CP). In two-phase systems the equilibrium curve terminates at the CP, where the difference between the coexisting phases disappears and the concepts of extraction and separation become meaningless (Fig. 1*a*). However, the response of the system to external influences is a maximum at the CP. Near the CP many other unique features of the critical state of matter become apparent due to the anomalous development of fluctuations and to the tendency of their correlation radius to increase towards infinity. Another important property of these systems is the loss of individuality of substances as the critical conditions are approached. The character of these properties is determined by the extent to which critical conditions are approached rather than by the individual character of the substances or even by the type of phase equilibrium. The conjunction of these two features produces uniquely favourable conditions for the realisation of various pathways for extraction, separation, and concentration processes using critical phases, thus creating methods of treatment which use no reagents and therefore emit no waste products.

The aim of this review is to examine by a unified approach the physicochemical foundations of the exploitation of the unique properties of the transcritical state of matter in extraction, separation, and concentration processes. The approach is based

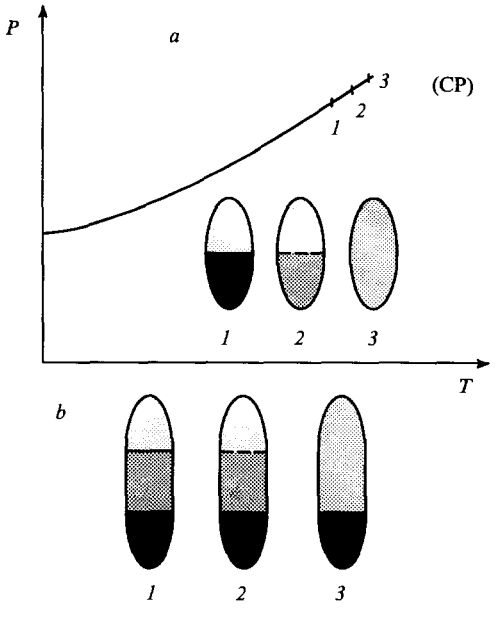


Figure 1. Equilibrium curve of two phases in temperature–pressure coordinates and schemes showing the gradual disappearance of the difference between the phases on approaching the critical point. *a*: (*1*) equilibrium of two noncritical phases; (*2*) equilibrium of two noncritical phases separated by a subcritical interface; (*3*) critical phase; *b*: (*1*) equilibrium of three noncritical phases: (*2*) equilibrium of two subcritical phases with a noncritical phase; (*3*) equilibrium of a critical with a noncritical phase.

V G Yurkin Physicochemical Research Laboratory, A A Bochvar All-Russia Research Institute for Inorganic Materials, ul. Rogova 5, 123060 Moscow, Russian Federation. Fax (7-095) 925 59 73

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on one of the most important conclusions of the modern theory of critical phenomena and of phase transitions: the existence of a unique and universal driving force[1,2] for the critical phenomena and phase transitions of the second kind.†

An alternative starting point is the postulate first put forward in Landau's classical theory of a continuous and monotonic replacement of one type of phase transition by another.[1] On the path towards the critical phase (or a 'pure' phase transition of the second kind) a phase transition of the first kind becomes increasingly 'weak', and increasingly sensitive to the effect of fluctuations on the character of the transition, i.e. it develops steadily increasing second-order properties.

A third (and very important) consideration is the hypothesis that transcritical and pre-transition phenomena in complex real multicomponent systems can be treated from the standpoint of the modern theory of critical phenomena, developed for the simplest model systems. In the first instance this refers particularly to a specific property of the transcritical state of matter: and enhanced solvent power of the transcritical phases, whose thermodynamic basis and molecular nature are most conveniently examined by considering the simplest two-component binary systems, i.e. critical solutions at infinite dilution. The concept of 'weak' phase transitions of the first kind and the postulate of universality in the properties of substances in the critical region allow the results of an analysis of the enhanced solvent power of critical phases to be applied to a wide range of real transcritical systems whose criticality (or degree of second-order nature) reveals itself not in a 'pure' form but in a form complicated by marked indications of first-order behaviour. A special case of this behaviour is the enhanced solvent power of systems containing an ultramicroheterogeneous dispersed phase.

The properties of the transcritical state can be exploited in extraction, separation, and concentration processes in various ways. In particular, extraction into critical phases from solid surfaces and extraction into critical phases through a noncritical interface have been used in liquid–gas systems. Supercritical fluid extraction processes near the gas–liquid critical point are known. Similar processes have been forecast for liquid–liquid systems. The use in extraction, separation, and concentration processes of the redistribution between phases in the subcritical region through the subcritical interface (Fig. 1*b*) and of the changes in the type of the phase transition under these conditions is new in principle. Processes of this type are known mostly in three-phase systems near the critical homogenisation point of two of the phases. In these processes an increased selectivity, determined by both universal physical effects and specific chemical effects, is observed when the system approaches the critical point, but in the subcritical rather than the supercritical region (in contrast to fluid supercritical extraction). The possibility of similar processes in ultramicroheterogeneous systems has been predicted.

These paths to transcritical superextraction all approach critical conditions, and therefore they can be analysed in terms of a unified concept leading to the prediction of several new phenomena.

II. Enhanced solvent power of critical phases

1. Thermodynamic causes

The thermodynamic causes of the increase in the solvent power as the system approaches the critical point (or a 'pure' phase transition of the second kind) are conveniently discussed in terms of a very simple binary system in which the solvent is a gas. In this case when a pure substance is dissolved in the gas under isothermal conditions (as a function of the gas pressure P) the solubility of the second component (N_2) varies according to the equation

$$\left(\frac{\partial N_2}{\partial P}\right)_{T,s} = \frac{v_2^0 - \left[v - (1-N_2)\dfrac{(\partial P/\partial N_2)_{T,v}}{(\partial P/\partial v)_{T,N_2}}\right]}{(\partial \mu_2/\partial N_2)_{T,P}}, \qquad (1)$$

where μ_2 is the chemical potential of the dissolved substance, v is the molar volume of the solution, and v_2^0 is the molar volume of the pure dissolved substance. The subscript s denotes differentiation along the coexistence curve. Eqn (1) follows from the generalised Gibbs–Duhem equation;[3] it has also been obtained[4] in terms of the quantitative theory of the solvent power of supercritical fluids. This equation describes the increase in the solvent power of a supercritical phase in terms of classical thermodynamics, resulting from the fall to zero of the derivatives $(\partial P/\partial v)_{T,N_2}$ and $(\partial \mu_2/\partial N_2)_{T,P}$ at the critical point. The role of the former of these derivatives is the more marked. Its tendency to zero on the path towards the critical point of the pure solvent depends on the chosen path, and therefore the thermodynamic properties of these solutions (and in particular the partial molar volumes) also depend on the path.[3,5] We note that all these authors[3–5] treat the approach to zero of $(\partial P/\partial v)_{T,N_2}$ near the critical point of the pure solvent under conditions of infinite dilution. Unless these conditions are stipulated the derivative $(\partial P/\partial v)_{T,N_2}$ is nonzero even on the gas–solute critical curve.[3–5] However, according to the modern fluctuation theory of the common nature of all critical phenomena (including phase transitions of the second kind[2]) and of the increased compressibility under all critical conditions[6] the derivative $(\partial P/\partial v)_{T,N_2}$ should decrease even if it does not vanish. This results in a growth of the solvent power of all critical phases. The problem lies in identifying the experimental conditions needed to observe this behaviour (the increased solvent power) experimentally, and the degree of approach towards the critical conditions. These arguments justify the assumption that Eqn (1) is universally applicable.

Let us examine the thermodynamic equations which describe the dependence of the partial molar volumes of the solvent ($\bar{v}_1$) and of the solute ($\bar{v}_2$) on N_1 and N_2 for the simplest two-component system:[7]

$$\bar{v}_1 = v + N_2\frac{(\partial P/\partial N_2)_{T,v}}{(\partial P/\partial v)_{T,N_2}}, \qquad (2)$$

$$\bar{v}_2 = v - N_1\frac{(\partial P/\partial N_2)_{T,v}}{(\partial P/\partial v)_{T,N_2}}. \qquad (3)$$

As it tends towards zero the derivative $(\partial P/\partial v)_{T,N_2}$ is always negative (in keeping with the classical thermodynamic stability conditions). Even more relevant to our problem is the nontrivial question of the sign of the derivative $(\partial P/\partial N_2)_{T,v}$. Under relevant conditions of divergence of the partial molar volumes this sign is assumed[2–5] to be arbitrary, though it has been stated[4] (without any evidence) that 'in practice' the derivative $(\partial P/\partial N_2)_{T,v}$ is positive. Allowing for Eqns (2) and (3) and for the negative sign of $(\partial P/\partial v)_{T,N_2}$, we may conclude that under conditions of divergent $\bar{v}_1$ and $\bar{v}_2$ (v being always finite) the sign of $(\partial P/\partial N_2)_{T,v}$ always agrees with that of the partial molar volume of the solute and is opposite to the sign of the partial molar volume of the solvent. This leads us to the universal thermodynamic conclusion that in keeping with the singularity of the partial molar volume of the solvent and irrespectively of its sign, the molar volume of the solution on the path towards the critical point always decreases. Thus, for negative values of $\bar{v}_1$ this decrease follows from the definition of a partial molar quantity, and for positive values of $\bar{v}_1$ it is produced by the negative value of $\bar{v}_2$ [of course, $(\partial P/\partial N_2)_{T,v} = -(\partial P/\partial N_1)_{T,v}$]. This important property of the molar volume of the solution of the path towards the critical point (i.e. towards the point for a 'pure' phase transition of the

† We shall treat the redistribution between phases as a phase transition of the second kind.

second kind) allows the general thermodynamic reason for the enhanced extraction of a substance into a critical phase to be identified in a specific case.

We note that in the modern theory of phase transitions both phase transitions of the second kind and 'weak' phase transitions of the first kind but close to the second kind are treated as critical phenomena.[2]

If the path to the critical point is examined under isobaric conditions an equation analogous to Eqn(1) can easily be obtained from the same generalised form of the Gibbs–Duhem equation:

$$\left(\frac{\partial N_2}{\partial T}\right)_{P,s} = \frac{-S_2^\circ + \left[S - (1-N_2)\dfrac{(\partial T/\partial N_2)_{P,T}}{(\partial T/\partial S)_{P,N_2}}\right]}{(\partial \mu_2/\partial N_2)_{P,T}} \qquad (4)$$

where S is the entropy of the solution, and S_2° is the molar entropy of the pure solute. This equation was first obtained in the author's laboratory.[8] The derivative $(\partial T/\partial S)_{P,N_2}$ in Eqn (4) plays the same role as $(\partial P/\partial v)_{T,N_2}$ in Eqn (1). Its decrease is the thermodynamic reason for the singularity in the partial molar entropy which enhances the solvent power of the critical phase as the critical point is approached. Equations similar to (2) and (3) can easily be obtained for the entropy, showing that the thermodynamic cause of the enhanced extraction into the critical phases under isobaric conditions is the increase in the molar entropy of the solution on the path towards the critical point. This increase is itself caused by the singularity in the partial molar entropy of the solvent, and is observed irrespectively of the sign of this singularity.

The general condition for a maximum in the isothermal dependence of the solubility on pressure in binary systems takes the form[7]

$$N_1^l(\bar{v}_1 - \bar{v}_1^l) + N_2(\bar{v}_2 - \bar{v}_2^l) = 0, \qquad (5)$$

where the subscripts denote the components and the superscripts denote the phase; the upper bar denotes a partial molar quantity. The presence of extrema on the composition dependence of the partial molar quantities predetermines the presence of extrema on the coexistence curve of the two equilibrium phases, i.e. on the solubility curve.[7] An analogous equation can be obtained for isobaric conditions.

By generalising the dependences described by Eqns (1), (4), and (5) we can establish not only that the solvent power of any critical phase is enhanced but also that the number of solubility maxima in the system is equal to the number of critical points.[8] In the special case of the solubility of an individual substance in a gas the solubility maximum is associated with the presence of a lower critical point in the gas–gas equilibrium, and if an upper critical point is also possible in the gas–gas equilibrium the solvent power of the gas phase should have a second maximum.[7]

2. Increase in the solvent power in 'weak' phase transitions of the first kind

The monotonic nature of the change in the type of the phase transition creates a very large class of so-called 'weak' phase transitions of the first kind, or phase transition of the first kind close to phase transitions of the second kind. The concept of weak phase transitions of the first kind and the widespread occurrence of transitions of this type in practical solutions have stimulated many attempts to find and to characterise various universal dependences in these solutions. The most important of these is the anomalously high response of a substance in the critical state to macroscopic and even to microscopic perturbations.[2] The stipulation of weak phase transitions of the first kind (close to transitions of the second kind) justifies the assumption of a universal enhancement of the solvent power in all cases of more or less clearly displayed second-order properties, i.e. λ-anomalies in the second derivatives of the thermodynamic potential with corresponding S-shaped changes in the first derivatives of the thermodynamic potential (enthalpy, volume, and entropy). The nature of the most important dependences can be determined from the results of studies of critical solutions at infinite dilution.[3]

Several uniquely anomalous dependences, apparently incompatible with classical thermodynamics,[3] have been observed in these solutions and explained in terms of the classical phenomenological theory.[5] The universality postulate suggests that in dilute critical solutions the most clearly marked effects are characteristic of the critical state as a whole, and that these effects should be observed to a greater or lesser extent in all practical critical phases during 'weak' phase transitions of the first kind. Indeed, at the critical point of the pure solvent

$$(\partial P/\partial v)_T = (\partial^2 P/\partial v^2)_T = 0,$$

whence it follows that

$$(\partial V/\partial P)_T = (\partial^2 V/\partial P^2)_T = \infty.$$

The anomalously high compressibility, observed not only in critical solutions at infinite dilution but also in solutions with 'weak' phase transitions of the first kind close to transitions of the second kind, should increase the solvent power. The universality of the anomalous properties of critical solutions at infinite dilution was first postulated in a general form by the writer,[9] and subsequently received independent confirmations.

3. Increased solvent power of ultramicroheterogeneous systems

The enhanced solvent power of systems containing an ultramicroheterogeneous dispersed phase, which increases with the dispersion as a result of changes in the type of the dispersed phase–medium phase transition from the first to the second kind, is of special interest.[10,11] A change in the type of phase transition on the surface of the dispersed phase as the system moves towards the critical point is phenomenologically consistent with Landau's assertion that the curve describing phase transitions of the first kind cannot terminate at a single point and must gradually be converted into a curve for phase transitions of the second kind, so that the two curves have a common tangent.[1] The effect is clearly illustrated in Fig. 2, which shows the dependence of the surface tension on both surfaces of the intermediate phase in a three-phase water–amphiphile–oil system upon the degree of enrichment of the intermediate phase by the components of the lower (water–salt) and the upper (oil) phase. Obviously, in the solubilisation within the droplet of the microemulsion by 'mechanical capture', without any allowance for the change in the type of phase transition and for the effect of this change on the interfacial redistribution, the size and nature of the solubilised volume should be strongly dependent on the type of microemulsion (the inverted microemulsion solubilises the aqueous phase, the normal solubilises the organic phase). This is indeed observed in practice: for surface tensions of 10^{-1}–10^{-2} dyne cm^{-1}, that is corresponding to microemulsion particles in which the intermediate amphiphilic phase is enriched with the components of the water-salt and the organic phase.[12] However, further lowering the surface tension (which corresponds to a decrease in the size of the microemulsion particles[12]), with a gradual transition from an amphiphilic to a micellar microemulsion phase (i.e. at surface tension values in the range 10^{-3}–10^{-5} dyne cm^{-1}), we can see not only an enrichment of the intermediate phase with the components of both the upper and the lower phase but also a decrease in the distance between the curves (see Fig. 2). Thus we observe an increase in the solvent power of the amphiphilic phase even in lyophilic ultramicroheterogeneous systems, with the approach of the 'weak' phase transition of the first kind to a 'pure' phase transition of the second kind. In this case the increase in the degree of criticality of the system is due to the increase in the fluctuations in the surface of the particles (micelles) with decrease in particle size. A thermodynamic driving force for the increased extraction into the micellar phase is provided by anomalies in the compressibility and in the change in the partial molar volumes.

Under isobaric-isothermal conditions the entropy of the ultramicroheterogeneous system increases with the degree of dispersion.[10,11] Allowing for these effects and for the primarily entropic nature of the subcritical redistribution of the components between the phases[13] we may assume that in multicomponent systems under isobaric–isothermal conditions the special properties of the partial molar entropies of the solute in the transcritical phases are the thermodynamic reason for the presence of maxima in the solubility.[10,11]

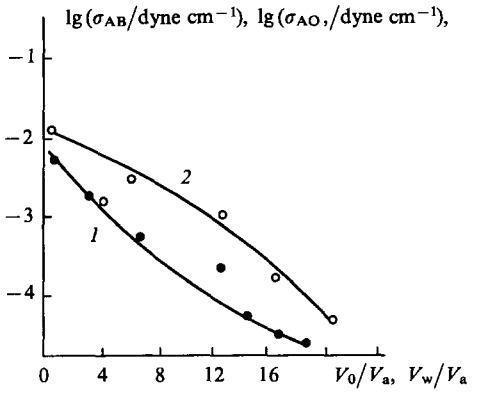


Figure 2. Plots of the surface tension σ in a three-phase system at the interfaces of an intermediate amphiphilic microemulsion-micellar phase with an upper (organic, *1*) and a lower (aqueous salt, *2*) phase against the bulk enrichment of the intermediate phase by the components of the upper (V_w/V_a) and the lower phase (V_0/V_a).[11]

We note that, as shown in Fig. 2, the solvent power of ultramicroheterogeneous systems varies only in the case of lyophilic ultramicroheterogeneous systems. Lyophobic ultramicroheterogeneous systems are thermodynamically unstable, they can be broken down by microscopic perturbations, and their enhanced solvent power can be observed only under conditions specially chosen to stabilise the degree of dispersion, for example by evolving hydrogen at a cathode, by cavitation produced by ultrasonic treatment of the liquids, or by forming Manegold spherical foams (gas emulsions) stabilised by surface-active substances. In all these cases we are dealing with the stabilisation of the gas–liquid interface in a dispersed system at the disappearance boundary of this surface, i.e. at the maximum spread of its fluctuations on the path from a colloidal dispersion to a true solution of a gas in a liquid. In most cases these phenomena have not been discussed from the point of view of changes in the nature of the phase transformation with increasing dispersion, but they can be easily incorporated into the concepts now being developed.

4. Molecular nature of the enhanced solvent power of critical phases

It is important to note that the enhanced solvent power of any critical phase is due to the special properties of partial molar quantities, as can easily be seen by examining the thermodynamics of the simplest binary transcritical systems. The left-hand sides of Eqns (1) and (4) exist only because of the singularity of the partial molar quantities. The signal of the partial molar quantities can be either positive or negative for both the solvent and the solute. The only universal feature is the nature of the decrease (in the critical region) of the molar volume of the solution as a result of the increased compressibility and of the anomalies in the partial molar volume. It has been shown[14] (in the case of critical dilute solution) that the compressibilty extrema correspond to the extrema of the partial molar quantities (Fig. 3). Under the same conditions maxima corresponding to clusters are observed in the solution: these are formations containing up to 10^2 molecules and having a local

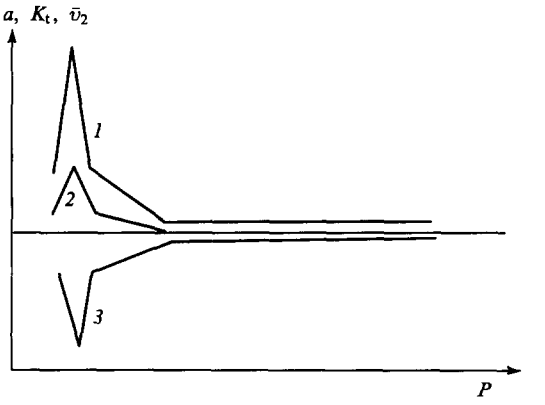


Figure 3. Plots of the size of the clusters (*1*), of the compressibility (*2*), and of the partial molar volumes (*3*) in the CBr_4-CO_2 system at infinite dilution.[14]

density higher than the average for the solution. Until recently the physical nature of the sign of the divergence of the partial molar quantities was not clear, but recent studies using molecular dynamics have thrown some light on the problem. According to Pelsche and Debenedetti[15] the anomaly in the partial molar volumes of a dissolved substance $\bar{v}_2$ is always (irrespectively of its sign) a universal phenomenon, accompanied by an increase in the size of the cluster (a shell surrounding the molecules of solute, with correlated fluctuations of the order parameter). Under these conditions infinitely dilute solutions of a Xe-like Lennard-Jones fluid in a Ne-like Lennard-Jones supercritical fluid show enhanced solvent–solute interactions near the critical point of the solvent, whereas in a 'symmetrical' system (an infinitely dilute solution of a Ne-like Lennard-Jones fluid in a Xe-like Lennard-Jones supercritical fluid) the shells surrounding the solute molecules are depleted of solvent. The stronger solvent–solute interactions correspond to an increased concentration of solvent in the cluster and to a negative divergence of $\bar{v}_2$ (tending to $-\infty$). On the other hand lowering the solvent content of the cluster corresponding to a positive divergence of $\bar{v}_2$ (tending to $+\infty$). In either case the local density of the cluster exceeds the average density of the solvent.

The same universality of the enhanced solvent power of the supercritical phases is observed in the extraction in liquid–liquid systems. Anomalies in the compressibility have been found even in solutions of liquid metals in the supercritical region (Fig. 4).

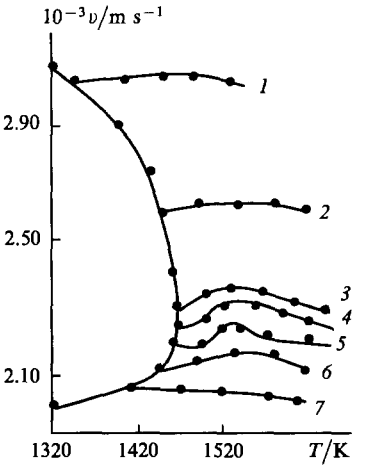


Figure 4. Compressibility anomalies in the critical region of the homogeneous phase-separating Cu–Te system. Plots of the velocity of ultrasound for alloys with an initial concentration of Te of 5 (*1*), 10 (*2*), 16 (*3*), 17.5 (*4*), 18 (*5*), 20 (*6*), and 29 at.% (*7*) (from data by Glazov et al.[16])

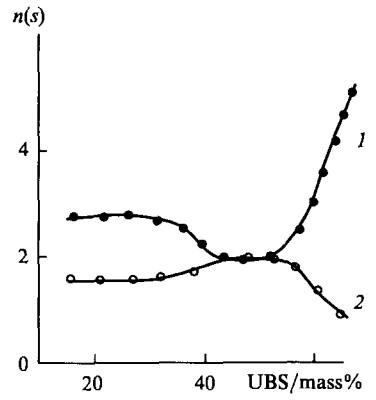


Figure 5. Dependence of the hydration number (*1*) and the solvation number (*2*) of the micelle-forming component uranyl benzenesulfonate (UBS) in the organic phase of the tributyl phosphate–water–UBS system on the concentration of UBS.[18]

The concept of universality in the extraction into micellar and liquid-crystalline phases due to the abundance in these phases of 'weak' transitions of the first kind with a 'diffuse' concentration[17] has provided explanations for several results previously treated as 'anomalous'.[10,11] The molecular nature of the enhanced solvent power of critical phases has been confirmed by a study by NMR of micellar extraction systems.[18] According to these results a region of universality is found in a tributyl phosphate (TBP)–water–uranyl benzenesulfonate (UBS) micellar solution in which the hydration and the solvation number in the hydration–solvation shell of the micelle-forming component become identical (Fig. 5). This means that the solvation shell of the micelle-forming component (in our case uranyl benzenesulfonate) contains both water and the hydrophobic solvent, i.e. that we have a region of universality. These experimental data confirm the validity of the concept of universality in the enhanced solvent power of the micellar phases and in the physical superextraction into these phases. The phenomenon has been called[18] reversible hydration. It confirms the concept of universality on a microscopic scale and contradicts the traditional explanation of solubilisation in the nucleus of a micelle in terms of 'mechanical' trapping of the conjugated phase. The observed solubilisation of both hydrophilic and hydrophobic substances is usually explained by the bicontinuous structures model proposed by Winsor,[19] according to which both normal and reversed-phase micelles are present in the micellar solution.

The concept of universality in the enhanced solvent power of ultramicroheterogeneous systems, produced by the fluctuational nature of the particle surfaces, is consistent with the well-known compression of knots of macromolecules produced by cross-linking within the knots.[20] Enhanced absorption of impurities in highly dispersed aerosols is also known. Evidently this effect becomes more marked as the degree of dispersion and therefore also the role of fluctuations are increased (as in the case of ultramicroheterogeneous liquid–liquid systems). This interpretation follows from the postulated universality of critical phenomena, and agrees well with the higher acidities observed in fog (up to pH 1.6) than in rain.[21] The assumption of fluctuations in critical phenomena allows us to predict other effects due to the development of fluctuations as the size of ultramicroheterogeneous particles is decreased: for example, a maximum in the absorption of CO_2 and SO_2 impurities during the condensation of superheated steam.[8]

5. Dependence of the solvent power of critical phases on the path to the critical state

A thermodynamic paradox, attributed to the 'nonclassicality' of critical phenomena, has been pointed out.[22] The effect of this paradox is that the thermodynamic state at the critical point is not uniquely defined by the conjugation of the available thermodynamic characteristics. This property of binary systems leads to several theoretical anomalies. As reported,[22] these anomalies are not experimentally accessible in liquid–gas systems, but it is thought that they could be observed near the liquid–liquid critical point in the case of two-component systems. We suggest that the ambiguity in the definition of the critical state by a conjunction of thermodynamic characteristics should produce a dependence of the properties of the critical phase on the path by which the critical point is approached.[8]

These dependences have been observed only in very dilute critical solutions. There are no reports of similar effects in concentrated solutions. One method of observing a dependence of the solvent properties of critical phases on the path by which these phases are produced is to study periodic colloid structures, whose composition and structure are known to depend on the method of preparation.[8]

Additional evidence for a dependence of the solvent power of a critical phase on its method of preparation is provided by the fluctuation theory of critical phenomena, according to which the partial derivatives of the concentration with respect to the chemical potential depend both on the degree of approach to the critical point and on the chosen path. In both cases we find a change in the critical index μ (see Anisimov's monograph[2]). Thus, if the critical point is approached by varying the concentration (φ) rather than the temperature the critical index for the surface tension, usually 1.26, takes the value

$$\frac{\mu}{\beta} \approx 3.9 \quad \text{and} \quad \sigma - \sigma_c \sim (\varphi - \varphi_c)^{\mu,\beta},$$

where β is also a critical index.

On the other hand if a concentration region to which the classical approximation applies exists at large distances from the critical point the deviation from the normal value at the critical point becomes less marked:[8,23]

$$\sigma - \sigma_c \sim (\varphi - \varphi_c)^3 \ln[(\varphi - \varphi_c)^{-1}].$$

This behaviour theoretically confirms the dependence of the solvent power of critical phases on the path by which the critical state is approached, since (as reported[10,24]) the σ values near the critical point are related to the solvent power of the critical phase and therefore also to the redistribution between phases. This allows the prediction of additional methods of exploiting the properties of the transcritical state of matter in extraction, separation, and concentration processes.

III. Pathways of transcritical superextraction

1. Superextraction through a noncritical interface

The simplest method of purification and deactivation of various solid surfaces is to use the universal solvent power of the critical phases. These extraction processes can be carried out both by using the macroscopic critical phase, corresponding to the end point of the equilibrium curve, and by relying on microscopic ultramicroheterogeneous lyophilic and lyophobic transcritical systems having a colloidal level of dispersion. Extraction is achieved by introducing into the system (in addition to the critical phase) another, noncritical interface which allows not only the removal but also the separation of the components to be extracted (see Fig. 1*b*). When the macroscopic critical phase is used this path is associated with the development of fluctuations in the volume between the two macroscopic subcritical phases which unite into a single critical phase under critical conditions.

A slightly different path to transcritical superextraction through a noncritical interface is also available: the creation of a critical extracting phase through microscopic critical phenomena in micellar ultramicroheterogeneous systems, in which we can observe the fluctuational erosion of the surface of the microscopic particles, ultimately leading to the fluctuational erosion of the interface between the dispersed phase and the dispersed medium. As in the case of extraction with ultramicroheterogeneous subcritical phases the processes of transcritical superextraction into ultramicroheterogeneous systems through a noncritical interface are usually not treated as subcritical. However, processes of this type are well known in membrane extraction processes in various types of emulsion, in which the formation of nanodispersions plays a controlling role.[25] Nanodispersions are formed with a change in the type of the phase transition on the surface of ultramicroheterogeneous particles, and as a result they not only stabilise a large number of emulsions but they also act as an extractant, able to control even the direction of the extraction process (in particular, they can lower the selectivity of the membrane extraction process in a multiple emulsion).

2. Fluid supercritical extraction processes

Fluid supercritical extraction processes[26] are among the most widely used methods of extraction through a noncritical interface into critical phases. Their main advantage is the ease of control through gradual changes in the gradient of the parameters of state and the physical nature of the extraction (which makes the process totally reversible). In supercritical fluid extraction from solutions the desired components can be isolated in a pure state. Control of the process (for example, the replacement of extraction by re-extraction) is carried out by gradually lowering the pressure, thus lowering the density of the fluid phase (upon which both the capacity and the selectivity of the fluid phase are strongly dependent).

Fluid supercritical extraction processes are used in the extraction, separation, and concentration of organic and of inorganic substances, in the purification of effluent waters, in the regeneration of adsorbents and catalysts, in the removal of toxic substances from soils, etc.[26] Because of the possibility of reagent-free re-extraction these processes offer a promising approach to the development of ecologically clean methods of separating and concentrating substances.[26] The most commonly used extractants are CO_2, ethane, and ethylene i.e. gases with a critical temperature close to 20 °C.[26-28] Other transcritical solvents have been suggested: for example, transcritical water vapour (classified[29] as a 'supersolvent').

Another feature of the fluid supercritical extraction process should be mentioned: in addition to having an anomalously high sensitivity to small changes in the parameters of state these processes are also anomalously sensitive to the presence of a third component (co-solvent) and to the chemical interaction (always quite weak) between the substance to be extracted and this component.[26-28] To produce an acceptable approximation to the experimental data in the physicochemical interpretation of the co-solvent effects in supercritical fluids we must allow for both the physical and the chemical components of the thermodynamic potential.[30] The addition of a co-solvent which interacts with the substance to be extracted can greatly increase the universal physical selectivity of the process as a result of the contribution from the specific chemical selectivity of the additive. If the active co-solvent is an alcohol (which is easily separated from the products) the complete reversibility of the process is retained since only the parameters of state (temperature and pressure) are varied. This feature is important from the point of view of developing technologies free from waste products. The use of fluid supercritical extraction in the technology of inorganic materials[31] (for example, for the separation of mixtures of liquid metals using inert gases as extractants) presents no theoretical difficulties. This would avoid the possibility of chemical decomposition of the extractant in work with very concentrated toxic or radioactive substances.

The extraction of inorganic salts (lanthanides and actinides) can be enhanced by modifying the extractant (CO_2) by additions of methanol with a selective complexing agent. Thus, in the fluid supercritical extraction of lanthanides and actinides from soils, the addition of co-extractants to the fluid superextractant has been suggested: these are compounds able to complex metal salts (dithiocarbamates, fluorinated β-diketones, tributyl phosphate).‡ It was found that tervalent lanthanides (La^{3+}, Eu^{3+}, Lu^{3+}), and also Th^{4+} and UO_2^{2+}, can be efficiently extracted from solid materials by using CO_2 modified by methanol and containing fluorinated β-diketones at 60 °C and 150 bar. It was also found that the addition of small amounts of water to the solid samples greatly increases the effectiveness of the extraction. A strong positive synergism is observed when tributyl phosphate is added together with β-diketones in the fluid supercritical extraction of lanthanides and actinides with CO_2 without modification by methanol. It is important to note that no synergism with tributyl phosphate is observed when the β-diketones do not contain fluorine substituents. Thus, chemical selective complex formation processes play a key role in the universal physical fluid superextraction, as in normal liquid–liquid processes. We note a serious shortcoming of these processes from the standpoint of their application to the extraction and concentration of radioactive substances: the need to work at relatively high pressures. In this context the application of superextraction processes near the critical conditions of liquid–liquid systems (which can be realised at atmospheric pressure) could be of interest.

3. Superextraction processes near the critical conditions for liquid–liquid systems

The possible realisation of supercritical extraction processes at atmospheric pressure near the critical conditions of liquid–liquid systems was theoretically substantiated,[32] and this was also predicted on the basis of the assumed universality of the properties of substances in the critical state.[33,34] More recently a maximum in the solvent power of a binary phase-separating liquid–liquid system near the critical consolute point was observed experimentally,[35] but none was found near the critical point of a ternary mixture.[32] It was shown[36] that the enhanced solvent power of liquid–liquid phases is associated with anomalous activity coefficients under critical conditions and is a universal property of critical phases. The universality is attributed to an increased compressibility. Because of the low compressibility of liquids near the critical phase separation point of a liquid–liquid system the concentration range of the subcritical conditions is very narrow, and therefore the practical possibilities of the method are problematic.[8]

Universal superextraction is more clearly seen in liquid–liquid systems in the case of phase transitions in micellar systems 'diffuse' in concentration, or in the case of abundant phase transitions close to the second kind, as in liquid–crystalline systems.[11,37] In these cases the extraction of substances by the critical liquid phases can reach enormous proportions (up to the complete homogenisation of the phases to be extracted). The increase in the homogenisation with increasing second-order properties of the micellar system (i.e. with decreasing micelle size) is illustrated in Fig. 2. A study of the extraction of uranyl benzenesulfonate by tributyl phosphate has shown[18] that the micellar–liquid-crystalline homogenisation of this system is physically reversible because of the reversibility of the hydration. As can be seen from Fig. 5 at high concentrations of uranyl benzenesulfonate the universality region (equality of the hydration and solvation numbers) disappears, the hydration

‡ See a recently published paper by C W Wai, Y Yen, and F Jean in *Pittsburg Conf. Anal. Chem. and Appl. Spectrosc., Chicago III, 27 Febr.–March 1994, Abstr.* (Chicago, 1994) p. 127

begins to predominate over the solvation, and the highly hydrated organic substance is no longer retained by the organic phase.

By combining the universal physical effects with specific chemical effects we can use the micellar extraction processes in separation and concentration experiments. Thus, the universality of the micellar extraction can be used for concentrating materials when the wanted component (aluminium) is held in the organic phase because of the formation of a complex between aluminium and the phenol–formaldehyde oligomer at the water re-extraction stage.[38] The formation of a complex with the phenol–formaldehyde oligomer in the same micellar extraction–re-extraction process allows gallium to be selectively concentrated and separated from aluminium.[39] Obviously the role of chemical reactions in processes of universal superextraction in liquid–liquid systems at atmospheric pressure is similar to the role of specific interactions with a co-solvent in the fluid supercritical extraction processes discussed above.

4. Universal superextraction processes through a subcritical interface

A new method of exploiting the special features of the transcritical state by using the redistribution of the components through a subcritical interface in the far subcritical region (see Fig. 1) is also of interest. These processes, so far observed only in phase-separating liquid–liquid systems, takes place when the system is moved away from the critical phase separation point, and are apparently unrelated to pretransition phenomena. However, for at least two reasons [the similarity in properties and composition of phases produced by the separation of one phase (usually the aqueous) and based on the same component (water)], these processes are related to the transcritical state of matter and they can be interpreted from this point of view. Detailed studies of three-phase extraction systems have been reported.[40–45] A new type of system, containing a third liquid phase similar in composition and properties to the equilibrium water phase, has been discovered. The third phase is found in ether(diisopropyl etc.)–aqueous hydrochloric acid systems containing metal chlorides both extractable and nonextractable by ether. It was shown[44] that the third phase is formed by the 'reversible extraction' of the ether into the aqueous phase by the hydrogen chloride in the form of the hydrated ether–HCl complex, which is poorly soluble in both water and ether. The second water phase formed under these conditions can extract all the components of the equilibrium water phase (without exception, but to different extents), including those which are poorly extractable or not extractable by ether. This accounts for the closeness of the system to the critical phase separation point.

5. Extraction in three-phase liquid systems near the critical homogenisation point of two of the phases

In this case the critical phase separation point for two subcritical phases is relatively far from the conditions of the experiment, which allows adequate selectivity in the extraction of the various components. For example, the distribution coefficients in the hydrochloric acid medium are greater than 200 for iron, 2–5 for tin and zinc, about 1 for cobalt, and less than 0.1 for nickel. The distribution and separation coefficients are markedly increased by the introduction of complex-formers. Thus, the formation of mixed metal–tin–chlorine complexes with hydrated ether allows the almost complete single-stage extraction of platinum, osmium, and iridium.[42,43] An analysis of these results[40–45] leads to the formulation of two principles of three-phase extraction equilibrium under subcritical conditions.

(1) The phase-forming component (poorly soluble in the phase-separating layer and insoluble or almost insoluble in the non-phase separating layer) becomes concentrated in the third phase, formed by the phase separation of one of the two liquid phases initially at equilibrium in the far subcritical region.

(2) The third liquid phase formed under the far subcritical conditions is an extractant for all the impurities of the separating phase.

The first principle explains the effects of forming a second aqueous phase and a second organic phase in extraction systems containing tributyl phosphate: the latter phase is well known as a concentrate of metal solvate ('red oil') in systems with uranyl nitrate and tributyl phosphate in a paraffin diluent. The extent of extraction of the components into the third phase through a subcritical interface in the far subcritical region is determined by universal physical effects and by highly selective chemical effects. It should be noted that the reported[40–45] enhancement of the extraction power and selectivity of the systems in the redistribution of the components between the phases is a consequence of the location of the system in the subcritical region. This property is independent of the presence in the system of a third (organic) phase, which plays no part in the separation processes.

A similar effect was noted in a study[46–48] of the increased extraction and separation in an extraction system consisting of two equilibrium aqueous phases one of which is strongly depleted of water by the addition of poly(ethylene glycol). In these systems the poly(ethylene glycol) acts not as an extractant but as a complex-former, which allows the formation of two aqueous phases having the same main component and similar compositions. The extraction is achieved by introducing complexing agents into the system. Supplementing the weak physical selectivity effects with clearly marked chemical effects produces results similar to those found in fluid supercritical extraction, but in this case the superextraction processes takes place in the subcritical rather than in the supercritical region.

6. Changes in the character of the phase transition during the redistribution between phases on the path to the critical point

According to Landau's views[1] on phase transitions of the first kind but close to the second, and to Fisher's postulate[49] of a continuous, purely entropic process leading to phase transitions in the critical state, we can formulate some conclusions on the type of changes in the nature of the phase transitions on the path to the critical point. If the redistribution between phases is treated as a phase transition of the first kind it should develop an increasing similarity to phase transitions of the second kind as the system approaches the critical point. The writer first proposed[13] (as a hypothesis) that the role of the entropy should increase along this path, and therefore in the equation

$$\Delta G = \Delta H - T\Delta S, \tag{6}$$

the enthalpic component (ΔH) of the change in the Gibbs free energy (ΔG) should tend to zero faster than the entropy component ($T\Delta S$). Therefore the plots of ΔH and $T\Delta S$ should converge into a single adiabatic curve. If this hypothesis is valid a region of adiabatic redistribution between phases should exist on the path to the critical point (as on the path to any phase transition of the second kind). In multicomponent two-phase systems this redistribution should show a maximum selectivity and a maximum sensitivity to small entropy differences between the redistributed components. In other words a region of adiabatic selectivity of the redistribution between phases should exist on the path to the critical point in multicomponent two-phase systems. The adiabaticity hypothesis was thermodynamically validated,[50] and the adiabaticity of weak phase transitions of the first kind was confirmed in terms of the classical theory of a two-phase flux near a liquid–gas critical point. By using a series expansion of the pressure near the critical point in powers of the difference between the time-dependent and the critical volume it was shown[51] that the equation for the phase equilibrium line coincides with the equation for the critical isentrope. This conclusion confirms the hypothesis of adiabaticity of the redistribution between phases, and it also explains the inconsistency between many experimental data and the adiabaticity hypothesis.

Thus, the specific heat λ-curves near the critical point are symmetrical because of the heat of the transition.[49] Critical solutions at infinite dilution are nonadiabatic.[3] This paradox can be resolved by noting that in a general derivation[51] the conclusion can be valid only if a region in which the classical theory of critical phenomena is applicable exists near the critical point. The classical theory of critical phenomena (region of low Ginzburg numbers) may be valid for conducting liquids[2] (solutions of electrolytes, liquid metals), and also for three-phase fluid systems[52] on the path to the tricritical point. Regions of subcritical adiabaticity of the redistribution between phases can exist only in these cases.[50]

The correctness of this conclusion is convincingly illustrated by considering the energetics of micelle formation. As we know, micelle formation is a weak phase transition of the first kind,[11] and therefore a decrease in the energy steps with temperature can be regarded as an increase in the criticality of the system. As can be seen from Fig. 6, as the criticality of the system is increased a tendency for the ΔG and $T\Delta S$ curves to merge into a single adiabatic curve is found only in electrolyte solutions. Thus the experimental data confirm the theoretical limitations to the possible existence of a subcritical adiabatic binodal.

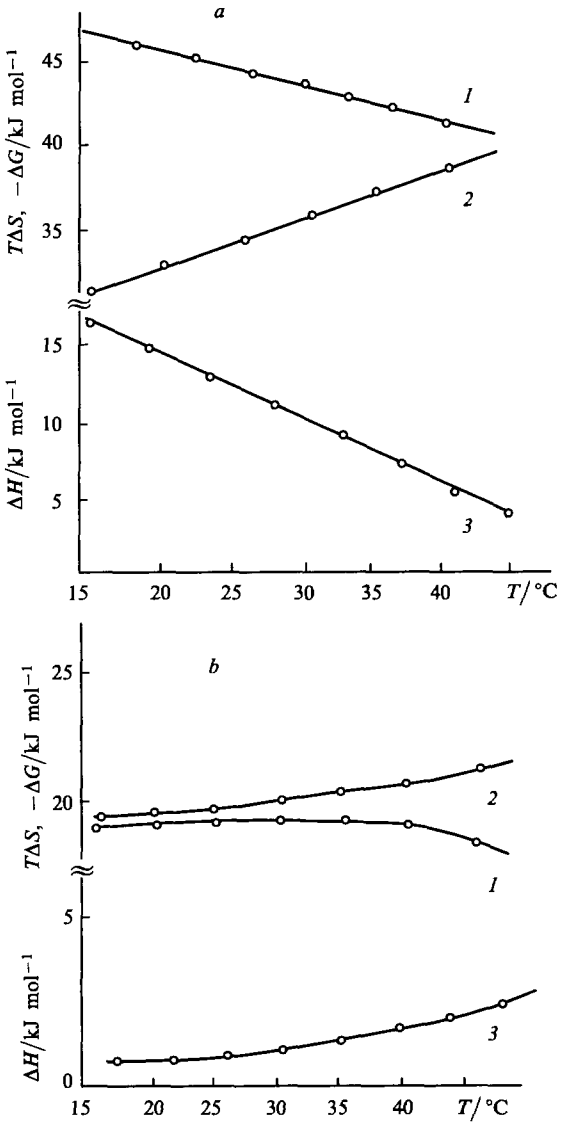


Figure 6. Temperature dependence of the trend towards adiabaticity of the micelle formation in aqueous solutions of nonionogenic SAS in the case of oxyethylated alcohol[53] (*a*) and dodecyltrimethylammonium bromide[54] (*b*): (*1*) $T\Delta S$, (*2*) ΔG, (*3*) ΔH.

7. Subcritical features of partial molar volumes and redistribution between phases

Proof of the existence of maxima in the subcritical selectivity follows from an analysis of the changes in the partial volumes on the path to the critical point. The relationship between extrema in the partial molar volume and in the solubility in critical phases was discussed above, including the simplest case of the solubility of a liquid in a gas.[7] For the far subcritical region it can be shown that because of the asymmetric location of the critical point relative to the coexistence curve we can expect extrema in the partial molar volume $\bar{v}$ and in the corresponding redistribution between phases.[50-55] As is shown in Fig. 7, in volume–composition coordinates the spinodal on the path to the critical point is tangential to a perpendicular to the composition axis at the point R. This point should correspond to an extremum in the partial molar volume $\bar{v}$. This statement becomes self-evident if in the condition for an extremum in the partial molar volume,

$$\left(\frac{\partial \bar{v}_2}{\partial x_2}\right) = 0,$$

$\bar{v}$ is replaced by the derivative of the chemical potential μ_2 with respect to pressure, and the order of the differentiation is changed,

$$\left(\frac{\partial \bar{v}_2}{\partial x_2}\right)_{P,T} = \left[\frac{\partial}{\partial P}\left(\frac{\partial \mu_2}{\partial x_2}\right)_{P,T}\right]_{x_2,T} = 0, \qquad (7)$$

(the subscript 2 denotes a dissolved substance). The condition (7) means that the $(\partial\mu_2/\partial x_2)_{P,T} = 0$ curves are independent of composition at the $\bar{v}$ extremum, i.e. they are tangential to a perpendicular to the composition axis. The spinodal $(\partial\mu_2/\partial x_2)_{P,T} = 0$ is a special case of these curves, and therefore it should also be tangential to the composition axis[50,55] at a point in the $\bar{v}$ extremum. This conclusion has a general thermodynamic significance: the extremum is due to the asymmetry in the position of the critical point on the binodal, and the asymmetry itself is a consequence of the failure of the critical points of the pure components to coincide. Furthermore, in liquid–liquid systems the critical points are usually located asymmetrically on

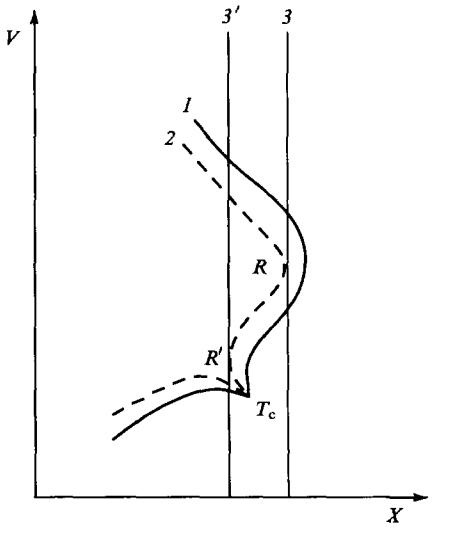


Figure 7. Asymmetry of the position of the critical point on the coexistence curve (*1*), making the spinodal (*2*) tangential to the perpendiculars to the composition axis in volume (V)–composition (X) coordinates at the extremal points R and R' in the far and the near subcritical region respectively (*3* and *3′* are the perpendiculars to the composition axes).[50]

the coexistence curve. The only exception is the rare case of a unit Hundt coefficient.[56] It is important to note that the solubility extrema are an individual characteristic of any binary system. Accordingly, in a multicomponent system the extremum points of the solvent power characterise the region of maximum selectivity in the solvent power of one phase with respect to the components of the other phase. This maximum is associated with the presence of extrema on the coexistence curve, and in general it can be located relatively far from the critical point, in the far subcritical region. However, the presence of extrema in the spinodal, at which the curve is tangential to a perpendicular to the composition axis in volume–composition coordinates (see Fig. 7), and its thermodynamic consequences regarding the distribution between phases, can be noted not only in the far but also in the near subcritical region, in which the theory predicts a singularity of the coexistence curve and of the associated spinodal.[57] The slope of the coexistence curve in the classical region near the critical point is one of the fundamental characteristics of any binary system.[58] The transition to universality (subcritical singularity) again confirms the validity of our proof of the presence of a maximum in the adiabatic selectivity of the subcritical redistribution between phases. The existence, under these conditions, of a region in which the spinodal is tangential to the perpendicular to the composition axis is a geometric necessity, as it is in the far critical region (see Fig. 7). Accordingly, in multicomponent two-phase systems two maxima in the subcritical selectivity should be found on the path to the critical point (in the far and in the near subcritical region respectively).[50]

8. Degree of generality of the predicted features of the transcritical selectivity of the redistribution between phases

According to Cahn[59] the bulk properties of the equilibrium phases in the subcritical region vary in the same sense as their surface properties. By developing and generalising this statement we may conclude that the regions of special features of the surface and of the bulk properties on the path towards the critical point are mutually related: in all cases the regions of changes in the wetting properties correspond to regions of adiabatic selectivity, and vice versa. In particular, in three-phase systems we should observe a maximum selectivity of the extraction into the wetting phase (for an adiabatic redistribution between phases) in the region of Cahn transitions from non-wetting to wetting of the α and β phases by the intermediate phase γ.

The general character of the predicted features is shown in Fig. 8. It can be seen that the curves describing the components of the thermodynamic potential for weak phase transitions of the first kind on the path to the critical path along the coexistence curve are in a symmetrical correspondence with the Nernst heat theorem.[60,61]

However, we should stress the fact that the generality of a subcritical adiabatic selectivity is limited to the case of classical subcritical fluids, i.e. to the existence (on the path to the critical point) of a region in which the classical theory of critical phenomena is applicable. The presence of two (rather than one) regions of subcritical adiabatic selectivity of the phase redistribution in multicomponent systems is also important. This assertion is also confirmed (in terms of the concepts considered here) by the experimentally observed sequence of Cahn transitions on the path to the critical point,[23] possibly related to the presence of several points of intersection of the ΔG and $T\Delta S$ curves in Fig. 8.

The regions of maximum separation (like the regions of the wetting transitions) can be far removed from the critical point along the coexistence curve. Thus, Cahn transitions have been observed several tens of degrees below the critical point.[23] By developing and generalising Cahn's views on the correspondence of surface and bulk properties, we may conclude that a well defined selectivity maximum with almost complete extraction of one of the components, and negligibly small extraction of the others, from the aqueous phase into propane has been observed in this region of Cahn transitions for the fluid extraction of various dyes in the presence of an aerosol of OT (sodium di-2-ethylhexylsulfosuccinate) at 25 °C, i.e. several tens of degrees from the critical point of propane (96.7 °C).[61] In this same region the homogenisation of the two-phase propane–OT aerosol–water system has been observed[62] under conditions which (like the selectivity conditions) depend strongly on the pressure. In this region we are dealing with physical superextraction, but since this superextraction takes place in a subcritical (rather than a critical) phase on the path to the critical point its universality is combined with universality of the maxima in the physical selectivity of the subcritical redistribution between phases whose existence has been predicted,[13] thermodynamically validated,[50] and experimentally demonstrated.[62]

The maximum in the selectivity of the phase redistribution through a subcritical interface into a transcritical region corresponds to the maximum in the selectivity of the extraction of the components of noncritical phases into a supercritical phase through a noncritical interface, i.e. under conditions of normal fluid supercritical extraction (Fig. 9). The existence of this maximum is illustrated in Fig. 9 for the fluid supercritical extraction of terpenes by carbon dioxide.[63] We note that in every case the selectivity maxima are located on the path to the critical path but not in its immediate vicinity. The presence of selective extraction in the region of the pretransition phenomena discussed in modern theories would be fundamentally incompatible with the modern theory of critical phenomena, one of whose main conclusions is the universality of the properties of matter

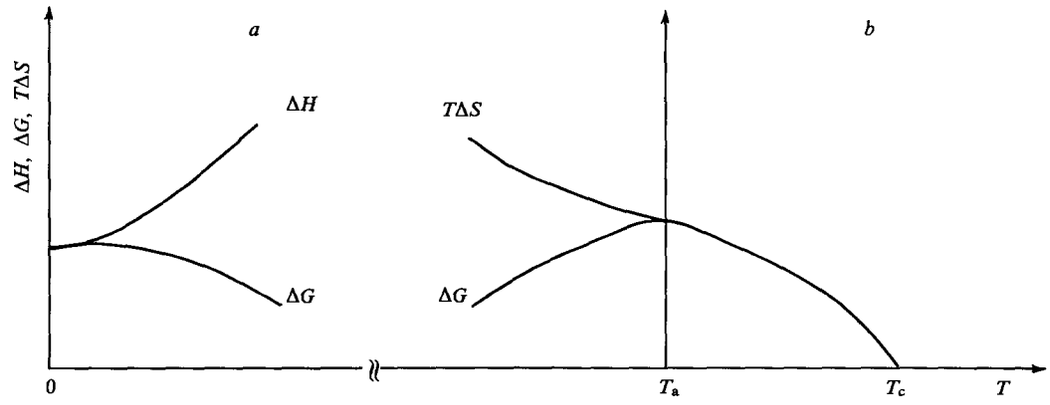


Figure 8. Symmetry of the Nernst heat theorem (*a*) and of the universal subcritical adiabaticity of the redistribution between phases in classical subcritical fluids (*b*). T_c is the critical temperature, T_a is the temperature of the transition to adiabaticity.

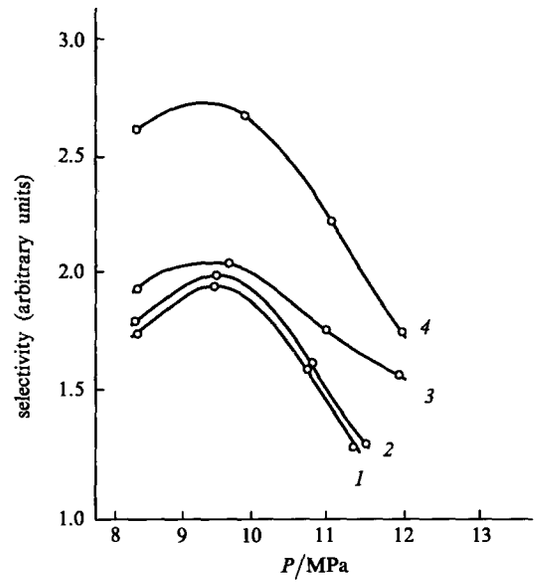


Figure 9. Selectivity in the supercritical region against pressure at different temperatures for the extraction of terpenes by CO_2 (see Ref. 63). (*1*) 40 °C, (*2*) 50 °C; (*3*) 60 °C, (*4*) 70 °C.

under these conditions. This conclusion has been confirmed experimentally[64] by showing that in equilibria between critical and ordinary phases dissolved substances are found in the phases in the same proportions. Another important conclusion is that in both regions of maximum transcritical selectivity (subcritical and supercritical) weak manifestations of universal physical selectivity can be enhanced by marked specific (chemical) effects due to selective complex formation. This is observed also in well known fluid supercritical extraction processes, and in recently described fluid subcritical superextraction processes.

IV. Possibility of subcritical selectivity in ultramicroheterogeneous systems

To conclude this phenomenological discussion of the features of transcritical superextraction we shall make one more observation concerning ultramicroheterogeneous subcritical systems. Wetting transitions accompanied by adiabatic and highly selective redistribution between phases should be found also in ultramicroheterogeneous liquid – liquid and liquid – gas systems on the path to a 'pure' phase transition of the second kind. Indeed, as long as the concept of an interface is meaningful in an ultramicroheterogeneous system it can be treated as a nominal 'wall' (C) with an equilibrium angle of contact, to which Young's law applies:

$$\sigma_{1,2}\cos\theta = \sigma_{1,3} - \sigma_{2,3}. \tag{8}$$

Following Cahn's approach[59] we shall assume that on the path to a 'pure' phase transition of the second kind the different between the interfacial energies $(\sigma_{1,3} - \sigma_{2,3})$ is determined mainly by the compositions of the equilibrium phases (J), and is dependent on temperature as is $(\varphi_2 - \varphi_1)$, i.e. in accordance with the universal scaling relation

$$(\varphi_2 - \varphi_1) \sim t^{\beta}, \tag{9}$$

where β is the critical index, equal to 0.33. On the path to a phase transition of the second kind, as on the path to the critical point, we can use the universal relationship

$$\sigma_{1,2} \sim t^{\mu}, \tag{10}$$

where μ is the critical index, equal to 1.26. From (8) – (10) we find

$$\cos\theta \sim t^{(\beta-\mu)}; \quad \beta - \mu = -0.93. \tag{11}$$

According to Eqn (11) the maximum wetting in a ternary two-phase ultramicroheterogeneous system should be observed at some distance from the phase transition of the second kind, i.e. on the path towards the phase transition, as in the wetting transitions on the path to the critical point in Cahn's original work.[59]

We can arrive at the same result by treating any third component as a nominal 'wall'. In this case on the path to a 'pure' phase transition of the second kind we find a maximum in the wetting of this component, and therefore also a maximum in the adsorption of its ultramicroheterogeneous particles. Since (at least, in three-component systems) the wetting phase is thermodynamically unstable (allowing for possible changes in the masses of the phases) it acts as the extracting phase. The combination of the maximum wetting and the maximum sorption points for various components defines the region of maximum selectivity.[50] Under these conditions the phase redistribution should be approximately adiabatic. In particular, this should be observed near adiabatic micelle formation transitions (see Fig. 6*b*).

V. Chemical reaction in the extractant phase and supercritical extraction into this phase

1. Chemical reaction and the critical phase

As reported,[3] in a critical solution in CO_2 at infinite dilution the apparent constant of the chemical dimerisation reaction ($2NO_2 = N_2O_4$) in the critical phase increases, and tends (if not to infinity) to a finite nonzero value. The thermodynamic dimerisation constant is expressed in terms of the chemical potentials, and therefore it cannot have singularities at the critical point (since the chemical potentials can have singularities only in their higher derivatives[2]).

A similar statement applies to the experimental data (discussed by Tveecrem et al.[65] and interpreted by this author[36]) on the dimerisation of nitrogen dioxide near the liquid – liquid critical point in the perfluorocyclohexane – carbon tetrachloride system. These data suggest the presence of singularities in the activity coefficients under critical conditions. It was shown that the data,[65] however interpreted, confirm the presence of superextraction in the liquid – liquid system near its critical phase separation point. On the other hand the apparent decrease in the rate constant of the chemical reaction under critical conditions is associated not only with anomalies in the activity coefficient but also with the tendency of the diffusion coefficients to vanish under critical conditions.[66]

Thus in micellar systems, in which criticality (fluctuation) conditions are found on the micelle surface rather than in the bulk of the phase, we observe an acceleration of chemical reactions ('micellar catalysis'[67,68]). But the problem of correlating chemical reactions and phase transitions has also other aspects. Thus, the polymerisation of sulfur in many organic solvents leads to the appearance of a new critical phase separation point.[69] Chemical reactions have a similar effect on phase transitions in H-bonded systems. Corrales and Wheeler[69] have examined theoretically other possible types of interaction between chemical reactions and phase transitions (not yet observed experimentally), in which the reaction acts as the driving force of the phase transition.

The possibility of stabilising (or, more strictly, metastabilising) the critical state by inducing a relatively slow chemical reaction in the homogeneous metastable critical phase has been pointed out.[70]

2. The chemical reaction as a weak phase transition of the first kind

The most interesting aspect of the interaction between chemical reactions and phase transitions of the second kind (or critical phenomena) is seen by treating the chemical reaction in the vicinity of the position of equilibrium (the equivalence point) as a

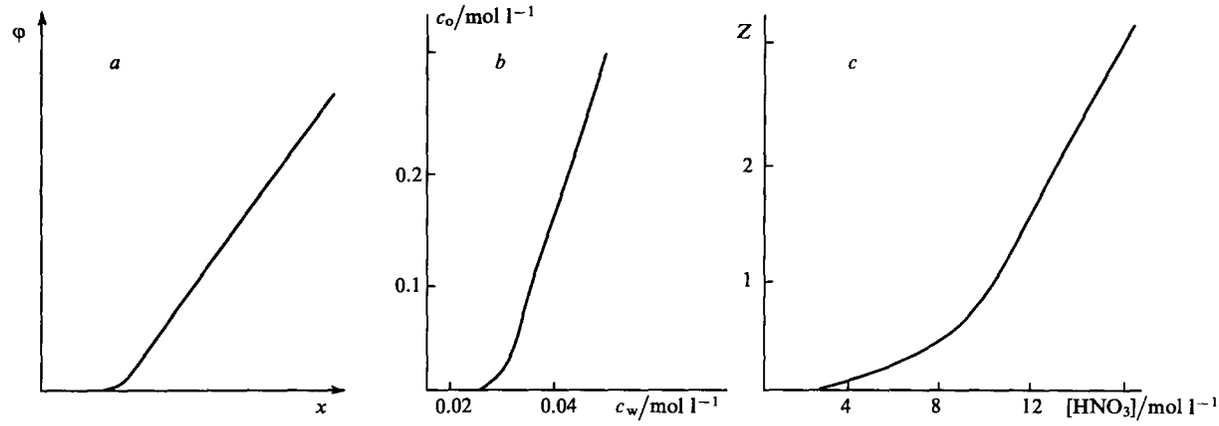


Figure 10. Plots of the concentration of monomers combined into micelles (φ) against the total concentration of monomers x (*a*); of the concentration of copper in the organic phase against its concentration in the aqueous phase in the micellar extraction by tetrachloromethane (*b*); of the concentration ratio of nitric acid and the tributyl phosphate solvate of uranyl nitrate in the organic phase (Z) against the concentration of nitric acid in the aqueous phase in the extraction of nitric acid into the tributyl phosphate solvate of uranyl nitrate (*c*). *a* and *b* from Ref. 11, *c* from Ref. 76.

weak phase transition of the first kind or as a special type of phase transition with marked second-order features. This problem has been examined theoretically[71,72] for the simplest one-dimensional model by studying reactions of the type

$$A \rightarrow X,$$

$$B+X \rightarrow Y+D,$$

$$2X+Y \rightarrow 3X_1,$$

$$X \rightarrow E.$$

It was assumed that the reactions take place near the equilibrium position. Features of transitions of the second kind were detected in the reactions by the reduced perturbation method.

By using Landau's theory it was shown[73] that a chemical reaction can be treated as a phase transition of the second kind even in regions far from equilibrium.

Published data on the superextraction by micellar liquid–crystalline alkylphenol phases at neutral pH values of all the components of conjugated phases are consistent with these theoretical considerations, according to which any manifestation of transitions of the second kind should lead to superextraction in the phase. These results were interpreted[10,11,17] as an indication of supercritical extraction at atmospheric pressure. It was also shown[74,75] that the extraction by metal solvates with tributyl phosphate and other organic extractants produces superstoichiometric supersaturation of the organic phase. The same workers[74,75] have treated the extraction of nitric acid by tributyl phosphate as a physical phenomenon. Rozen and Andrutskii[76] have pointed out the weakness of these conclusions[74,75] on the dimerisation of nitric acid in an organic phase. The formation in the organic phase of mono-, di-, tri-, and tetrasolvates of nitric acid was postulated in order to explain the observed phenomena. However, in this variant four empirical constants are needed to account for the almost linear extraction isotherm (without any indication of saturation) inferred[76] from the published data[74,75] for the dependence of the extraction of nitric acid into the tributyl phosphate solvate of uranyl nitrate on the concentration of nitric acid in the aqueous phase. But it has been shown[10] that similar isotherms without any indication of saturation are observed for micelle formation described as a phase transition of the second kind,[77] and also in the micellar extraction of copper dibutyl phosphate by tetrachloromethane.[10,18]

It can be seen from Fig. 10 that the special features of micelle formation, micellar extraction, and extraction by metal solvates are similar: the extraction into the organic phase shows no sign of saturation (i.e. of a horizontal asymptote for the isotherm). The micelle formation isotherm observed as a phase transition of the first kind which is close to the second kind has exactly the same shape. This experimental fact agrees well with the assertion[78] that many phenomena traditionally treated as chemical are in fact physical effects (in this case effects of universal physical superextraction at atmospheric pressure). The mechanism of this process is still unclear: is it due to a transition of the second kind or (as suggested[79]) is it an experimental observation of anisotropy in the solvates, caused by liquid-crystalline transitions? In any case it is clear that we are dealing with supercritical extraction at atmospheric pressure, but if this extraction is induced by second-order features of a chemical reaction the extractant can be any solvate or other chemical compound in the organic phase, and salts of any metal can be the extracted salts. On the other hand if the superextraction takes place because of the second-order properties of liquid-crystalline transitions only mesogen molecules can be the extractants.

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Regularities in the concentration and separation of surfactants in a foam

T N Khaskova, P M Kruglyakov

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Abstract. The theoretical and experimental studies devoted to the regularities of foam adsorption concentration and separation of substances occurring in the liquid phase in molecular, ionic, or micellar form are surveyed. The main characteristics of foam concentration and separation, their analytical dependences on the structural parameters of the foam, and their interdependences are analysed. Quantitative relationships for the characteristics of foam separation with due regard to the influence of foam destruction have been obtained. The dependences of the concentration coefficient on the expansion factor and dispersity of the foam and also on the capillary pressure in polyhedral (dry) foams prepared from solutions of individual surfactants and their mixtures are analysed. The reasons for concentration restrictions (upper and lower limits) of the foam concentration method are discussed. Examples of partial separation of surfactants in a foam and foam chromatography are considered. Brief information on equilibrium displacement and acceleration of chemical reactions in a foam is presented. The bibliography includes 77 references.

I. Introduction

Surface separation and concentration of substances comprise a group of related processes based on the regularities of adsorption and wetting. The longest used and best known among these processes is foam flotation. There exist several methods for the concentration of minerals based on flotation. According to one of these, mixtures of solid particles of various natures and degrees of dispersity are dispersed in an aqueous suspension by a gas. As this takes place, hydrophobic particles adhere to the rising bubbles, while hydrophilic particles remain in the bulk. Another method involves pumping of a suspension being separated onto a foam. This flotation process was called[1] foam separation. In the oil flotation process, drops of an emulsion to which ore particles adhere are used instead of gas bubbles. In the case of film flotation, the crushed ore is poured onto a constantly moving water surface; the easily wetted particles sink, while the poorly wettable ones remain at the surface and are then collected with the aid of a special device. A similar principle of flotation, but involving other properties of collecting agents, is also used for separation of drops of the organic phase from dilute emulsions, specifically, for the purification of waste water from oil impurities.

During the last two decades a large number of studies have been reported (see, for example, Refs. 2—6) on nonchromatographic methods of surface separation of dissolved substances (molecules and ions) and highly dispersed particles (colloids and other small particles), to which the regularities of normal flotation are inapplicable. Among these methods are isolation of ions, surfactants, proteins, dyes, and other organic compounds, colloidal particles, and microorganisms. Surfactants can be extracted from a solution or separated from each other (if in a mixture of surfactants) owing to different degrees of adsorption of components. In order to extract inactive components (in particular, ions), one should use collecting agents, which increase the ability of compounds to concentrate at the surface. The most frequently used collecting agents are diphilic compounds. Mechanisms of the action of these compounds are varied and depend on the type of species being extracted (ions, proteins, or colloidal particles). For example, ionogenic surfactants with high surface activities are typical collecting agents in the flotation of ions and molecules. As a result of ion exchange, the collecting agent attracts the substance being extracted (colligend) to the surface and forms an insoluble surface active compound with it (for example, iron ions can replace sodium ions in an anionic surfactant). This ion exchange reaction occurs most frequently in the bulk solution. In this case, the collecting agent acts as a precipitant that participates in the formation of a hydrophobised poorly soluble compound (sublate) in the bulk of the dispersive medium.

The processes of surface separation of dissolved compounds and particles of a colloidal degree of dispersion have been classified according to various criteria:[2–5] the substances being isolated (electrolyte ions, surfactants, organic compounds with high molecular weights, colloidal particles, microorganisms, etc.);[4] the type of particles in the composition of which the colligend is collected; the aggregative state of the phase in which the particles being flotated are collected; the type of interaction (binding) of the collecting agent with the compound being extracted, and according to other criteria.

T N Khaskova, P M Kruglyakov Department of Chemistry, Penza State Architectural and Building Institute, ul. Titova 28, 440028 Penza, Russian Federation, Fax (7-841) 262 04 10

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The methods of surface separation are named differently in various papers: in the case of extraction of surfactants they have been referred to as adsorption flotation,[2] foam flotation,[3] foam in fractionation, foam separation, or adsorption concentration,[5] and in the case of extraction of ions, the methods of ion flotation,[2] foam flotation of hydrophobic precipitates, etc. have been reported.

All these methods have many common features, but, at the same time, they are noticeably distinct. For example, in foam flotation of macroscopic particles (suspensions), separation is governed by wetting and adhesion and involves the step of the water–particle–gas three-phase contact; the concentration and separation of surfactants in a foam are determined by the adsorption ability, the rate of diffusion of the surfactant, and the properties of the foam (especially its stability). The principle of accumulation of substances at a surface and similarity of the equipment should be considered to be common features of these processes.

In the present review we shall restrict ourselves to the analysis of the foam method of concentration and separation of compounds that exist in solution as ions, molecules, or micelles (without formation of dispersions or precipitates). This method is based on the regularities of adsorption and the properties of a stable foam. The adsorption-bubble separation without foam formation, as well as flotation extraction and ion flotation with accumulation of a thin layer of the hydrophobic product at a surface, are outside the framework of our present review.

Depending on the purpose of foam separation, it will be referred to as adsorption foam concentration (separation of dissolved species from the solvent) or foam separation (in the case of partial or complete separation of dissolved species from one another).

II. Characteristic features of the adsorption concentration of surfactants in a highly expanded polyhedral foam and methods for determining its structural parameters

Concentration of surfactants in a foam occurs due to their adsorption on the bubbles of the gas, which is passed through a layer of the solution, followed by the separation of the foam from the solution. This process can be either batch or continuous. The surface separation is mostly achieved due to the single-stage distribution of compounds between the bulk phase and the surface layers of foam bubbles. Transformation of a gas dispersion into foam is accompanied by segregation of the excess liquid from the latter (syneresis of the foam), which brings the composition of the foam product closer to that of the adsorption layers, by the change of the spherical shape of bubbles into polyhedral, by a partial internal destruction of the foam (a decrease in the liquid–gas interface due to coalescence of bubbles and diffusional transfer of gas from small bubbles into larger ones), and by distribution of the foam column as a whole. Desorption of the surfactant from the vanishing surfaces results in an increase in its concentration within the Plateau–Gibbs† channels and in three-dimensional parts of the films. Syneresis of a foam results in additional adsorption of the surfactant at the surface of bubbles lying below, and where several surfactants are present, because the desorption-adsorption event is repeated many times, some redistribution of the surfactants with height and in an increase in the lifetime of the foam occurs.

The return of the liquid phase partially enriched in the surfactant into subsequent portions of the foam is called internal dephlegmation. Its contribution to variations of the effectiveness of the concentration and separation becomes substantial at low concentrations of surfactants [below the critical concentration for micelle formation (CCM)].

The adsorption concentration is normally carried out under the conditions of the gravity separation of the liquid from the foam.[2–4,6] The equipment used in these processes has been described in detail in a number of monographs.[2–4,6] A method for the adsorption concentration of surfactants under the conditions of accelerated and more complete drying of foams by creating a pressure differential in the liquid phase of a foam and the corresponding high capillary pressure in the Plateau–Gibbs channels in the course of the liquid separation, has been suggested in a series of papers.[7–10]

The use of polyhedral foams for the processes of adsorption concentration and separation increases the effectiveness of the latter. The relative simplicity of the geometry of the Plateau–Gibbs channels and films (compared with a nonpolyhedral foam) allows one to obtain quantitative dependence of various characteristics of the adsorption concentration on structural parameters of a foam (expansion factor, dispersity, size of the channels).

Below we present technological features of concentration and separation of surfactants carried out under the conditions of capillary drying of a foam and also some characteristics of 'dry' foams.

For preparation of a highly expanded dry foam by the capillary method, a foam is brought into contact with a porous plate, beneath which a reduced pressure P_0' is created (see Refs. 11 and 12). The pressure differential

$$\Delta P = P_0 - P_0',$$

(P_0' is the external pressure above the foam; usually, ambient pressure) should not exceed the capillary pressure in the pores of the filter

$$\Delta P_m = \frac{2\sigma \cos\theta}{r},$$

(where σ is the surface tension of the solution; θ the contact angle of wetting of the material of the filter; r the radius of a pore),‡ otherwise not only the liquid, but also the gas, would pass through the pores of the filter.

Under the action of the pressure differential in the liquid phase of the foam, the liquid quickly flows out until this differential is equilibrated by the capillary pressure in the foam. The porous partitions can be made of ceramics, metal ceramics, or glass, or be dense grids.

The increase in the expansion factor and in the capillary pressure in a dry foam is accompanied by the simultaneous decrease in the stability of the foam and increase in the time necessary for the equilibrium capillary pressure, corresponding to the pressure differential applied, to be established. Therefore, the optimum pressure differential, which will ensure the necessary expansion factor of the foam and a lifetime sufficient for its technological processing, should be selected experimentally.

The scheme of a laboratory unit for investigating the adsorption foam concentration in the continuous regime is presented in Fig. 1.

Separation column (*1*) is a vertical cylinder placed in a temperature-controlling jacket (*2*); in the bottom of the column there is a gas dispenser, viz. a removable glass filter (*3*), which allows gas dispensers of various porosities to be applied. In the lower section of the column there is also a cock (*4*), which serves for withdrawing samples of the solution subjected to separation. In the upper section of the column a number of holes are situated at various levels with respect to the solution surface (*5*–*7*) for the egress of the foam and for disposition of electrodes (*8*) and a capillary micromanometer (*9*), which measures pressure in the Plateau–Gibbs channels. The foam is dried with the aid of a cartridge filter (*10*), which is a metal frame covered with a

† Plateau borders in Western literature (Editor).

‡ If there are pores with different radii, the greatest one is meant.

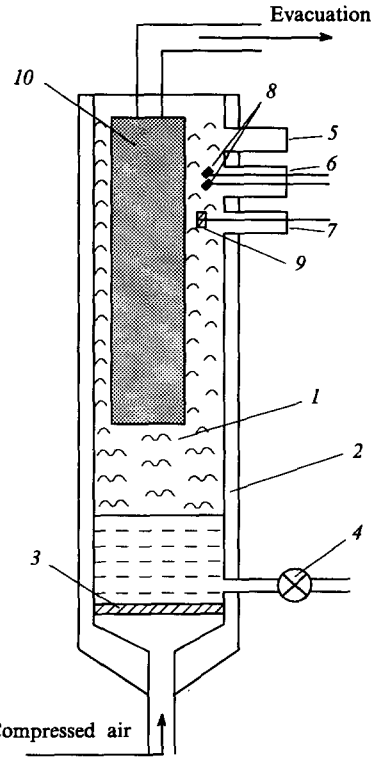


Figure 1. The scheme of a laboratory unit for adsorption concentration in 'dry' foams. (*1*) A separation column; (*2*) a temperature-controlling jacket; (*3*) a removable glass filter; (*4*) a cock for withdrawing samples of the liquid; (*5–7*) holes for the egress of the foam; (*8*) platinum electrodes; (*9*) a micromanometer; (*10*) a cartridge filter.

metallic grid having a mesh of 60 μm. A cylinder smaller in diameter than the column acts as the cartridge. It occupies 1/3 of the height of the column and is located 5–15 cm above the level of the liquid. A reduced pressure (ΔP_L = 1.0 – 2.0 kPa) of no more than the capillary pressure in the pores of the filter (grid) is produced within the cartridge. Under the action of the pressure differential, the liquid from the foam is drawn off into the cartridge. The liquid that finds its way into the cartridge is collected in a glass sampler, which makes it possible to determine the surfactant concentration and to evaluate the losses. Hereafter this liquid will be referred to as 'filtrate'.

It should also be noted that a dry polyhedral foam is very sensitive to external factors, including the rate of its movement and the diameter of vessels and tubes in which it moves. Special rheological studies§ have shown that intense destruction of a foam occurs at expansion factors of more than 300 even when the foam moves in the sliding mode (piston mode). For this reason, in the case of continuous drying of a moving foam the coefficient of the concentration of a surfactant is lower than in the case of a stationary foam in a batch-operating unit, the pressure in the Plateau–Gibbs channels being the same.[7,8]

A major part of the physicochemical characteristics of foam concentration correlates quantitatively with the expansion factor and dispersity of the foam. The expansion factor of a foam (n) characterises the volume proportion of liquid in the foam:

$$n = \frac{V_F}{V_{L,F}}, \tag{1}$$

where V_F is the volume of the foam and $V_{L,F}$ is the volume of liquid in it.

§ See, for example, P M Kruglyakov, T V Meshkova *Kolloidn. Zh.* **52** 487 (1990).

To determine the expansion factor, especially of dry foams, the conductometric method is most commonly used,[1,8,9] as

$$n = \frac{\kappa_F}{\kappa_L B}, \tag{2}$$

where κ_F and κ_L are the specific electric conductivities of the foam and the solution of a foam-forming agent respectively, B (= 1.5 to 3) is a coefficient depending on the distribution of the liquid between the channels and films.[13–15] For a polyhedral foam with a purely channel conduction mechanism, where the liquid in films may be neglected, $B = 3$, and for a foam with a film conduction mechanism, where the contribution of channels may be neglected, $B = 1.5$ (see Ref. 14).

Analysis of experimental data carried out by Lemlich[14] has shown that the coefficient B increases monotonically from 1.5 to 3 as the expansion factor increases from 4 to 200, and that the experimental data obtained for bubbling foams are well approximated by the relationship

$$B = 3 - 2.5\left(\frac{\kappa_F}{\kappa_L}\right)^{1/3} + 0.5\left(\frac{\kappa_F}{\kappa_L}\right). \tag{3}$$

Characteristics of foam concentration depend substantially on the dispersity of the foam,[2–6] for which a variety of methods exist for its determination, for example, microphotography, an optical method, a method based on the measurement of the gauge pressure after destruction of the foam, and others (for details, see Refs. 5, 16, and 7).

A method based on the simultaneous measurement of the local expansion factor and the pressure in the Plateau–Gibbs channels at the same level in a foam[18] is very convenient for kinetic studies of the variation of the dispersity in highly expanded foams. The expression used is

$$a = (0.46\sqrt{n} - 1.8)\frac{\sigma}{\Delta P_L}, \tag{4}$$

where a is the size of the edge of a polyhedron (from here on, a dodecahedron), n the expansion factor of the foam at a given instant τ, σ the surface tension of the foam-forming solution, and ΔP_L the gauge pressure measured by a micromanometer at time τ.

Relationship (4) is obtained by simultaneous solution of the equation that relates the expansion factor to the size of the edge of a polyhedral bubble and to the radius of curvature of the Plateau–Gibbs channels and the dependence of the capillary pressure on the surface tension of the solution and the gauge (reduced) pressure in the channels.[5] Eqn (4) is valid for a monodisperse foam. A real foam is a polydisperse system. The dispersity of such a system can be expressed quantitatively via average values for size, surface area, and volume of particles. These average values can be determined from the known function of size distribution of bubbles. Then the average linear (a_L), average surface (a_S), and average volume (a_V) magnitudes of the parameter a will be expressed by the relationships

$$a_L = \int_0^\infty F(a)a\,da, \tag{5}$$

$$a_S^2 = \int_0^\infty F(a)a^2 da, \tag{6}$$

$$a_V^3 = \int_0^\infty F(a)a^3 da, \tag{7}$$

where $F(a)$ is the size distribution function for bubbles.

From Eqns (5)–(7) the volume–surface averaged parameter a may be written as follows[19]

$$a_{VS} = \frac{a_V^3}{a_S^2} = (0.46\sqrt{n} f_a' - 1.8)\frac{\sigma}{\Delta P_L} , \quad (8)$$

where

$$f_a' = \frac{a_V^{3/2} a_L^{1/2}}{a_S^2} .$$

To calculate the coefficient f_a', taking into account polydispersity of the system, we used various functions suggested as distribution functions for foams.[5] It turned out that the resulting values of the parameter differ from each other by no more than 5%. For example, when the de Vries[20] function,

$$F(R) = \frac{6\alpha R}{(1+\alpha R^2)^4} \quad (9)$$

(α is the distribution parameter), or the γ-function,

$$F(R) = cR^{\alpha-1}\exp(-\lambda R) , \quad (10)$$

(α and λ are distribution parameters selected from normalisation conditions

$$\int_0^\infty F(R)\mathrm{d}R = 1) ,$$

was taken as the distribution function, the resulting values of the coefficient f_a' were 1.15 and 1.14 (at $\alpha = 2$ and 3, respectively) for the γ-function and 1.16 for the de Vries function.

In the discussion of experimental data throughout the subsequent sections of the review we have used the volume–surface averaging of the parameter a based on the de Vries distribution function.

III. Characteristics of the effectiveness of concentration, separation, and purification of solutions of surfactants

The process of foam separation of surfactants is used for solving various problems: the concentration of surfactants in a foam aimed at their extraction or at purification of the solution from the surface active impurities; complete or partial extraction of one of the components or fractionation of surfactants for the purpose of separating them from each other; displacement of a chemical equilibrium in the foam with respect to the initial solution, for example, to increase the degree of hydrolysis of a soap.

To evaluate the effectiveness of foam separation processes, various physicochemical characteristics are used, for example, the degree of extraction, concentration coefficients, selectivity coefficient, carry-over of the liquid, etc.[2, 21, 22]

Distribution of a surfactant between a foam and a solution is characterised by the coefficient (constant) of concentration (R^f). The small (R_{min}^f) and large (R_{max}^f) coefficients of concentration are distinguished:[2,4,5,26]

$$R_{min}^f = \frac{c_F}{c_{L,0}} , \quad (11a)$$

$$R_{max}^f = \frac{c_F}{c_{L,R}} , \quad (11b)$$

where c_F is the surfactant concentration in the foam including the substance of the adsorption layers; $c_{L,0}$ and $c_{L,R}$ are surfactant concentrations in the solution prior to and after the process. Equations connecting the coefficient of concentration to parameters of the foam structure (dispersity, expansion factor, and the radius of curvature of the Plateau–Gibbs channels) can be derived from the balance equations for the surfactant and the liquid phase, and data on the foam structure.

The total amount of a surfactant in a foam (G_F) is given by

$$G_F = G_L + G_S = V_{L,F}\, c_{L,F} + \Gamma_S , \quad (12)$$

where G_L is the amount of the surfactant in the liquid phase of the foam (channels and films) without considering adsorption layers, G_S is the amount of the surfactant in adsorption layers, $V_{L,F}$ the volume of the liquid phase of the foam, $c_{L,F}$ the concentration of the surfactant in the liquid phase of the foam, S the total interfacial area in the foam, and Γ the degree of adsorption.

The total concentration of the surfactant in the foam is

$$c_F = \frac{G_F}{V_{L,F}} = c_{L,F} + \frac{\Gamma S}{V_{L,F}} . \quad (13)$$

On the one hand, if one considers a unit volume of the foam containing υ bubbles of radius R, then the total interfacial area in this foam is $S = \upsilon 4\pi R^2$, and the volume of gas bubbles is

$$V_g = \upsilon\frac{4}{3}\pi R^3 .$$

On the other hand, $V_g = 1 - V_{L,F}$, therefore

$$\upsilon = \frac{3(1 - V_{L,F})}{4\pi R^3} .$$

Taking into account the number of bubbles, we have

$$\frac{S}{V_{L,F}} = \frac{3(1 - V_{L,F})}{RV_{L,F}} = \frac{3(n-1)}{R} . \quad (14)$$

From Eqn (11a) with allowance for (13) and (14) we obtain

$$R_{min}^f = \frac{c_{L,F}}{c_{L,0}} + \frac{3\Gamma(n-1)}{c_{L,0}R} . \quad (15)$$

Rubin and Gaden,[22] who assumed that $c_{L,F} = c_{L,0}$ and that the liquid volume in the foam can be neglected in relation to the total volume of the foam, derived a relationship for the concentration coefficient:

$$R_{min}^f = 1 + \frac{k\Gamma n}{Rc_{L,0}} , \quad (15a)$$

where k is a geometric coefficient for the shape of bubbles ($k = 3$ for a spherical foam and $k = 3.3$ for a polyhedral foam of the pentagonal dodecahedron type). However, the $V_{L,F}$ value for a spherical foam is substantial and amounts to 48% of the total foam volume for simple cubic packing and 26% for hexagonal close packing; the expansion factor varies at these packings from 2.01 to 3.85, which may introduce large errors into the calculations of the numerical value for R_{min}^f. In a polyhedral foam the volume of liquid may be neglected in comparison with the foam volume, but for determination of $R_{min}^f(n)$ more detailed information on the structure of the foam is required.

The ratio of the interfacial area to the volume of liquid in a foam can be expressed via unit cell parameters of the foam. If a pentagonal dodecahedron is taken as the unit cell, this ratio will be[5]

$$\frac{S}{V_{L,S}} = \frac{20.7a^2}{6\times 1.725\, a^2h + 10\times 0.16\, r^2a} = \frac{20.7a^2}{10.35\, a^2h + 1.6\, r^2a} , \quad (16)$$

where $20.7a^2$ is the area of the dodecahedron surface, 6 and 10 are the numbers of films and channels that belong to one polyhedron, $1.725a^2$ is the area of a dodecahedron face (a film), h the thickness of the film, $0.16r^2$ the cross-section area of a channel of curvature radius r.

From Eqn (11a) and relationships (13) and (16), formulae can be derived for calculating concentration coefficients at various distributions of liquid between the channels and the films.

For the film model of foam (where all the liquid is located in the films, $10.35a^2h \gg 1.16r^2a$) the concentration coefficient R^f_{min} is

$$R^f_{min} = \frac{c_{L,F}}{c_{L,0}} + \frac{2\Gamma}{hc_{L,0}} . \quad (17)$$

For the channel model of foam (where all the liquid is located in the channels, $10.35a^2h \ll 1.16r^2a$), with allowance for the fact that the foam expansion factor for this model is

$$n = \frac{7.66\,a^3}{1.6\,ar^2} = 4.8\frac{a^2}{r^2} ,$$

the concentration coefficient is given by

$$R^f_{min} = \frac{c_{L,F}}{c_{L,0}} + \frac{\Gamma n}{0.37\,c_{L,0}a} . \quad (18)$$

If the radius of curvature of the Plateau–Gibbs channels is expressed in terms of the capillary pressure $R = P_\sigma/\sigma$, then the equation for the concentration coefficient assumes the form

$$R^f_{min} = \frac{c_{L,F}}{c_{L,0}} + \frac{\Gamma a}{0.77\,c_{L,0}} \left(\frac{P_\sigma}{\sigma}\right)^2 . \quad (18a)$$

Relationship (18) indicates that when $\Gamma = \text{const}$ and $n = \text{const}$, the concentration coefficient is determined by the dispersity of the foam, and when $\Gamma = \text{const}$ and $a = \text{const}$, it is determined by the expansion factor of the foam and the capillary pressure.

The parameter a can be expressed in terms of the radius of a sphere whose volume is equivalent to that of the dodecahedron ($7.66a^3 = \frac{4}{3}\pi R^3$), that is

$$a = 0.816R.$$

By substituting this dependence into Eqn (18) we obtain

$$R^f_{min} = \frac{c_{L,F}}{c_{L,0}} + \frac{\Gamma n}{0.302\,c_{L,0}R} . \quad (18b)$$

The resulting expression is analogous to relationship (15a). In the absence of internal disruption when the surfactant concentration in the bulk parts of the foam $c_{L,F}$ is equal to its concentration in the solution from which the surfactant is extracted, the first term in Eqns (18) and (18b) is equal to unity.

When internal disruption occurs, i.e. diffusion of the gas between the bubbles and coalescence or destruction of the foam column, the liquid phase is enriched in the surfactant that is desorbed from the surfaces of vanishing films. The more intense the destruction process, the larger the quantity of the substance desorbed returning into the bulk of the foam. The increase in the concentration of the substance in the liquid phase of the foam occurring in the course of destruction is expressed by the dependence[23]

$$c_{L,F} = c_{L,0} + \int_{\varepsilon_\tau}^{\varepsilon_0} \Gamma n\,d\varepsilon . \quad (19)$$

where $c_{L,F}$ is the surfactant concentration in the liquid phase of the foam at a given instant, $c_{L,0}$ the initial surfactant concentration in the liquid phase of the foam, ε_τ and ε_0 are specific surface areas of the foam at time τ and at the initial instant, respectively, n the expansion factor of the foam corresponding to the given specific surface area at a given instant. Thus, if the destruction proceeded at a constant expansion factor and a constant adsorption, the increase in the substance concentration in the foam bulk ($\Delta c = -\Gamma n \Delta\varepsilon$) would correspond exactly to the diminution of the substance due to desorption from the surface layers.

In view of Eqn (19) expression (18) assumes the form

$$R_{min} = 1 + \frac{1}{c_{L,0}} \int_{\varepsilon_\tau}^{\varepsilon_0} \Gamma n\,d\varepsilon + \frac{\Gamma n_\tau}{0.37 c_{L,0} a_\tau} , \quad (20)$$

where n_τ is the expansion factor of the foam at time τ, a_τ the size of the edge of a polyhedron at time τ, n a variable expansion factor which varies from $n(\varepsilon_0)$ to $n(\varepsilon_\tau)$ in the course of concentration.

In the case where the foam is stable and the duration of the process is low, the concentration caused by the internal breakdown is not very great. For unstable foams and prolonged processes the concentration resulting from the internal disruption and destruction of the column is comparable with that occurring in the adsorption layers. In addition, if concentration is carried out with increase in the expansion factor in the course of gravity syneresis or by the method of the capillary drying of the foam, then the excess of the substance that accumulates in the bulk sections of the foam owing to its destruction would be removed with the liquid being drawn off from the foam and would result in a diminution of the effectiveness of the concentration processes.

When the concentration of a mixture of surfactants is carried out, the selectivity of foam separation is evaluated from the selectivity coefficients, which are generally represented by the ratios between the coefficients of concentration of the ith (R_i^f) and jth (R_j^f) components:[2,5]

$$K_{ij} = \frac{R_i^f}{R_j^f} . \quad (21)$$

It should be noted that the selectivity coefficient like the concentration coefficient is a relative value depending not only on the nature of substance but also on the initial concentration of the surfactant in the solution.[3, 24–26]

In order to evaluate the effectiveness of isolation of surfactants in the course of foam separation, especially in a foam being destroyed, it is expedient to introduce a parameter γ characterising the quantity of the substance extracted with the foam (G_F) per unit volume of the gas consumed (V_g):

$$\gamma = \frac{G_F}{V_g} . \quad (22)$$

If we assume that adsorption reaches a constant equilibrium value during foam concentration, the foam is not destroyed, and the whole bulk of the gas remains in the foam, then using Eqn (22) and taking into account the balance of the substance in the foam (12) we obtain the following dependence

$$\gamma = \frac{c_{L,F}V_{L,F} + \Gamma S}{V_g} = \frac{c_{L,F}}{n-1} + \Gamma\varepsilon \simeq \frac{c_{L,F}}{n} + \Gamma\varepsilon , \quad (23)$$

where $(n-1) \approx n$ for highly expanded foams.

It follows from Eqn (23) that with the expansion factor of the foam being constant the effectiveness of the extraction is mostly determined by the degree of its dispersity, since normally $c_{L,F}/n \ll \Gamma\varepsilon$.

The coefficient of the effectiveness of extraction is related to the concentration coefficient by the following relationship

$$\gamma = R^f_{min} \frac{c_{L,0}V_{L,F}}{V_g} = R^f_{min} \frac{c_{L,0}}{n} . \quad (24)$$

Thus, the greater R^f_{min}, the greater the coefficient of extraction effectiveness at $c_{L,F} = \text{const}$ and $n = \text{const}$. Eqn (24) also shows that when the extraction is carried out from solutions with different initial concentrations of surfactants (at $R = \text{const}$), to achieve equal effectivenesses of the process different amounts of the gas are required.

With allowance for the internal destruction [Eqn (19)] the dependence (23) assumes the form

$$\gamma = \frac{c_{L,0}}{n_\tau} + \frac{1}{n_\tau}\int_{\varepsilon_\tau}^{\varepsilon_0} \Gamma n \, d\varepsilon + \Gamma\varepsilon_\tau \ , \tag{25}$$

where n_τ is the expansion factor of the foam at time τ, and ε_τ the specific surface area of the foam at time τ.

Carry-over of a liquid with a foam during foam separation is reflected by the volume factor R_V [21,22] and the water flooding coefficient β_V.[28]

$$R_V = \frac{V_{L,F}}{V_{L,0} - V_{L,F}}, \tag{26a}$$

$$\beta = \frac{V_{L,F}}{V_{L,0}} \ , \tag{26b}$$

where $V_{L,F}$ is the volume of the liquid in the foam product and $V_{L,0}$ is the initial volume of the liquid at the beginning of separation.

The same parameters can be expressed in terms of the expansion factor of a foam

$$R_V = \frac{n_0}{n - n_0} \ , \tag{27a}$$

$$\beta = \frac{n_0}{n} \ , \tag{27b}$$

where n is the expansion factor of the foam as it leaves the separation column, n_0 the foam expansion factor on the assumption that the whole liquid has been converted into the foam.

The influences of various factors on the carry-over of liquid with the foam have been studied by many authors.[21,29–33] In particular, empirical equations relating the reciprocal of the expansion coefficient to the viscosity and density of the foam-forming solution, the diameter of foam bubbles, and the rate of its movement were obtained.[32,33]

In the general case, it is rather difficult to predict quantitatively the carry-over of a liquid with a foam. Analytical equations describing the distribution of liquid with height have been obtained only for a hydrostatically equilibriated foam.[34–36]

The distribution of liquid throughout the height of the column of a moving foam can be calculated only for the simplest (steady-state) regime.[36] This calculation is possible only for the channel variant of foam with stationary surfaces of the channels if the rate of the foam movement is lower than the rate of gravity syneresis in a spherical foam V ($V = 1$ cm s^{-1}).[36]

Some results on the distribution of liquid with height for a foam being continuously generated have also been obtained by numerical methods on a computer with the aid of various hydrodynamic models.[37–41]

The volume of liquid carried away with a foam is determined, on the one hand, by the rate at which the liquid is incorporated into the foam (which is proportional to the rate of bubbling of the gas) and, on the other hand, by the rate at which this liquid flows out of the foam (the rate of syneresis). In fact, when the consumption of the gas is low and the whole excess liquid has time to flow out from the foam, then a foam with an expansion factor close to the hydrostatically equilibriated distribution of liquid with height should be formed at the outlet from a foam generator. Conversely, when the consumption of the gas is high, the expansion factor should diminish and approach asymptotically that of a spherical foam.

In the medium region of gas consumption the expansion factor of the foam at the outlet from the foam generator depends substantially not only on the rate of bubbling but also on physicochemical properties of the solution of a foam-forming agent (viscosity, surface tension) and the structural parameters of the foam (dispersity). To analyse the experimental data obtained for this region one can use the equation of syneresis in a gravitation field[42] which contains two empirical constants, the value for one of which ($V'_{L,0}$) is known:

$$\Delta V'_L = V'_{L,0}\frac{\tau}{\tau + V_{L,0}/w_0} \ , \tag{28}$$

where V'_L is the volume of liquid that has flowed out of the foam by time τ (referred to unit cross-sectional area of the foam), $V'_{L,0}$ is the initial volume of liquid in the foam referred to unit surface area, and w_0 is the initial volumetric rate of syneresis.

The analytical dependence of w_0 on the structural parameters of a foam is unknown. Therefore, to carry out a semiquantitative estimation of the influence of the structural parameters of a foam and the properties of a foam-forming solution, one may use the equation for the flow rate of homogeneous polyhedral foam for the channel variant [36]

$$\begin{aligned} w_0 &= 3.6 \times 10^{-4}\frac{r^4}{\eta R^2}\left[\rho g - \left(\frac{\partial p}{\partial H}\right)_0\right] \\ &= 3.3 \times 10^{-3}\frac{R^2}{\eta n^2}\left[\rho g - \left(\frac{\partial p}{\partial H}\right)_0\right] \ , \end{aligned} \tag{29}$$

where 3.6×10^{-4} and 3.3×10^{-4} are hydrodynamic coefficients, R the average radius of a bubble, η the dynamic viscosity, r the radius of curvature of Plateau–Gibbs channels, ρ the density of the foam-forming solution, g the acceleration due to gravity, and $(\partial p/\partial H)$ the gradient of the capillary pressure with the height of the foam column at the beginning of syneresis.

It has been found [29,30] that at low specific gas consumptions (< 0.8 cm min^{-1}) a foam with a distribution of liquid hydrostatically equilibriated with height leaves the foam generator regardless of the type of surfactant. At high specific gas consumptions (> 20 cm min^{-1}) a foam with an expansion factor of 10–12 comes out of the foam generator. The authors did not manage to achieve further decrease in the expansion factor owing to the very high rates of syneresis in slightly expanded foams and the 'break-down' of the foam formation on further increase in the gas consumption.

When the rate of gas consumption falls within the limits $0.8 < W_g < 20$ cm min^{-1} the carry-over of a liquid with a foam depends considerably on the rate of syneresis. All the factors that decrease the rate of syneresis [diminution of bubble size and of the surface tension, increase in the surface and dynamic viscosities, and lowering of the foam column [see Eqn (29)] resulted in increase in the carry-over of the liquid with the foam. Conversely, all the factors increasing the rate of syneresis diminished the carry-over of the liquid with the foam.

A detailed study of Eqns (25a)–(25b) and identification of the relationship of characteristics of foam separation to structural parameters of the foam and to each other are possible on the basis of the material balance equations for the substance in the foam and in the solution, including those taking into account destruction of the foam.

The material balance for a substance involved in foam separation is given by the formula

$$G_0 = G_F + G_R \ , \tag{30}$$

where G_0 is the amount of the substance in the original solution, G_F is the amount of the substance in the foam, and G_R is the amount of the substance in the solution after the separation.

In view of Eqn (12) the material balance may be written as follows:

$$G_0 = G_L + G_S + G_R \ . \tag{31}$$

The total volume of the liquid involved in foam separation is given as:

$$V_{L,0} = V_{L,F} + V_{L,R} , \quad (32)$$

where $V_{L,0}$ is the volume of the solution subjected to foam separation, $V_{L,F}$ is the volume of the liquid phase in the foam, and $V_{L,R}$ is the residual volume of the solution after foam separation.

If we express the substance amounts by means of the corresponding concentrations and volumes, we obtain

$$c_{L,0}V_{L,0} = c_{L,F}V_{L,F} + \Gamma S + c_{L,R}V_{L,R} , \quad (33)$$

where $c_{L,0}$ is the surfactant concentration in the solution subjected to separation, $c_{L,F}$ the surfactant concentration in the liquid phase of the foam, $c_{L,R}$ the surfactant concentration in the solution after separation, and S the total interfacial area in the foam. All these parameters are values averaged through the whole period of foam separation.

If there is no internal disruption in the foam or destruction of the foam column, then $c_{L,F}$ varies from $c_{L,0}$ to $c_{L,n}$ in the course of separation. On the assumption that the specific interfacial area in the foam is constant and the concentration in the liquid phase of the foam is close to the initial value, Eqn (33) with account taken of Eqn (31) can be represented as follows:

$$c_{L,0}V_{L,0} = c_{L,0}V_{L,F} + \Gamma S + c_{L,R}(V_{L,0} - V_{L,F}) . \quad (34)$$

Taking into account that $n = V_F/V_{L,F}$, $S/V_F = \varepsilon$, and $c_{L,0} = c_{L,F}$, we obtain from Eqns (34) and (26b)

$$\frac{\Delta c}{\beta} = \Delta c + \Gamma \varepsilon n . \quad (35)$$

Here β is the water flooding coefficient

$$\beta = \frac{\Delta c}{\Delta c + \Gamma \varepsilon n}, \quad (36)$$

where $\Delta c = c_{L,0} - c_{L,n}$, ε and n are the specific surface area and the expansion factor of the foam (average values throughout the process).

The water flooding coefficient is related to the volume factor (R_V) by the relationship[27]

$$R_V = \frac{\beta}{1 - \beta} \quad (37)$$

The combination of Eqns (36) and (37) gives

$$R_V = \frac{\Delta c}{\Gamma \varepsilon n} . \quad (38)$$

For the process of foam separation in which the foam is dried through the action of a pressure differential in the Plateau–Gibbs channels Eqns (31), (32), and (34) assume the form

$$G_0 = G_L + G_S + G_D + G_R , \quad (39)$$

$$V_{L,0} = V_{L,F} + V_{L,D} + V_{L,R} , \quad (40)$$

$$c_{L,0}V_{L,0} = c_{L,F}V_{L,F} + \Gamma S + c_{L,D}V_{L,D} + c_{L,R}V_{L,0} - c_{L,R}V_{L,F} - c_{L,R}V_{L,D} . \quad (41)$$

The index D designates the corresponding values in the 'filtrate'. Considering that $c_{L,D} = c_{L,F}$, $S = V_F\varepsilon$, $n = V_F/V_{L,F}$, and $\beta = V_{L,F}/V_{L,0}$, we obtain from Eqn (41)

$$\beta_F = \frac{\Delta c_{max}}{(c_{L,F} - c_{L,R})(1 + \delta) + \Gamma \varepsilon n} \quad (42)$$

where $\Delta c_{max} = c_{L,0} - c_{L,R}$, β_F is the flooding coefficient of the foam that emerges from the column (irrespective of the liquid carried away with the 'filtrate'), $\delta = \beta_D/\beta_F$ is the constant of drying, and $\beta_D = V_{L,D}/V_{L,0}$ is the coefficient of carry-over of the liquid with the 'filtrate'.

As the process is carried out, the concentration of the substance in the liquid phase of the foam varies within the range $c_{L,R} \leqslant c_{L,F} \leqslant c_{L,0}$.

At the start, $c_{L,0} = c_{L,F} = c_{L,D}$, and the water flooding coefficient is given by

$$\beta_{F(0)} = \frac{\Delta c_{max}}{\Delta c_{max}(1 + \delta) + \Gamma \varepsilon_0 n_0} . \quad (43)$$

At the end of the process $c_{L,F} = c_{L,R}$, and

$$\beta_{F(R)} = \frac{\Delta c_{max}}{\Gamma \varepsilon_R n_R} . \quad (44)$$

The overall flooding coefficient of the foam, β_Σ, with allowance for the liquid extracted during drying ('filtrate'), is found from the equation

$$\beta_\Sigma = \beta_F + \beta_D = \frac{\Delta c_{max}}{(c_{L,F} - c_{L,R})(1 + \delta) + \Gamma \varepsilon n}(1 + \delta) . \quad (45)$$

From Eqn (34), taking into account (19), one can obtain the following expression for the foams destroyed during the foam separation:

$$c_{L,0}V_{L,0} = \left(c_{L,F} + \int_{\varepsilon_\tau}^{\varepsilon_0} \Gamma n \, d\varepsilon\right) V_{L,F} + \Gamma S_\tau + c_{L,R}V_{L,R} , \quad (46)$$

where S_τ is the surface area of bubbles in the foam at time τ.

From Eqn (36), the general expression for the carry-over of the liquid phase with a foam, which undergoes destruction, can be obtained from

$$\beta = \frac{\Delta c_{max}}{\Delta c_{max} + \int_{\varepsilon_\tau}^{\varepsilon_0} \Gamma n \, d\varepsilon + \Gamma \varepsilon_{min} n_\tau}, \quad (47)$$

where $\Delta c = c_{L,0} - c_{L,R}$, and ε_{min} is the specific surface area of the foam at the outlet from the column at time τ.

For the process of foam concentration involving capillary drying, an equation can be obtained which relates the water flooding coefficient to the structural parameters of the foam.[43]

The mass (α_m) and concentration (α_c) degrees of extraction are characteristics of the completeness of the extraction of a substance:

$$\alpha_m = 100 \frac{G_0 - G_R}{G_0}, \quad (48)$$

$$\alpha_c = 100 \frac{c_{L,0} - c_{L,R}}{c_{L,0}} \quad (49)$$

The equations of the material balance during the foam separation and dependence (48) make it possible to obtain an equation relating R^f_{min}, β to α

$$\alpha = 100\frac{G_0 - G_R}{G_0} = 100\frac{G_F}{G_0}$$

$$= 100\left(\frac{c_{L,F}V_{L,F} + \Gamma S}{c_{L,0}V_{L,0}}\right)$$

$$= 100\left(\frac{c_{L,F}}{c_{L,0}} + \frac{\Gamma S}{c_{L,0}V_{L,F}}\right)\frac{V_{L,F}}{V_{L,0}} = 100R^f_{min} \quad (50)$$

It can be seen from Eqn (50) that only two of the three characteristics of the adsorption concentration are independent. For example, at different concentration coefficients, the same degree of extraction can be achieved by the appropriate variation of the water flooding coefficient.

The effectiveness of the removal of impurities from a solution is characterised by the purification coefficient (factor)

$$o = \frac{c_{L,0}}{c_{L,R}} . \quad (51)$$

From the material balance equation, one can obtain an expression for the purification coefficient containing the structural characteristics of foam:[5]

$$o = \frac{c_{L,0}}{c_{L,R}} = 1 + \frac{\Gamma S}{c_{L,R} V_{L,R}} = 1 + \frac{2.7\,\Gamma n}{c_{L,R} a} . \quad (52)$$

Eqns (51) and (52) are of little use for determining the limiting values of the purification coefficient, since in the case of low surfactant concentrations the stability of the foam dramatically decreases, and the foam layer containing the adsorbed product has no time to separate from the solution.

For this reason determination of the minimum residual surfactant concentration necessary to obtain a stable foam provides more precise information on the purification coefficient. The minimum residual concentration is close to that for the formation of black spots (c_b) in microscopic foam films ($c_{L,0} = c_{St} = c_b$) in the circumstances where they are formed

$$o_{max} = \frac{c_{L,0}}{c_b} . \quad (53)$$

Some researchers, for example, Skvirskii et al[44] and Sontag and Strenge,[45] maintain that a stable foam is formed only when the concentrations of surfactants correspond to the limiting degrees of their adsorption (Γ_∞), while others, for example, Venstrem and Rebinder[46] and Ekserova and Sheludko[47], have noted that a stable foam can also be obtained when the surfactant concentrations are much lower than those necessary to reach Γ_∞. In fact, a dramatic increase in the lifetime of a foam is typical of the concentration regions corresponding to the formation of black spots in microscopic foam films.[5,48]

The formation of black spots in thermodynamically non-equilibrium films has a probability character.[49,50] It can be observed experimentally if the lifetime of a black spot is greater than the time resolution of the instrument. The probability of the detection can be calculated from experimental data as the ratio of the number of films in which black spots have been observed to the total number of films examined.

The probability (W_b) of observing black spots in an ordinary black film from a solution of sodium dodecyl sulfonate exists over a wide concentration range, 2.5×10^{-6} to 3.5×10^{-4} mol l^{-1}. It rises substantially in the initial section, up to a concentration of $\sim 10^{-5}$ mol l^{-1} when the degree of filling of the adsorption layer, Γ/Γ_∞, is 0.4. However, even when this probability is equal to unity, the complete saturation of the adsorption layer is not yet reached [$\Gamma/\Gamma_\infty = 1$ at $c = (5.0 \pm 0.2) \times 10^{-4}$ mol l^{-1}].

The increase in the probability of the formation of Newton black films for the same surfactants lies within a narrow range of surfactant concentrations (from 8×10^{-5} to 2×10^{-4} mol l^{-1}) that correspond to the saturated adsorption layer ($\Gamma/\Gamma_\infty = 1$ at $c = 1.1 \times 10^{4}$ mol l^{-1}). It is important to keep in mind this distinction between the concentration dependence of the probability of detecting black spots and the lifetime of the foam, while determining the minimum residual concentration of the surfactant.

A necessary and sufficient condition for the principal possibility of foam separation is that a substance is concentrated in the foam, i.e. $R^f_{min} > 1$.

Eqn (18) implies that in a polyhedral foam the condition $R^f_{min} > 1$ is satisfied when $\Gamma n/0.37a > c_{L,0}$, since $c_{L,F}/c_{L,0} \simeq 1$. This inequality determines both the lower and the upper limits of foam concentration, outside of which concentration is impossible ($R^f = 1$). However, the reasons why this relationship no longer holds are different. Thus, the upper limit of the applicability of the foam separation method is often attributed to the CCM,[4,51] since at this concentration σ = const, and $d\sigma/dc = 0$. However, in the region of concentrations not far exceeding the CCM, where $\sigma(c)$ = const, adsorption of a surfactant has a positive value, which is indicated by direct measurements of adsorption in this region. The calculation according to Eqn (18) shows that for typical micelle-forming surfactants ($\Gamma = 3 \times 10^{-10}$ mol cm^{-2}, $a = 10^{-2}$ cm) $R^f_{min} > 1$ already at $n > 40$. This expansion factor can be achieved both by using the method of drying with the aid of porous plates and by drying in a gravitational field at a low gas consumption in the separation column and with a high foam column. Thus, if the lifetime of a foam is sufficient for technological processing ($\tau = 10-15$ min), then its high expansion factor can be achieved and adsorption concentration of a substance can be carried out at $c_{L,0} >$ CCM.[22,52]

IV. Experimental studies on the concentration of individual surfactants and mixtures

The distribution of a substance being extracted between a liquid and a foam, which is characterised by the concentration coefficient, has been studied in foam separation processes under conditions both of gravity[2,22,23,43] and of accelerated syneresis.[7,10,43,52,53]

Under the conditions of gravity syneresis, R^f_{max} diminishes with decrease in the height of foam in the separation column (at a constant specific rate of gas delivery to the separation column) or with increase in the rate of bubbling at a constant height of the foam column.[43]

The concentration coefficient R^f_{min} increases with decrease in the size of bubbles only if n = const [Eqn (18)]. If the expansion factor changes simultaneously with dispersity (as is often the case under the conditions of gravity syneresis, since the decrease in the sizes of foam bubbles results in a decrease in the rate of syneresis and in the formation of a foam with a lower expansion factor at the outlet from the foam generator), then a decrease in the size of bubbles often leads to a decrease in R^f_{min}, rather than to its increase.[4,43]

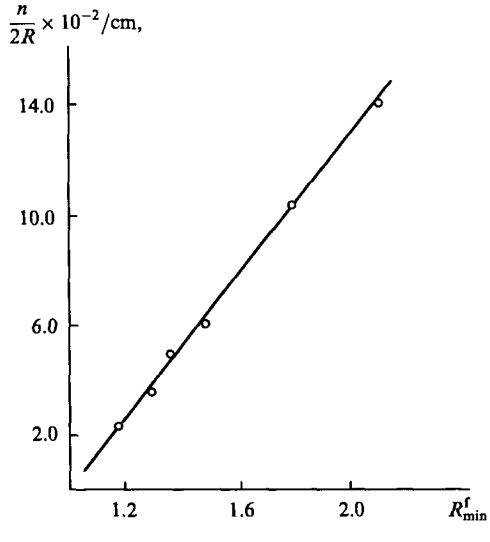


Figure 2. The dependence of the ratio $n/2R$ on the coefficient of concentration of sodium butyl diphenylsulfonate in a foam. The initial concentration of the surfactant in the solution was 2.4×10^{-3} mol l^{-1}.

A study of foam separation of sodium butyl diphenyl sulfonate in an ordinary slightly expanded foam has shown[22] that the concentration coefficient increases linearly with increase in the $n/2R$ value in conformity with relationship (15a) (Fig. 2).

An expansion factor of more than 100 is rarely achieved in standard separation columns, and therefore, under these conditions, the concentration coefficient is of the order of several tens or, occasionally, several hundreds.

Greater magnitudes of the concentration coefficient can be reached in dry foams.[5,7-10,52,53] Kruglyakov and Kuznetsova[7] have studied the influence of the capillary pressure, the expansion factor, and dispersity on R^f_{min}. The foam was prepared from solutions of sodium dodecyl benzenesulfonate (DDBSNa) and 20-oxyethylated nonylphenol (NP-20). The concentration coefficient R^f_{min} increased in direct proportion to the expansion factor (at $a = \text{const}$) and in inverse proportion to the parameter a (at $n = \text{const}$) (Fig. 3 *a*, *b*).

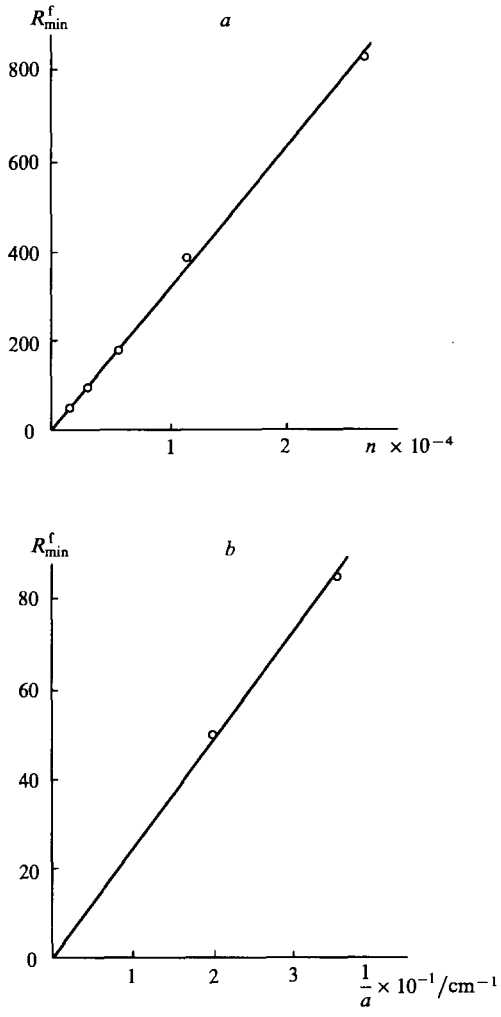


Figure 3. The dependence of the coefficient of concentration of a surfactant in a foam on the expansion factor (*a*) and dispersity (*b*) of the foam. (*a*) $a = \text{const}$; (*b*) $n = 1000$.

Interesting results have been obtained in a study of concentration of proteins in a dry foam.[53] Under the conditions of gravity syneresis a foam prepared from proteins has a low expansion factor ($n = 20-30$) and a concentration coefficient of 1.5–3. In the case of accelerated syneresis under the action of high pressure differentials, the foam expansion factor can be as high as 500 and the concentration coefficient is 50–70 (Fig. 4).

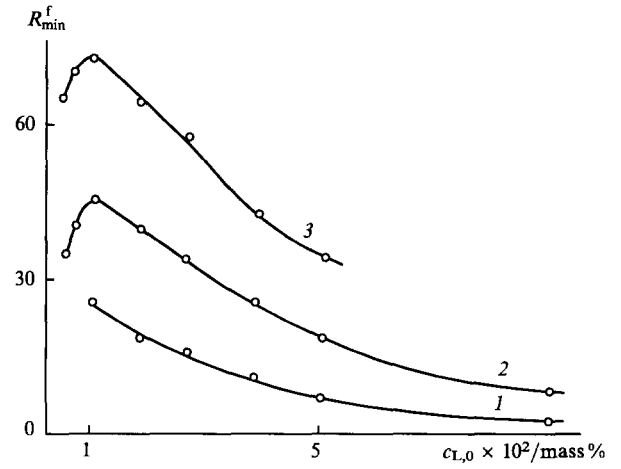


Figure 4. The dependence of the concentration coefficient for serum albumin on its initial concentration in a foam-forming system at various degrees of expansion of the foam. *n*: (*1*) 150; (*2*) 300; (*3*) 500.

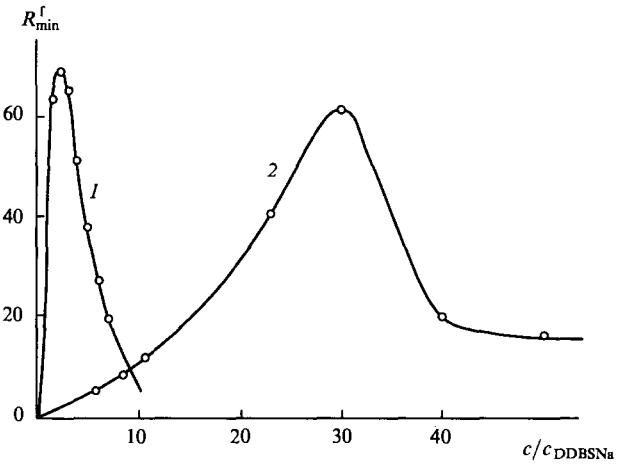


Figure 5. The dependence of the coefficient of concentration of saponin (*1*) and valeric acid (*2*) on component concentration ratios in mixtures with DDBSNa. The concentrations of the components in the mixtures are given in percent (*1*) and in mol l^{-1} (*2*).

If a surfactant is not a good foam-forming agent it cannot be concentrated in a dry foam; therefore a good foam-forming agent is introduced in the solution of such compound, and concentration of the resulting mixture is carried out. Valeric acid, saponin, and α-chymotrypsin were concentrated in such a manner (DDBSNa and DDSNa were used as foam-forming agents).[9] When concentration is carried out from a mixture, the dependence of R^f_{min} on the ratio between the components has an extreme character (Fig. 5).

The low-molecular-mass protein antibiotic nisin was successfully concentrated from a culture liquid in a highly expanded foam stabilised by the foam-forming agent Tween-80. In the absence of a special foam-forming agent no stable foam is produced from the culture liquid. By adding Tween-80 one can extract nisin; however, the concentration coefficient in a foam under the conditions of gravity syneresis does not exceed 4–5 (see Ref. 54). To increase the degree of concentration, a multistep process involving destruction of foam and subsequent foaming is required. When nisin is concentrated in a dry foam (dried with the aid of filtering partitions) the degree of concentration can be increased to $R^f_{min} = 350$.

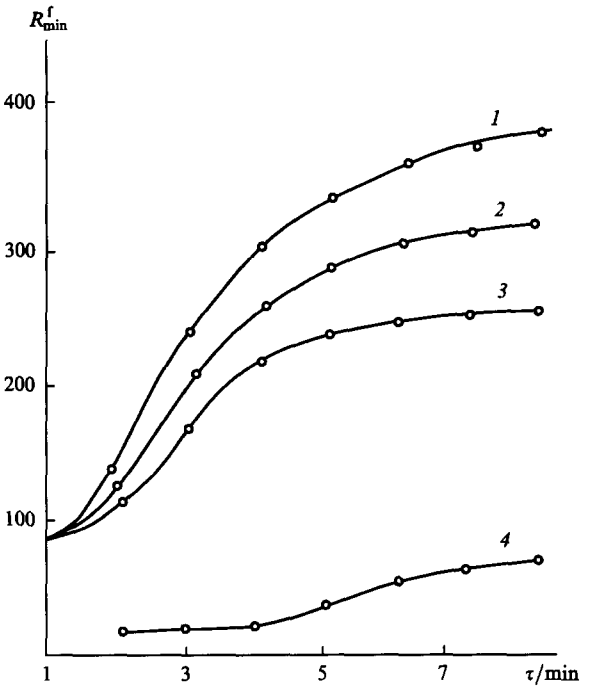


Figure 6. The time dependence of the concentration coefficient and its constituents for a foam prepared from a DDBSNa solution.
(*1*) $R_1^f = \Gamma n_\tau / 0.37\, c_{L,0}\, a_0$; (*2*) $R_2^f = R_3^f + R_4^f$;
(*3*) $R_3^f = \Gamma n_\tau / 0.37\, c_{L,0}\, a_\tau$; (*4*) $R_4^f = \int_{\varepsilon_\tau}^{\varepsilon_0} \Gamma n\, d\varepsilon \Big/ c_{L,0}$.

The influence of the internal disruption on the parameters of foam concentration has been experimentally studied by Khaskova and Kruglyakov.[27,43] They carried out quantitative evaluation of the effect of the internal disruption on the variation of the concentration and extraction coefficients for foams prepared from solutions of DDBSNa and sodium oleate (NaOL) having distinct destruction kinetics.[27,43] Fig. 6 shows the kinetic dependence of the concentration coefficient and its constituents for a foam prepared from a solution of DDBSNa [see Eqn (20)]. Curve *1* corresponds to the variation of R^f occurring as the foam is dried provided that there is no destruction in it. Curve *2* shows the variation of R^f with allowance for foam destruction. Curve *3* reflects the accumulation of the substance in adsorption layers provided $a = \text{const}$, and curve *4* shows the accumulation of the substance in the liquid phase of the foam owing to its internal disruption. The second term of Eqn (20) was calculated by graphical integration on the basis of the $n = f(\varepsilon)$ dependence. One can see that foam destruction results in a decrease in the concentration coefficient.

Similar results were obtained for a foam prepared from a solution of NaOL. In this case, the influence of foam destruction on the concentration coefficient was still more pronounced. The proportion of the quantity

$$\frac{1}{c_{L,0}} \int_{\varepsilon_\tau}^{\varepsilon_0} \Gamma n d\varepsilon$$

in foams prepared from NaOL solutions was $\sim 50\%$ of the theoretical R^f value (in the concentration without destruction). The coefficient of extraction effectiveness is affected by the foam destruction to an even greater degree: for a foam formed from a solution of DDBSNa it varies from 5.4×10^{-8} (at the beginning of the process) to 4.7×10^{-8} mol cm^{-3} (at the end), and for a foam obtained from a solution of NaOL, it varies from 10.8×10^{-8} to 3.89×10^{-8} mol cm^{-3} (see Refs 27, 43).

In the course of drying, some liquid is removed from the foam and, if the specific surface area of the foam considerably decreases, the liquid is substantially enriched in the substance being extracted. To determine the loss of a substance with the filtrate one can use the following characteristics

$$\alpha_{D,\tau} = \frac{G_D}{G_{F,\tau}}, \tag{54}$$

$$\alpha_{D,0} = \frac{G_D}{G_{F,0}}, \tag{55}$$

where G_D is the amount of the substance removed from the system with the filtrate, $G_{F,0}$ the initial amount of the substance in the foam, and $G_{F,\tau}$ the amount of the substance in the foam at time τ. The characteristics $\alpha_{D,\tau}$ and $\alpha_{D,0}$, similarly to R_V, R^f, and γ, can be expressed in terms of the foam structural parameters, adsorption, and concentration of the surfactant in the solution.[43] If $\alpha_{D,0} \ll 1$ and $\alpha_{D,\tau} \ll 1$, the losses during drying are small.

The losses with the filtrate have been determined under steady-state conditions: a foam with a known volume was prepared from a definite volume of liquid in a separate cell, this foam was then dried in the same cell by increasing the pressure to $\Delta P = 1.6$ kPa. Variations of the expansion coefficient, the pressure in the Plateau–Gibbs channels, and dispersity in the foam were monitored. In the filtrate produced by the drying process the concentration of the surfactant was determined and the losses of the substance to be extracted, which occurred during drying and destruction of the foam, were found from Eqn (54).

The $\alpha_{D,0}$ values for stable foams obtained from solutions of DDBSNa with 0.01 or 0.1 mol l^{-1} of NaCl added are 0.2 and 0.3, respectively. Foams produced from solutions of sodium oleate are destroyed under conditions of forced syneresis much more intensely, and in this case the losses with the filtrate reach $\alpha_{D,0} \simeq 0.6$. When $\alpha_{D,0} > 0.4-0.5$, the filtrate should be returned to the separation column in order to diminish losses of the substance extracted by foam separation.

A negative influence of foam destruction on the concentration and extraction coefficients has also been found[27,43] in the separation of foams with various stabilities carried out under the conditions of gravity syneresis: as a result of the internal disruption of a foam these coefficients decrease over a wide range of concentrations of the surfactant being extracted.

A positive influence of the internal disruption on the concentration coefficient (i.e. its increase) is observed only in the cases where a very small $c_{L,0}$ value lies in the range $c_b < c_{L,0} < c_{\Gamma,\infty}$ ($c_{\Gamma,\infty}$ corresponds to the saturated adsorption layer). This is caused by the fact that desorption from film surfaces during the foam destruction increases the surfactant concentration in the liquid phase of the foam, and, as a consequence, the degree of adsorption increases to the values that ensure formation of a small volume of a stable foam. It therefore becomes possible to separate the foam from the original solution with $R^f > 1$.

A positive influence of the internal destruction on the concentration coefficient due to the internal return of the solution (dephlegmation) has been found experimentally in foam separation processes carried out for solutions of DDBSNa and lysozyme at $c_b < c_{L,0} < c_{\Gamma,\infty}$.[43,55]

Studies on the identification of the upper and lower concentration limits of the applicability of the foam separation method have been reported.[43,52,55]

It was found experimentally that concentration from solutions of surfactants with a concentration $c_{L,0} = (2-3)$CCM is possible with $R^f_{min} = 6-9$ (for foams obtained from solutions of NaOL) or $R^f_{min} = 27-30$ (for foams obtained from solutions of DDBSNa).[43,52]

To evaluate the minimum residual concentration, a rather simple method can be used involving determination of the surfactant concentration above which a stable foam is formed under the conditions of steady-state operation of a separation

column (when the height of the foam column remains constant during the delivery of a gas).[55] The foam-forming ability is estimated based on the ratio V_F/V_g (where V_F is the greatest volume of foam obtained in a separation column over period τ in the steady-stade regime and V_g is the volume of the gas bubbled into the column over the same period), the parameter a and the rate of gas bubbling being constant during the course of the experiment. The experimental dependences $V_F/V_g = f(c)$, $\tau = f(c)$, and $\Delta N/N = f(c)$ (τ is the lifetime of the foam and foam films, $\Delta N/N$ the probability of the detection of black films) have similar characters for all surfactant types studied (DDSNa, DDBSNa, lysozyme). The minimum residual concentration is, as a rule, equal to the concentration at which black films arise with a probability of more than 50%. Moreover, if the $V_F/V_g = f(c)$, $\tau = f(c)$, and $\Delta N/N = f(c)$ curves vary by jumps, then the dependences of the concentration coefficient also vary by jumps. The variations described are characteristic of systems in which black spots (ordinary or Newton black films) arise in microscopic films at a definite concentration. If ordinary thin foam films are formed in a system (DDSNa and DDBSNa without an electrolyte, or lysozyme not at the isoelectric point), the lower threshold concentration cannot be distinguished unambiguously. In these systems, the minimum concentration is found from the particular conditions under which the process is conducted (the rate of gas bubbling, dispersity, the foam height in the column, etc) and has no clear-cut limit.

V. Separation of components of a mixture of surfactants in a foam

In the previous sections we have mostly considered the results of concentration of surfactants in a foam or purification of a solution from surfactants in binary systems. Our goal has been to increase the concentration coefficient or the degree of extraction of one of the components with the aid of the other, rather than to separate the components of the system from one another.

A partial or complete separation of two dissolved components can be carried out by the foam separation process. The separation occurs most easily when one of the components is surface inactive or has very low surface activity. For example, soaps and various synthetic surfactants can be readily separated (purified) from electrolytes; proteins can be separated from amino acids; and so on.

The separation of ions is most frequently carried out by ion flotation methods (without formation of a stable foam) involving ion exchange reactions, formation of nondissociated compounds, precipitation, coprecipitation, and other expedients.[2-4,6] The possibility of separating components without resort to ion flotation methods has been shown for the first time for mixtures of soap and dyes. Ostwald and coworkers[56-58] demonstrated the possibility of separating blue (triphenylmethane) and crimson-red (novococacine azo dye) dyes. With identical concentrations of these dyes in the initial solution (0.01 %), the concentration of the blue dye in the foam reached 0.22%, that for the red dye was 0.02 %. Their concentrations in the residual solution were 0.003 % and 0.01 %, respectively. A similar separation of bromothymol blue into a yellow dye (in the foam) and a blue dye (the residue), and also the separation of congorubin into a wine-red dye and a violet dye, respectively, were achieved in the experiments of Thiele.[59] Separation of other dyes has been considered by Skomorski.[60]

Other papers deal with the processes of partial separation of soap mixtures (sodium oleate and laurate), mixtures of salts of cholic and fatty acids, and a mixture of saponin, sodium oleate, and gelatin.[61-63]

A large number of examples of partial separations, including those of proteins, polymers, and other compounds, are presented in a book by Cassidy[64] and in other papers.[65,66] Analysis of these works shows that purification of sodium dodecylsulfonate from a dodecyl alcohol admixture is perhaps the only example of complete separation of one of the components of the mixture from the other (apart from inactive electrolytes) and that this separation in an ordinary foam is possible only when the concentration of the alcohol is low compared with that of sodium dodecylsulonfate.[64] The thermodynamic theory of the surface separation processes, based on the difference between the compositions of the surface layer and the bulk phases, has been outlined in a monograph.[4]

The fundamental relationship connecting the mole fraction of the i-th component of the system (N_i) to the change in the total number of moles (m) during the surface separation can be presented in the following way

$$\Delta N_i = (N_i^S - N_i)\frac{\Delta m}{m} . \qquad (56)$$

Here N_i^S is the mole fraction of the ith component in the surface layer.

If the dependence of N_i^S on the composition of the system is known, one can integrate Eqn (56) and follow the variation of the composition of a solution during foam separation in the concentration space (i.e. follow the course of the lines of surface separation). Experimental studies on the thermodynamic theory of surface separation (in particular on the course of lines of surface separation which show the manner in which the solution composition varies during foam separation) for ternary systems, the components of which do not interact chemically with one another, have been carried out in a number of studies.[4,67]

Surface separation theory implies that the effectiveness of the separation is determined mostly by the selectivity coefficients of the components.

The results of separation in a foam are strongly affected, apart from the adsorption ability, by the stability of the foam, which depends on the nature and concentrations of the components, since it takes a rather long time ($\sim 10-15$ min) for the adsorption equilibrium to be reached and for the excess liquid to separate without destruction of the foam column. The selectivity of foam separation for two or three surfactants from aqueous solutions has been considered in many papers (see, for example, Refs 3, 26, 68, 69). Shinoda and Mashio[68] studied the selectivity for several pairs of anionic surfactants differing in the length of the hydrocarbon radical and the nature of the polar group. It was shown, for example, that the selectivity coefficient for the DDBSNa/DDSNa pair in molecular solutions is 35–50, and for the DDBSNa/potassium undecylsulfonate pair is 180–200. In the case of micellar solutions, the coefficient of selectivity is substantially lower, for example, it amounted to 5–8 for the DDBSNa/TDSNa (TDSNa is sodium tetradecylsulfonate) and $C_{15}H_{31}COOK/C_{13}H_{27}COOK$ pairs; however, the difference in the carbon chain length in these pairs was also much smaller.

At low concentrations of surfactants the selectivity coefficient increased by a factor of 2.75 when one methylene group was added. The introduction of a benzene ring in the hydrocarbon chain was equivalent to the introduction of 3.5–4 methylene groups.

The selectivity of the isolation of inorganic ions in a foam[69] during their simultaneous adsorption with the cetylpyridinium chloride ion (0.75–1.0 mol l^{-1}) increased in the sequence $Cl^- < Br^- < I^- < SCN^-$. The adsorption increased in this sequence from 1.39×10^{-10} to 2.8×10^{-10} mol cm^{-2}. The use of recycling (dephlegmation), which changes the ratio between the components, allows the effectiveness of the separation to be increased, especially for pairs of substances whose surface activities are slightly different.[3]

Hargis and Rogers,[70] who studied foam separation of DDSNa/DDBSNa and DDSNa/BSNa mixtures (BSNa is sodium benzenesulfonate), have noted that the concentration coefficients of these surfactants remain constant over a wide concentration range regardless of the presence of the other component.

The partial separation of components occurring during movement of gas bubbles through a layer of a surfactant solution is regarded by some researchers as a modification of chromatography (see, for example, Refs 4, 64, and 66). One cannot achieve the complete separation of substances by this method because it involves only single-stage adsorption of the components of a mixture, and because of the low concentration coefficients in a foam in which syneresis occurs only under the action of gravity.

The effectiveness of the separation of components dramatically increases when dry foams, prepared under the action of the pressure differential in Plateau–Gibbs channels with the aid of porous plates, are used.[5,7,10,52,53] In this way a complete separation of proteins from deoxyribonucleic acid has been carried out.[10]

The possibility of chromatographic separation of surfactants in a foam has been reported.[71] To perform this process a foam with controlled size of Plateau–Gibbs channels was used. A solution of the mixture of surfactants to be separated (thymol blue dye, 5×10^{-4} mol l^{-1}, and DDBSNa, 1.5×10^{-3} mol l^{-1}) was passed through a layer of a foam prepared from a DDSNa solution with 0.4 mol l^{-1} of NaCl added. The foam was con-fined on both sides by porous partitions. The pressures on the outside of these partitions were dissimilar and lower than those on the inside by an amount not exceeding the capillary pressure in the partition pores. The solution of the mixture was delivered through that partition where the outside pressure was higher. Separation of the mixture was achieved owing to the multistage selective adsorption of the components at the surface of foam bubbles with the rate of the solution flow under the action of pressure differential ($\Delta P = 1.3$ kPa) being controlled.

In the mixture under study, DDBSNa and DDSNa are less active than the dye. As a consequence, DDBSNa appeared in the samples from the effluent, together with DDSNa, within 15 min, and within 30 min the effluent contained only DDBSNa. It was not until 40 min after the beginning of the process that traces of the dye appeared, i.e. one of the components (DDBSNa) was isolated by frontal analysis. It should be noted that foam chromatography, which has much in common with conventional liquid chromatography with a solid adsorbent, also has significant differences from it. The first of these is that it is impossible to obtain surfactant-free layers (sections) in foam chromatography. Other peculiarities are associated with the continuous decrease in the surface of the adsorbent (foam). The possibilities of foam chromatography have so far been poorly investigated.

Foam separation can also be used for shifting chemical equilibria or changing the rates of chemical reactions in a foam. If a reversible reaction, for example, the hydrolysis of a soap $NaR + H_2O = NaOH + HR$, can occur between dissolved compounds, the equilibrium in this reaction can be shifted in either direction depending on which component (NaR or HR) is more active. The change in the equilibrium constant in the surface layer compared with its magnitude in the bulk of the solution has been attributed to the concentration of the reactants in the surface layer (and the corresponding change in the activity) and change in the surface energy.[26]

The first quantitative experiments on moving an equilibrium in a foam have been carried out for soap solutions.[26] It was found that the foam, which underwent destruction, was acidic, whereas the remaining solution was alkaline, and the surface tension of this solution was twice as high as that of the liquid obtained from the foam. The hydrolysis is especially pronounced in dilute solutions. When the concentration of sodium oleate was 0.0002%, the ratio between the proportions of the acid and a base in the foam was 2.7, and it was only slightly dependent on the nature of the base. Similar results have been obtained for the foam prepared from a sodium laurate solution.[26]

Catalytic action of cationic surfactants (quaternary pyridinium chlorides) in the hydrolysis of 2,4-dinitrochlorobenzene and in the reaction with aniline in a foam has been observed.[74,75] For example, in the presence of quaternary pyridinium bases, the rate constant of the hydrolysis in a foam increased from 1.42×10^{-7} (without the surfactant) to 2.7×10^{-2} m^3 mol^{-1} s^{-1} (with surfactant), which is greater than in the case of catalysis in micelles (8.3×10^{-6} m^3 mol^{-1} s^{-1}). A similar acceleration of acid hydrolysis occurs also in the presence of anionic surfactants.[76,77]

In a series of papers[74–77] this catalytic action has been explained in the context of the mechanism of micellar catalysis and has been attributed to the concentration of reactants in adsorption layers of a foam, to a local change in the pH, and to the influence of orientation of reactant molecules in the adsorption layers and of the surface charge on the formation of the transition state (intermediate complex). The higher effectiveness of the film catalysis in a foam as compared with micellar catalysis has been accounted for by the structural features of the surface layers in a foam (the type of adsorption film) that facilitate attainment of transition states of reactions. However, the authors[74–77] undertook no special studies that would have unambiguously confirmed these assumptions.

To the best of our knowledge the influence of the foam structure and especially of the type of thin films (the ordinary and Newton black ones) on the rate of reactions has not been investigated.

VI. Conclusion

The drying of a foam by developing a pressure differential in the liquid phase with the aid of porous plates allows one to obtain high concentration coefficients for individual surfactants and their mixtures in the case where at least one of the compounds is a good foam-forming agent, and ensures chromatographic separation of substances in a foam.

The identification of the analytical relationships of characteristics of foam separation with the structural parameters of a foam and the properties of a surfactant makes it possible to optimise the process and to take into account the influence of foam destruction on various characteristics of surface concentration.

The internal disruption of a foam and the destruction of a foam column degrade the characteristics of the concentration. A positive influence of foam destruction (internal recycling) and, hence, of the external recycling and multistage separation on the concentration of individual surfactants, is manifested at low surfactant concentrations close to that for the formation of black spots in microscopic foam films.

Investigation of some reactions in a foam demonstrated a more pronounced catalytic action of surfactants in adsorption layers of a foam compared with their catalytic action in micelles.

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Polymeric electrolytes for lithium chemical power sources

V G Syromyatnikov, L P Paskal', O A Mashkin

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Abstract. The review deals with the properties of solid and polymeric electrolytes incorporating (co)polymers or mixtures of polymers and copolymers doped with inorganic lithium salts. Such electrolytes are used for lithium chemical power sources. Attention is concentrated on the methods for the modification of the structure and composition of these systems by means of amorphous and network (co)polymers, additives promoting conversion into an amorphous form, crown-ethers, plasticisers, and ceramic powders, which increase the ionic conductivity of polymeric electrolytes. The methods for the preparation of thin films of polymeric electrolytes by plasma polymerisation and also procedures for the modification of the electrodes of lithium chemical power sources with polymeric electrolytes are considered.

Data on the ionic conductivities of the systems described are presented. The bibliography includes 129 references.

I. Introduction

Considerable efforts by specialists in the development and manufacture of chemical power sources (CPS) are nowadays directed to the creation of superminiaturised autonomous power sources. Studies in the last 10 years have shown that this problem can be solved with the aid of film-type polymeric electrolytes (PE). High specific characteristics are then attained (for example, a power capacity up to 200 W h kg^{-1} subject to a high degree of discharge) and satisfactory storage properties. The use of PE for the creation of rechargeable accumulators with a lithium anode is of special interest. The principal advantages of such accumulators are virtually total safety in use, the possibility of preparing CPS of any shape, the absence of liquid and gaseous components, a high resistance to mechanical influences, and a capacity for operation at high temperatures. Lithium accumulators with PE are employed most effectively in electric automobiles, in military and space technology, in microelectronics, in communication devices, and, especially, in combination with solar batteries.

According to the estimates of a number of investigators, lithium CPS with a polymeric electrolyte can replace in the future sulfuric acid-sodium batteries, accumulators based on systems of the Li/metal sulfide type, and even, partially, nickel–cadmium batteries.[1] Apart from their use in CPS, PE can be employed in sensor devices, condensers, and other solid state electrochemical devices.[2]

The principal task in the creation of solid PE involves nowadays the search for new compositions with a high ionic conductivity for ions of different species over a wide temperature range. The stability of the PE in air, their low cost, and the ease of their technological application are also very important. It is noteworthy that the possibility of constructing thin 0.5–100 μm films from electrolytes of the class considered and their elasticity constitute their major advantages compared with ceramic electrolytes. Furthermore, in terms of their transport properties, PE are only slightly inferior to liquid electrolytes.

Depending on the nature of the ionogenic centre, PE can be divided into two groups: (1) polymeric complexes — complexes of functional polymers with metal salts; (2) composite PE — compositions comprising film-forming polymers with low-molecular-mass solvents and electrolytic salts.

The polymeric complexes may be synthesised from polyesters, polynitriles, polyamides, polysulfones, and other functional polymers. By varying the structure of the polymer matrix and the composition of the complex, it is possible to obtain compounds with conductivities σ up to 10^{-2} S cm^{-1}. However, the variation of the properties under the conditions of constant current polarisation constitutes a significant disadvantage of this type of PE.

Composite PE may be obtained from a wide variety of polymers, solvents, and ionogenic salts. This makes it possible to regulate their properties over a wide range. The conductivity of the composite electrolytes is extremely sensitive to their composition and methods of preparation. After prolonged storage and also after polarisation with a direct current, an irreversible change in their structure takes place in many instances and leads to a significant decrease in conductivity. In order to obtain solid electrolytes, it is essential to have polymers with a high flexibility of the chain, a low cohesion

V G Syromyatnikov, L P Paskal' Department of the Chemistry of Macromolecular Compounds, Shevchenko Kiev University, ul. Vladimirskaya 64, 252017 Kiev, Ukraine. Fax (7-044) 225 12 73. Tel. (7-044) 274 85 70, (7-044) 221 02 82 (V G Syromyatnikov)
O A Mashkin Institute of General and Inorganic Chemistry, National Academy of Sciences of Ukraine, prosp. akademika Palladina 32/34, 252142 Kiev, Ukraine. Fax (7-044) 444 30 70

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energy density, etc. The necessary and sufficient conditions for the employment of various polymers and matrices in polymeric electrolytes for CPS have been most fully considered in the review of Bruce and Vincent.[3]

In the present review, attention is concentrated on questions of the modification of solid polymeric electrolytes in order to increase their conductivity, of the influence of the purity of the PE components on the ionic conductivity and the electrical parameters of the CPS, and also of the chemical interaction in the lithium anode–polymeric electrolyte system.

II. The mechanism of ionic conduction in solid polymeric electrolytes

In composite PE, the driving force leading to the dissolution of the salt in the polymer arises from the oxygen, nitrogen, or sulfur atoms forming part of the composition of the polymer molecule and surrounding the lithium cations. The coordination groups in PE are the oxyalkanes $-CH_2-CH_2-O-$, azoalkanes $-CH_2-CH_2-NH-$, thioalkanes $-CH_2-CH_2-S-$, and the esters $-CH_2-CH_2-OCO-$. The following types of polymers are used for the preparation of the PE: linear homopolymers — poly(ethylene oxide) (PEO), poly(propylene oxide) (PPO), and polyethyleneimine (PEI), nonordered polymers–PEO/PPO; network polymers (with cross-links); cellular-branched copolymer blocks.

The organic polymers used for the preparation of the PE are usually insulators themselves. Their insignificant conductivity (of the order of $10^{-12}-10^{-10}$ S cm^{-1}) is due to the presence of impurities and is due to the diffusion of ions through the free volume of their macromolecules. Therefore fairly satisfactory ionic conductors can be obtained by dispersing various salts in the polymers at the molecular level. Among metal ions, those of lithium are the smallest and have the lowest activation energy and for this reason lithium salts are frequently employed to prepare electrically conducting compositions for different purposes. With increase in the size of the cation, there is an increase in the degree of binding of the salts to the macromolecules. An increase in the complexity of the structure of the cations lowers the degree of solvation of the low-molecular-mass ions by the macromolecules. The donor capacity (DN) of the solvents also influences the complex formation process. For example, in acetonitrile ($DN = 14.3$), the degree of association of polyesters with low-molecular-mass salts is higher than in methanol ($DN = 19.0$) solutions.[4–6]

The mechanism of the conduction in polymeric electrolytes, first proposed by Armand et al.,[7] presupposes ionic conduction in continuous conducting regions of the helical structure of the PEO and also the fact that it is effective predominantly in the amorphous phase of the PEO–salt system. Under these conditions, the ion migrates between the polymer chains by virtue of the segmental motions of the polymer matrix. It may be that such movement in the polymer is an important factor which determines the order of magnitude of the ionic conductivity in the solid state.

Bruce and Vincent[8] investigated ionic transport in polymeric electrolytes — amorphous PEO–$LiClO_4$ complexes — by an e.m.f. method for different compositions of the complexes. In this case, the steady-state current during polarisation by a permanent field was attained after several hours and was determined by the mobility of both Li^+ and ClO_4^- ions, while at a high salt concentration ion pairs are also mobile.[9] According to the data quoted by Gray,[10] at a fixed temperature the dependence of the conductivity on the perchlorate concentration is a complex function. At low concentrations, the conductivity σ diminishes rapidly with increase in the salt content. It then increases to a maximum, the position of which depends on the temperature, after which it again falls. The form of the observed dependences of σ on temperature and perchlorate concentration is caused, according to the authors, by charge transfer involving the Li^+ and ClO_4^- ions, the mobilities of which are influenced by the incomplete dissociation of the salt and by the formation of the cluster ions $Li(ClO_4)_2^-$ and $Li_2(ClO_4)^+$.

It has been shown by Brillouin and photon-correlation spectroscopy[11] that the cooperative movement of ~20 monomer units of the polymer is needed for ion transport. For $n > 4$, short-lived ion–polymer cross-links, restricting the mobility of the polymer segments, arise in the electrolyte. The density of the cross-links diminishes sharply with increase in temperature as a consequence of the formation of ion pairs, which exert a plasticising effect on the electrolyte.

In the study of the ionic association of the PPO–$LiClO_4$ complexes, the constancy of the number of dissociated ions under conditions when the monomer : salt ratio varies from 1000 to 30 was noted.[12] With increase in the salt concentration in PPO, the rate of formation of ion pairs also rises. The main contribution to the increase in the conductivity of the PE at low $LiClO_4$ concentrations comes from the increase in the number of dissociated ions and not from their mobility. The IR and polarised Raman spectra of the PPO–$LiCF_3SO_3$ complexes indicate the existence of three types of associated species: two differently coordinated ion pairs and a triple ion. It is claimed[13] that the free ions which had been believed previously to exist in these polymer–salt complexes are in fact cation–anion pairs in which the cation interacts weakly with the terminal CF_3 group of the anion.

The data of Arumugam et al.[14] on the diffusion coefficients of Li^+ and PF_6^- in the amorphous PEO–$LiPF_6$ electrolyte obtained using ^7Li and ^{31}P NMR with a pulsed field gradient over a wide range of temperatures (25–100 °C) and salt concentrations (up to 0.25 M) indicate different mechanisms of the transport of the cation and anion at a high salt concentration. A reduced sensitivity of the diffusion of the cation to the salt concentration and a deviation from the Nernst–Einstein relation have been observed. Cation jumps between ionic clusters and the diffusion of neutral ion pairs have been proposed as mechanisms to account for the results.

III. Modification of the polymeric electrolytes used in lithium chemical power sources

The main obstacle in the creation of low-temperature solid-state batteries with a polymeric electrolyte is the marked impairment of its ionic conductivity during storage caused by the crystallisation of the PE and a sharp increase in the size of its particles.[15] One of the ways of solving this problem is to base the electrolytes on complex polymeric compounds or to use these to modify the traditionally employed PE.

A survey of the experimental studies in recent years demonstrated that complexes of PEO with lithium salts are mainly employed as the solid PE, but their practical use in the manufacture of CPS is difficult, firstly, as a consequence of the tendency of PEO to crystallise, secondly, as a consequence of the hygroscopicity of the films based on it, and, thirdly, due to the small transport numbers of the cations.

Analysis of the literature data makes it possible to differentiate the following principal modification methods which increase the ionic conductivity of the polymeric electrolytes: the use of amorphous polymers and additives inducing conversion into an amorphous structure; the formation of a network system (cross-links); the introduction of crown-ethers, plasticisers, and ceramic powders. The application of such methods makes it possible to employ the PE in lithium CPS at normal temperatures.

The efforts of investigators engaged in the development of the PE have been directed mainly to the stabilisation of the state of the polymers containing amorphous sections or their preparation in the amorphous state. This is associated with the fact that the majority of polymeric electrolytes containing lithium salts have the maximum ionic conductivity when they exist in the amorphous state, which is the reason for the level of working

temperatures being approximately 100 °C. The possibility of creating electrolytes in a stable amorphous form, i.e. the preparation of polymers with a secondary structure having optimum electrochemical and mechanical properties, has therefore been discussed in recent years.[18,19] In particular, an amorphous single-state solid electrolyte with an improved ionic conductivity, the absence of crystallinity, and a satisfactory elasticity at 20 °C has been obtained by copolymerising ethylene oxide and other oxides of the type $-CH_2-CH(R)-O-$, where R = alkyl, alkenyl or alkynyl, containing between 1 and 12 carbon atoms, or $-CH_2-O-R'-R$, where R' is a polyether $-(CH_2-CH_2-O-)_p$ (p is an integer in the range from 0 to 10), or a cyclic ether containing more than three carbon atoms in the ring.[20] The oxides are selected from the group comprising tetrahydrofuran, dioxolane, and their derivatives. Short cross-links in the electrolyte are ensured by adding silicon, cadmium, boron, titanium, zinc, magnesium, or tin compounds. The polymeric electrolyte contains between 1.5 and 25 mass% of $LiClO_4$ or $LiCF_3SO_3$.

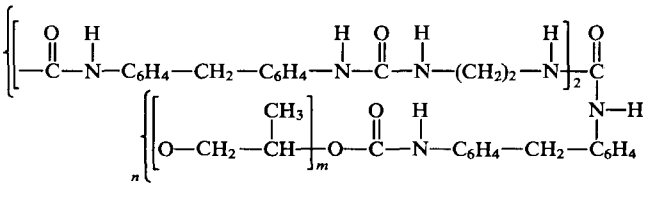
A PE with $LiClO_4$ has been obtained from an amorphous copolymer of ethylene and propylene oxides and allyl glycidyl ether (the content of the amorphous phase was 98%). Its maximum conductivity proved to be 75×10^{-5} S cm^{-1} at 25 °C for an electrolyte composition with a lithium : oxygen ratio of 0.05.[21]

In another study,[22] the polymer matrix was PEO, each monomer unit of the main chain of which contained the $-(CH_2-CH_2O)_x-R$ side chain, where $1 < x < 20$ and R is an alkyl group. The bond between the main and side chains in the polymer is formed via an ether group. The molecular mass (M) of the main polymer chain was $10^4-5 \times 10^6$, while that of the side chain was 50–2000. Such a solid PE has a high conductivity at 20 °C and may be used in lithium accumulators.

It proved possible to increase the conductivity of the PEO–$LiClO_4$ and PEO–$LiCF_3SO_3$ systems at low temperatures by adding low-molecular-mass polyethers $CH_3(OCH_2.CH_2)_nOCH_3$.[23–25] The materials obtained behave similarly to a solution of salts in the polymer of the dimethyl ether of ethylene glycol ($\sigma = 10^{-4}$ S cm^{-1} at 40 °C), but their mechanical properties turned out to be unsatisfactory.

The PE based on PEO may be modified by introducing various lithium salts of fluorinated monobasic salts. The complex of PEO with $LiCF_3SO_3$ has the highest conductivity among the complexes investigated ($\sigma \approx 4 \times 10^{-4}$ S cm^{-1} at 100 °C). An increase in the size of the anion in these salts leads to a decrease in σ. This has been attributed to a change in the interactions and mobilities of the ions. In the case of the $LiCF_3SO_3$ and NaI salts, there is a significant increase in the conductivity of the PEO-based PE and a decrease in the microviscosity.[26] It has been suggested that the observed effect is associated with the strong influence of the fraction of the amorphous 'elastomeric' phase and also with the inhomogeneity of the distribution of various cations and anions in different phases.

The PE can also be maintained in the amorphous state by creating segmented block copolymers in which the regularity of the chain is disturbed and hence crystallisation is hindered. A series of materials have been investigated[27,28] in which this principle holds, especially the system employed as the primary polymeric crystal, namely segmented polyether-polyurethane-urea, which has the structure $(A-B)_n$, where A is the solid segmented polyurethane-urea (~30 mass%) and B is a soft polyether segment.

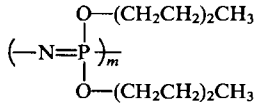


The polyurethane-urea segments tend to aggregate as a result of the formation of hydrogen bonds and of a two-phase microstructure, ensuring thereby that the electrolyte has excellent mechanical properties. Salts such as $LiClO_4$ dissolve selectively in the polyether. The relation between the morphologies, the dynamic-mechanical properties, and the ionic conductivities of the materials has been described.[28,29]

A similar matrix polymer — polyurethane-urea (PUU) — has been described.[30] 4,4-Dimethylbis(phenylene isocyanate)ethylenediamine and poly(ethylene glycol) ($M = 1000$) were used as the starting materials for its synthesis. The molecular mass of the soft (polyether) segment of the polymer is 1000, the mass fraction of the hard segment (polyurethane-urea) is 35, and the melting point of the polymer is 180 °C. A film formed from a complex of an alkali metal salt with PUU has a high ionic conductivity ($\sigma = 1 \times 10^{-5}$ S cm^{-1}) at 33 °C and a fairly high mechanical strength.

A method has been proposed for the preparation of the PE by the mechanical mixing in a solvent at room temperature of an acrylic poly(alkylene oxide) and a lithium salt with polyurethane (PU) or polyurethane-urea and subsequent heat treatment of the mixture.[31] The resulting solid electrolyte has $\sigma = 1.5 \times 10^{-5}$ S cm^{-1} and satisfactory mechanical properties. When the salt $LiClO_4$ is introduced into polyurethane, the ionic conductivity increases by three orders of magnitude: $\sigma_{max} = 10^{-4}$ S cm^{-1} at 20 °C is attained in PU : $LiClO_4$ = 8 : 1 mixtures.[32] In the presence of high contents of $LiClO_4$, the conductivity falls owing to the increase in viscosity. The difference between the conductivities of the PE based on PEO and PU is especially significant at temperatures below 80 °C, since a decrease in temperature entails a sharp (by a factor of ~10) decrease in the conductivity of PEO due to a structural rearrangement. Experiments in which lithium electrodes were employed established that the transport numbers of the lithium cations at 50–100 °C are 0.5–0.8. In order to prevent the impairment of the characteristics of batteries having PE as a result of prolonged storage, it has been suggested that a polymer having a urethane-like structure, in which the hydrogen atoms have been replaced by alkali or alkaline earth metal atoms, be used as the electrolyte.[33]

More flexible comb-branched systems may be obtained from polymers the main chain of which has a low glass point. These probably result in the formation of electrolytes with a maximum conductivity.[34] In order to synthesise such PE, a study has been made[35–37] of systems based on phosphazene and siloxane polymers. One of the most successful PE has been synthesised by substituting the chlorine atoms in poly(dichlorophosphazene) by alkyl groups as a result of treatment with the sodium salt of 2-(2-methoxyethoxy)ethanol in the presence of tetra-n-butylammonium bromide, which results in the formation of a compound having the formula

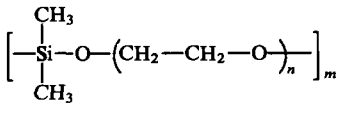


This polymer gives rise to single-phase amorphous electrolytes with different univalent, divalent, and trivalent salts.[35] The dependence of the ionic conductivity of the solid-phase polymeric complexes of an oligo(ethylene oxide) graft copolymer with polyphosphazene on temperature and concentration has been investigated.[38] The maximum value of σ ($\sigma_{max} = 10^{-4}$ S cm^{-1}) was observed for complexes of the copolymers with $LiClO_4$ at 25 °C and for a salt content of 15%. For the complexes of $LiClO_4$ (salt content 7.5%) with polyphosphazene modified by the grafting of oligo-oxyethylene with a degree of oligomerisation of 7, $\sigma = 3.5 \times 10^{-4}$ S cm^{-1}. For structurally involved complexes of a polycyclotriphosphazene with $LiClO_4$, the conductivity was $\sigma = 1.2 \times 10^{-4}$ S cm^{-1} (at 90 °C), the

maximum in σ shifting towards a higher salt concentration with increase in temperature.[39]

The main advances in the field of ionic polymeric conductors based on linear phosphazenes and polyacrylates containing PEO with different degrees of polarisation as substituents in the side chains have been considered in reviews.[40,41] It was shown that the complexes of the above polymers with the salts $LiCF_3SO_3$ and $AgCF_3SO_3$ exhibit an anomalously high conductivity with respect to the metal cations (up to 10^{-3} S cm^{-1}). These results agree well with the experimentally determined diffusion coefficients of the cations. A polymeric electrolyte, consisting of a mixture of the complex salt of poly[bis(methoxyethoxyethoxide)-phosphazole] (I) and PEO (II) and doped with $LiCF_3SO_3$ or $LiClO_4$ was cast from a I + II solution in acetonitrile and dried in vacuo at 100 °C.[42] For the ratio I : II = 1 : 1, the specific conductance of the electrolyte was 2×10^{-4} S cm^{-1} at 20 °C and 5×10^{-2} S cm^{-1} at 100 °C. A method of synthesis of oligoethyleneoxypolyphosphazene (OPP), containing allyl groups, has been proposed.[43] The method includes a stage in which hexachlorotriphosphonitrile is converted into dichlorophosphonitrile and the latter interacts with the corresponding alkoxides. During the synthesis, up to 5 mass% of $LiClO_4$ is introduced into the OPP, which ensures a fairly high conductivity of the PE with respect to lithium ions.

Polymers with a very low glass point have been obtained by the polycondensation of dichlorodimethylsilane with poly-(ethylene glycol).[44]



The high flexibility of the main chain and the absence of crystallinity (as a consequence of the irregularity of the chain) ensure a high conductivity of such polymers — much higher than the conductivity of poly[bis(methoxyethoxyethoxide)phosphazene].[35] The conductivity is comparable to that of the comb-branched siloxanes.[45] However, the practical employment of such systems is held back by the high sensitivity of siloxanes to hydrolysis.

PE based on poly-*p*-phenylenevinylene (PPV) have also been proposed for the manufacture of accumulator batteries.[46] The films consist of a mixture of aqueous solutions of polymeric precursors of PPV (a water-soluble sulfonium salt) and a water-soluble polymer such as PEO, methylcellulose, or hydroxypropylcellulose in proportions of 1 : 1. PPV is obtained from the precursor salt form by heat treatment of it. The best results were obtained for mixtures of PPV and PEO doped with $LiClO_4$. Such mixtures are resistant to thermal degradation (up to 225 °C) and possess satisfactory mechanical properties.

Polymeric electrolytes with an amorphous structure are formed from a copolymer of acrylonitrile and sulfoalkyl methacrylate.[47] The conductivity of different salt forms of the PE then varies in the sequence lithium salt > sodium salts > potassium salts and increases with increasing oxygen : lithium ratio in the range 20 – 100. The new PE based on the copolymers with poly(vinyl alcohol), PVA, and polyacrylamide have a high thermal stability combined with a fairly high conductivity.[48]

One of the methods for retarding the transition of the polymer from the amorphous to the crystalline state involves the cross-linking of the polymer matrix, for example the cross-linking of PEO by exposure to γ-radiation or an electron beam.[49] In this case, one obtains PE with an improved conductivity with respect to lithium ions at a reduced temperature. The mechanisms of the radiolytic degradation and cross-linking of PEO in the solid state and in aqueous solutions have been investigated by the EPR method.[50] The decrease in crystallinity, the improvement in mechanical properties, and the increase in conductivity at 20 °C of the cross-linked polymeric materials indicate that γ-irradiation is a simple and effective method for the preparation of highly conducting and mechanically stable PE. However, the effect of the γ-irradiation of PE specimens based on PEO and lithium salts ($LiClO_4$ and $LiCF_3SO_3$) at 78 °C has not been confirmed.[51]

The cross-linking of a polymer composition consisting of PEO units with terminal C(O) – CH=CH – C_6H_4R (R = NO_2, Cl, OCH_3), C(O) – CH=CH – CH=CH – C_6H_5, C(O) – C(NC)= CH – C_6H_5, and C(O) – C(NC)=CH – CH=CH – C_6H_5 groups has been described.[52] The cross-linking takes place under the influence of accelerated electrons or UV irradiation. A thin-film PE (in a mixture with lithium salts) with a degree of cross-linking of 90% and an ionic conductivity of 1.7×10^{-4} S cm^{-1} at 20 °C was obtained.

Chemical methods for the cross-linking of the polymer matrix have been described in a series of studies. For example, film PE with satisfactory conductivity at 30 °C[53] as well as a strong and elastic PE with $\sigma = 6 \times 10^{-5}$ S cm^{-1} at 25 °C[54] have been obtained by mixing the product of the copolymerisation of polyglycerol with ethylene oxide or a mixture of ethylene and propylene oxides with a polyfunctional cross-linking agent (polyisocyanate) at 50 – 200 °C and a pressure of >10 kg cm^{-2}. The methods of preparation of PE based on lithium salts and poly(ethylene glycols) cross-linked by siloxane tetraisocyanate have been described.[55]

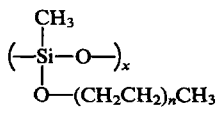
It has been suggested that a cross-linked copolymer of ethylene oxide and propylene oxide be used as the base of a polymeric electrolyte for a lithium accumulator.[56] In combination with a lithium salt, such a PE ensures a specific conductance of the lithium ions of the order of 10^{-5} S cm^{-1} at 25 °C. The product of the copolymerisation of the vinyl ether R – (O – CH_2 – CH_2)$_n$ – O – CH= CH_2 (R = Me or Et, n = 1 – 6) with the divinyl ether [CH_2=CH – (O – CH_2 – CH_2)$_n$ – O – CH=CH_2] (n = 1 – 6) is a cross-linked polyether with a glass point of 60 – 80 °C, which has been used as the matrix for the preparation of a solid PE.[57] The cross-linking of PEO-based resins by vinyl polymers has been described.[58] Before cross-linking, the (PEO-400)-maleate-isophthalate resins by styrene (St), vinylpyrrolidinone (VP), or vinylpyridine (VPD), $LiClO_4$ was added to the resins. For the ratio [PEO]/[Li^+] = 50, the conductivity of the PE obtained increases in the sequence VPD < VP < St. This sequence is correlated with the increase in the strength of binding of Li^+ on passing to more polar comonomers.

A polymeric electrolyte with stable characteristics,[59] capable of being used for a long time without a decrease in capacity, has been obtained from a polyether with cross-links of the urethane type. It contained the (O – CO – NR) (R = an inert group or an element in Group I of the Periodic System other than hydrogen) repeating unit. The electrolyte also contained an inorganic salt and an inert additive.

A polymeric electrolyte — a modified polyurethane network obtained from polydimethylsiloxane containing grafted PEO, cross-linked by an aliphatic diisocyanate, and incorporating 10% of $LiClO_4$ — has an ionic conductivity of 10^{-5} S cm^{-1} at 30 °C. It was used in solid-state electrochemical lithium batteries. Analysis of voltammetric data showed that, after the completion of the synthesis of the polyurethane network, the unreacted cross-linking agent may interfere with the diffusion of lithium ions at the electrode – electrolyte interface. The limiting currents were determined from the cathodic branches of the voltammogram. The internal resistance of the RuO_2/Li accumulator with a PE was determined from its discharge curves recorded at 60 and 80 °C. It proved to be 5 kΩ. After two discharge cycles with degrees of discharge of 95% and 73%, the adhesion of the PE film to RuO_2 and Li remained unchanged.

The morphology and physical properties of the electrolytes prepared from linear segmented polyurethanes based on PEG and alkali metal salts have been described in fair detail.[61] Systems based on siloxane polymers may be obtained by mixing in a common solvent lithium salts with an organopolysiloxane containing more than two COOH groups in the molecule.[62]

The conductivity of such a PE at 25 °C is 5.6×10^{-5} S cm^{-1}. Liquid comb-branched polymers of the type



may be additionally cross-linked by heating to 150 °C (in order to form rubber-like films).[45] The length of the side chain exerts only a slight influence in this case on the conductivities of the electrolytes. For a PE of this kind, containing $LiClO_4$ as the ionogenic additive, $\sigma = 1 \times 10^{-4}$ S cm^{-1} at 25 °C.

A number of authors patented liquid solidifying organosiloxane-oxyalkylene copolymers with acrylate functional groups into which $LiCF_3SO_3$ and azobisisobutyronitrile (AIBN) had been introduced. After solidifying at 85–90 °C for 30 min, elastic films 1 mm thick and with $\sigma = 1.6 \times 10^{-5}$ S cm^{-1} were obtained.

It is noteworthy that the assignment of a particular polymeric electrolyte in terms of the method of modification to the first or second group is arbitrary, since the appearance of cross-links between the macromolecules is a means of fixing the amorphous state.

One of the promising ways of modifying PE involves the introduction of crown-ether additives, which greatly increase the ionic conductivity.[64] Studies on the electrical and electrochemical properties of PE films consisting of PEO and the salts $LiCF_3SO_3$, $LiBF_4$, or $LiClO_4$, both containing and not containing 12-crown-4 (12Cr4), showed[65] that at a constant temperature σ for each salt depends on the concentration of the crown-ether, which is a maximum for the concentration ratio [12Cr4]:[Li] = 0.003.

The kinetics of the complex formation reactions between alkali metal cations and macrocyclic ligands — 12-crown-4, 18-crown-6, and 15-crown-5 — have been investigated.[66] Crown ethers of the 16-crown-5 group were also introduced into polyphosphazenes (PP) as side groups.[67,68] The temperature dependences of the conductivities of such PE, containing $LiClO_4$ or $NaClO_4$, have been investigated. The lg $\sigma - 1/T$ relation was linearised with the aid of the Vogel–Tammann–Fulcher relation. The highest value of σ was attained for PP–$NaClO_4$, which is associated with the higher degree of ionisation of the salt bound to the macromolecular part of the polyphosphazene. The introduction of 12-crown-4-ether both into the solid PE consisting of PEO and $LiBF_4$ and into a cathodic composition consisting of Li_xCoO_2, PEO, and $LiBF_4$ improves the ionic conductivity of the PE.[69] The electrolyte has a very low leakage current. The addition of a crown-ether improves the operation of the cell, lowers the dissociation peak and the resistance to charge transfer, and increases the current capacity and reversibility of the cell (this has been observed in the case of CoO_2 and TiS_2 cathodes).

Apart from crown-ethers, a bicyclic compound (cryptand), which also forms a complex with lithium ions, may be used as an additive.[70]

The addition of low-molecular-mass plasticisers such as ethylene and propylene carbonates to electrolytes based on PEO,[71,72] polyacrylonitrile (PAN) poly(tetraethylene glycol diacrylate), or polyvinylpyrrolidinone and also into hybrid films based on PMMA, polystyrene, PVC, PVA, PAN, and poly(vinylidene fluoride) in amounts up to 30 mol.% increased σ to 10^{-5}–10^{-3} S cm^{-1}.[74] The suitability of the hybrid films as PE in solid-state batteries is indicated by the stable potential of the Li/specimen/MnO_2 galvanic cell operating for more than 70 h without the decomposition of the electrolyte. The possibility of plasticising the PEO-based compositions by introducing poly(ethylene glycols) with different molecular masses has been investigated.[75,76] Such plasticisation increases σ by increasing the content of the amorphous phase in the electrolyte and simultaneously increasing the salt concentration in this phase.

The study of the conductivites of solid polyelectrolytic complexes of the alkali metal salts NaSCN, $NaCF_3SO_3$, and $LiCF_3SO_3$ with polymers based on methoxypoly(ethylene glycol methacrylate) $CH_2{=}C(CH_3)COO(CH_2CH_2O)_nCH_3$ [$n = 8$ (PMG-8) and $n = 22$ (PMG-22)] as a function of temperature and salt concentration showed[77] that the systems based on the copolymers of PMG-22 with polystyrene as well as systems plasticised by poly(propylene carbonates) have much higher values of σ than systems based on the homopolymers. Compositions based on a mixture of an alkyl acrylate (alkyl C_{1-8}) and/or alkoxyacrylate (alkoxy C_{2-5}) polymer with 5%–100% (relative to the mass of the acrylate polymer) of $LiClO_4$ or the lithium salt of a polymeric acid (polystyrenesulfonic acid, polyethenesulfonic acid) with a high conductivity, used as a thin-film electrolyte, have been described.[78] The organic solvent, with a high relative permittivity, serves as both the plasticiser and the solvent.

An interesting phenomenon — a sharp increase in the conductivity of the PE on mixing it with Al_2O_3 powder — has been observed by the authors of a series of investigations. Such PE were investigated by impedance spectroscopy, X-ray diffraction, and NMR. It was shown[79] that the conductivity of the polymeric PEO–NaI electrolyte increases on mixing with Al_2O_3, reaching a value in excess of 10^{-5} S cm^{-1} at room temperature.

An increase in conductivity and satisfactory mechanical properties are also manifested by the PE having the composition $(PEO)_8LiClO_4$ into which powdered β-Al_2O_3 with a small grain size (< 5 μm) have been introduced by mixing with a solution of PEO and $LiClO_4$ in acetonitrile.[80] The addition of Al_2O_3 [81] and of ceramic $LiAlO_2$ microspheres 1 μm in diameter[82] (up to a concentration of 10%–30%) has a positive effect on the mechanical properties and conductivities of solid PE. An increase in the conductivity by an order of magnitude is attained by introducing β-Al_2O_3, Li_2O–B_2O_3–SiO_2 ionic glasses, and ion-exchange resins in the lithium-form as fillers into PEO-based.[83,84] Since the ratio of the pre-exponential factor for the conduction and the activation energy satisfies the Mayer–Neldel rule for the entire range of filler concentrations, the authors concluded that the ion-conducting fillers do not participate in charge transfer through the solid electrolyte and that their presence leads merely to the composites being more amorphous.

IV. The influence of the purity of the components of the polymeric electrolyte on its electrochemical characteristics

It was noted above that the composition for the preparation of the PE consists as a rule of a polymeric binder, an ionogenic alkali metal salt, and the solvent. PEO is the polymer most often employed in PE and has been most thoroughly investigated, but it is extremely hygroscopic like many other polymers employed in the PE; the lithium salts are also hygroscopic. The stability of the properties of the PE films is largely determined by the purity of the components and their moisture content. Therefore all manipulations involving the PE component are as a rule carried out under a dry or inert atmosphere.

A high-molecular-mass highly pure PEO is obtained by anionic polymerisation. The mechanism of the absorption of water by polymers, including poly(ethylene oxide), and the influence of the polymer structure on this process have been described.[85] It was shown that the absorption of water depends greatly on the composition of the aqueous solution: it diminishes with increase in the salt concentration, and to a greater extent the higher the ionic charge. The interactions of PEO with water have been investigated by differential scanning calorimetry (DSC) and NMR spectroscopy.[86] The plasticised PEO was characterised by the ratio of the number of moles of D_2O to the number of moles of monomer units (R). The DSC results showed that an increase in R to 0.6 leads to a monotonic decrease in the melting point of

the PEO from 56 to 35.9 °C. For $R > 0.135$, another low-temperature fusion isotherm appears, which has been attributed to the decomposition of the eutectic mixture. It was observed that an increase in R leads, on the one hand, to a decrease in the melting point from 22.7 to 11.9 °C and, on the other, to a linear increase in the enthalpy of fusion. The absence of a low-temperature endotherm for lower R has been attributed to the small size of the pores through which D_2O diffuses. Analysis of the NMR line shape indicates the presence of a doublet for $R = 0.07$ and 0.096, which has been explained by the low rate of exchange (on the time scale of the NMR experiment) between the bound and free water.

Studies showed that the method of preparation of the PEO has actually no influence on the properties of the PEO–lithium salt polymeric electrolyte.[87] On the other hand, the purity of the solvent employed for the preparation of the composition (acetonitrile) is strongly reflected in the properties of the polymeric complexes formed. In 'dry' solvents, complexes with high melting points and high degrees of crystallinity are formed, whereas in 'moist' solvents the complexes produced have low melting points. Complexes with low melting points are suitable as electrolytes for use at 120 °C and above.

The dehydration of the PE films is necessary, since an insulating coating comprising lithium hydroxide is formed on the lithium anode when the latter comes into contact with moisture. In order to protect the lithium electrode against oxidation, Japanese investigators[88] introduced tin salts into the liquid electrolyte. Tin ions are substituted by metallic lithium and a thin coating of metallic tin, suppressing the formation of lithium hydroxide, is formed on the surface of the negative electrode.

The study of the influence of hydration and dehydration processes on the conductivity of films of a PEO-based solid electrolyte showed that the hydration of the PE having the initial composition $(PEO)_8NiBr_2$ results in the formation of at least two types of bound water:[89] weakly bound water, which is removed at temperatures of approximately 80 °C, and strongly bound water which can be removed only at 130–140 °C. It is suggested that the strongly bound water is present as the complex $(PEO)_8NiBr_2 \cdot 6H_2O$. The ionic conductivity depends greatly on the degree of hydration of the electrolyte, increasing by ~8–10 orders of magnitude during the moisture absorption process. A method for the preparation of anhydrous films comprising polymers (PEO, PPO) and salts (mercury and sodium perchlorates) from their hydrated forms has been described.[90]

Thus the electrochemical properties of polymeric electrolyte films can be easily reproduced, provided that the water content in the components and the solvent is strictly controlled and also when films in a dry, inert form are employed.

V. Preparation of thin films of polymeric electrolytes by plasma polymerisation

One of the most important problems in the development of solid polymeric electrolytes is that of the preparation of thin films with a high mechanical strength. Japanese investigators developed a technology for the preparation of thin polymeric films with ionic conductivity for lithium accumulators by plasma polymerisation.[91] Hybrid layers of the polymeric product, exhibiting ionic conductivity, are obtained in three consecutive stages: (1) plasma polymerisation (PM) of the monomer in a vacuum with a residual inert gas, (2) spraying of a lithium salt solution over the polymer layer (0.5 μm), and (3) plasma polymerisation of a fresh portion of the monomer. The characteristics of the solid PE which depend on the plasma parameters have been established.[91] A relative increase in the energy of the glow discharge leads to an increase in the number of cross-links in poly[tris(2-methoxyethoxyvinyl)-silane] and to a decrease in its conductivity. Ultrathin films (~1 μm) of a homogeneous PE have been obtained by the plasma polymerisation of methyl acrylate (MA) and tris(2-methoxy-ethoxyvinyl)silane (TMVS).[92] According to IR spectroscopic data, the structure of the polymer obtained is close to that of the MA–TMVS copolymer. A layer of LiI was sprayed on to the polymer layer and then a further polymer layer was deposited. The three-layer composite was maintained for 24 h in vacuo (10^{-3} Torr). On interaction with LiI, the ester group $COOCH_3$ is then converted into the carboxylate group. The conductivity of such PE at 20 °C is 10^{-8} S cm^{-1}, which is less than the value for the TMVS–$LiClO_4$ complex (10^{-6} S cm^{-1}).

A technology for the preparation of ultrathin solid-state lithium accumulators involving the use of a plasma-polymerised solid polymeric electrolyte has been described.[93] A layer of TiS_2 (~12 μm) was deposited on a borosilicate glass support by the vacuum spraying of $TiCl_4 + H_2S$ vapour; a layer of a solid PE (~1.5 μm) was then deposited on it by the plasma polymerisation of the 1:10 TMVS–Ar mixture in vacuo. A 3% methanol solution of $LiClO_4$ was sprayed onto the polymer film at 60 °C and then a further layer of the polymer and a layer of the lithium salt (~1.5 μm) were deposited. After being kept in vacuo at 80 °C, the resulting solid PE had a conductivity of 10^{-4}–10^{-3} S cm^{-1} at 20 °C. The accumulators operated at a current density of 100 mA m^{-2}.

The properties of such a thin three-layer PE film with a high conductivity, laid on a glass plate with gold deposited from a high-frequency plasma in a stream of gold and TMVS vapour, have been investigated.[94] It was noted that there are no alkene groups in the polymer film and the distribution of the ClO_4^- ions with respect to thickness is nearly homogeneous, which corresponds to a homogeneous distribution of lithium ions. Pin holes were not detected in the film by electron microscopy. For the films containing 7% of $LiClO_4$, the conductivities are respectively 4.4×10^{-5}, 4.5×10^{-6}, and 3×10^{-7} S cm^{-1} at 100, 50, and 10 °C.

Apart from the plasma-generated TMVS polymers, a solid polymeric electrolyte for chemical lithium batteries has been obtained from polyoctamethylcyclotetrasiloxane and $LiClO_4$ by plasma polymerisation under glow discharge conditions. The conductivity of such films, reaching 10^{-6} S cm^{-1}, is determined by the $LiClO_4$ content.[95] A solid-state lithium accumulator with a thin-film (10–15 μm) cathode comprising TiS_2 and a PE film obtained by the plasma polymerisation of octamethylcyclotetra-siloxane with subsequent grafting of the poly(propylene oxide)–$LiClO_4$ complex has also been described.[96,97] The structure of this plasma-generated polymer is similar to that of polydimethyl-siloxane. The ionic conductivity of the hybrid PE reaches 2.6×10^{-6} S cm^{-1} at 60 °C. For a current density of 8 μA cm^{-2} and room temperature, the discharge plateau for the first discharge of the accumulator corresponded to the 85% utilisation of the cathodic material. The chargeability of the accumulator was satisfactory, but its internal resistance was fairly high.

A CPS with an increased operating lifetime, capacity, and number of charge-discharge cycles has been patented.[98] In this CPS, the solid PE consists of a plasma-polymerised layer of an organic compound containing an alkali metal ion and an element with a higher electronegativity.

VI. Electrochemical stability of solid polymeric electrolytes

When polymeric electrolytes are employed in lithium accumulators, complex problems associated with the electrochemical stability of the electrolytes arise. However, the number of publications devoted to this problem is small.

Thus Armand noted[99] that the electrochemical stability of polyethers is comparable to that of aprotic solvents such as tetrahydrofuran and propylene carbonate. The kinetics of the electrochemical process occurring in the lithium cell and involving the PEO–$LiClO_4$ solid electrolyte are as a rule controlled by the diffusion of ions.[100] The study of the PE films based on phosphazenes with $LiCF_3SO_3$ showed that the limits of the electrochemical stability are determined by the

reduction of the lithium salt.[101] Molecular complexes of lithium salts with poly[bis(methoxyethoxyethoxide)phosphazene] (MEEP) and its analogues with a high ionic conductivity, but are unstable.[102,103] In order to increase the stability of the polymeric structure, the MEEP was cross-linked by poly(ethylene glycol) ($M = 1000$), since the cross-linked macromolecules are very stable. This made it possible to employ their complexes with $LiCF_3SO_3$ as ionic conductors up to 140 °C. Stable polymeric electrolytes for lithium CPS, in which the dimensions are satisfactorily maintained during operation and the conductivity is 6.7×10^{-5} S cm^{-1} at 25 °C, have been obtained from MEEP and PEO–[$LiN(CF_3SO_3)_2$].[104] Cyclic voltammograms indicate the stability of the PE at potentials up to 4.5 V relative to the Li^+/Li electrode. Their use in the Li/TiS_2 lithium cell ensures 200 charge-discharge cycles.

Preliminary data on their cyclic nature and stability have been obtained for PE based on Li/poly[*N*-3,6-dioxaheptylpyrrole] to which [poly(ethylene oxide)-styrene macromonomer]$_{20}$–$LiClO_4$ had been added.[105] The possibility of using such PE at room temperatures was demonstrated.

Films based on the complex $(PEO)_9LiCF_3SO_3$ were investigated in the temperature range 100–170 °C using voltammetry at a low scanning rate.[16] The reversible reduction of the electrolytes was observed over a wide range of external conditions and subject to the stipulation that a certain threshold potential was not exceeded. It was shown that the stability of the reduction of the PE is limited by the discharge of Li^+ and the stability of the oxidation is limited by the discharge of $CF_3SO_3^-$. At temperatures of about 140 °C, the region of the oxidative-reductive stability of the film exceeds 3.3 V. In the range 140–160 °C, the stability region diminishes by 1 V as a result of the oxidation of $CF_3SO_3^-$. The authors[16] note that, by virtue of their high electrochemical stability and effective mechanical properties, the PE films investigated may find an application in solid-state batteries.

In order to devise batteries of a similar type capable of working with satisfactory operating characteristics for a long time, it is necessary to suppress the crystallisation process in the PE, which is achieved by adding an elastomer (a butadiene–acrylonitrile copolymer) and a macromonomer based on styrene and PEO.[106] It has been shown by X-ray diffraction that, when the elastomer and the macromonomer are added, the PEO crystal cell remains monoclinic. In the course of 15 months, the diffraction patterns and the conductivities remained unaltered. The stabilisation of the conductivity was also achieved by the partial replacement of the PEO by oligo(ethylene oxide) (OEO) with terminal styrene groups keeping the ethylene oxide unit/Li^+ ratio unaltered.[107] Best results ($\sigma = 2 \times 10^{-4}$ S cm^{-1}) were obtained by employing $LiCF_3SO_3$ and by introducing from 20% to 50% of a low-molecular-mass oligo(ethylene oxide) with $M = 550$.

VII. Chemical interaction at the lithium anode – polymeric electrolyte interface

The electrochemical reactions at the electrode/polymeric electrolyte interface have been considered in a review.[108] It was shown that although an analogy with the reactions in a liquid electrolyte is in fact observed, the former reactions are more complex. Under open-circuit conditions, the formation and growth of a passivating film are observed at the lithium/polymeric electrolyte interface. The growth kinetics depend on the nature and composition of the electrolyte, which agrees well with data on the phase diagram of the PEO–electrolyte system.[109] It was established that the behaviour of the passivating film on polarisation of the lithium electrode cannot be described in terms of a simple model comprising a solid electrolytic or polymeric surface film, and a model comprising an ion-conducting film of a modified polymeric electrolyte with a high resistance was therefore proposed. The stability of the vacuum-sputtered lithium electrode in an ultrathin film electrochemical cell of the type Ni/PE/Li with PEO, PPO, and the oxyethylene–oxymethylene copolymer as the polymeric electrolyte was therefore investigated by impedance spectroscopy at room temperature.[110] The most intense reactions at the interface are observed in the case of PPO. This is due to the rapid reaction between lithium and the amorphous copolymer, which was demonstrated with the aid of cyclic voltammetry. Owing to the phenomenon of passivation, the Faraday efficiency depends to a large extent on the rate of scanning of the potential. Its decrease from 20 to 5 mV s^{-1} decreases the degree of reduction of lithium from 85% to 30%.[111]

The resistance at the lithium/PE interface was investigated in thin secondary CPS with a solid PE (PEO–$LiClO_4$).[112] It was shown that the discharge characteristics of the CPS are impaired during storage, which is apparently associated with the increase in the internal resistance of the polymeric electrolyte.

In order to improve the mutual adhesion and to reduce the ohmic resistance at the negative electrode/PE interface, it was suggested that an intermediate layer of the halide of the metal constituting the anode (Li, Na, K, Ag) be formed on the electrode surface. Such a layer exhibits cationic conductivity and plays the role of the solid electrolyte.[113] Small transitional resistances are established between this layer, on the one hand, and the metallic anode and the PE on the other.

Overall, the study of the processes at the lithium/PEO interface leads to the conclusion that the characteristics of the lithium accumulators with PE are limited not so much by the intrinsic ionic conductivity of the polymeric electrolyte as by the charge transfer to the interface.

VIII. Modification of the electrodes in lithium chemical power sources with a polymeric electrolyte

In selecting the PE for use in solid-state batteries, it is necessary to take into account not only their ionic conductivity and transport numbers but also their compatibility with the anodic and cathodic materials.

In assembling the primary cells based on PEO and lithium salts, metallic lithium or its alloy with aluminium are employed as the anode and MnO_2 [114] TiS_2, MoO_2, or V_6O_{13} [115,116] as the cathode. The composite cathode contains as a rule a metal oxide, carbon black, and a polymeric electrolyte. For example, the active mass of the positive electrode contained 45 vol.% of V_6O_{13}, 5 vol.% of acetylenic carbon black, and 50 vol.% of the PEO–$LiClO_4$ composition[32,116] or 75 mass% TiS_2, 10 mass% of graphite powder, and 15 mass% of PEO + NaI.[117]

The improvement of parameters of the cells such as the current density and the specific capacity is achieved by improving the technique for the preparation of the composite cathode.[118] In the first discharge cycle, 100% and 50% utilisations of the active material of the cathode are attained at current densities of 0.27 and 0.8 mA cm^{-2} respectively. The increase in the size of the cells from 1 to 100 cm does not impair their properties. A sol-gel technology for the preparation of positive electrodes has been described.[119]

Japanese investigators[120] proposed five compositions of the negative active substance: an alkali metal, an alkali metal alloy, an electrically conducting polymer, a complex of an alkali metal and an electrically conducting polymer, and a layered interstitial compound. The characteristics of thin-film rechargeable accumulators operating at 20 °C and employing solid polymerisation redox electrodes have been investigated.[121] The anodes were prepared from various substances: the product of the polymerisation of salt synthesised by the interaction of 2,5-dimercapto-1,3,4-thiadiazole with LiOH; carbon black; a mixture of poly(ethylene oxide) with a lithium salt. Such accumulators withstood 100 charge-discharge cycles without a significant impairment of the parameters.

The Bridgestone Corporation and Seiko Electronic Components Ltd (Japan) have jointly developed a series of rechargeable polymeric lithium power sources[122] having a capacity three times as great as that of the existing lithium accumulators and a 2–3 times greater potential compared with the nickel–cadmium batteries. In the new lithium accumulators, a Li–Al alloys, ensuring a high capacity, is employed as the negative electrode, and a conducting polymer is used as the positive electrode. The nominal potential of the accumulators is 3 V and the capacity is 2 mA h.

The development of lithium accumulators is hindered by the poor rechargeability of the negative electrode associated with the formation of lithium dendrites at a current density > 0.5 mA cm^{-2}.[123] It has therefore been suggested that a negative electrode consisting of interstitial lithium compounds be employed. It has been proposed that Wood's alloys (Pb–Sn–Cd–Bi), having low melting points and ensuring a high diffusion coefficient of lithium, be used as the material of such electrodes.

The reversibility of the lithium electrode, operating in conjunction with polymeric electrolytes $(PEO)_x \cdot LiCF_3SO_3$, where x is in the range $4 < x < 16$, has been investigated[124] by potentiometric and polarographic methods in the temperature range 100–170 °C. Satisfactory results were obtained.

A tendency has arisen in recent years to employ polymeric electrodes in chemical batteries with polymeric electrolytes. Thus an accumulator with a PE has been described.[125] Its negative electrode was made of an alkali metal (Li, Na, K) and a conducting polymer or a composite of a conducting polymer and an alkali metal, while the cathodic mass consisted of a composite of a conducting polymer and a polymeric electrolyte. The composite cathode for solid-state lithium accumulators may also consist of polypyrrole (PP),[126] into which between 0% and 50% of PEO of polybithiophene (PBT)[127] has been added. It was shown that the capacity of the PBT electrode in contact with the solid PE is lower than that of the substance in contact with a liquid electrolyte (propylene carbonate–$LiClO_4$), but increases with increase in temperature from 50 to 70 °C.

The possibility of creating thin-film polymer batteries with a high energy capacity from a complex of PEO and $LiClO_4$ has been described.[128] The use of TiS_2 or V_6O_{13} as the cathodes and of metallic lithium as the anode makes it possible to create batteries which ensure a current density of 0.5–1.0 mA cm^{-2} at 80–100 °C and can undergo up to 250 charge-discharge cycles.[129] The Faraday efficiency is 80%–90% and the specific energy capacity is not less than 100 Wh kg^{-1}. The replacement of $LiClO_4$ by $LiCF_3SO_3$ in the polymer complex impairs the characteristics of the cell (the efficiency is $< 15\%$) and requires an increase in the working temperature to 130 °C. The authors suggest that the new PE based on PEO make it possible to create CPS operating at room temperature and likely to be useful in transport systems.

The data presented indicate the undoubted growth of interest in the theoretical and practical studies on the creation of new solid polymeric electrolytes and the construction on their basis of CPS with a high energy capacity.

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The synthesis, properties, and applications of *N*-acyl-α-aminoacids

A P Mikhalkin

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Abstract. The review gives a systematic account of, and surveys the literature data on, the methods of synthesis, the physical and colloidal properties, and applications of acyl derivatives of aminoacids. The bibliography includes 369 references.

I. Introduction

Aminoacid derivatives, in particular *N*-acyl-α-aminoacids, the molecules of which include the peptide and carboxy-groups (or the sulfo-group in the case of aminosulfonic acids) have aroused continuous interest because of their exceptionally broad spectrum of activity. The presence of the acyl fragment in the molecule imparts hydrophobic properties to these compounds and enables them to exhibit surface-active properties. Aminoacids and higher carboxylic acids (HCA) are used for the manufacture of *N*-acyl-α-aminoacids. The practical application of *N*-acyl-α-aminoacids in industry and in human vital activity merits special attention. They are biologically 'soft' and are readily decomposed by bacteria under natural conditions, which is very important in our era of progressive pollution of the environment by industrial and domestic waste.

The chemistry of aminoacids, including the practical aspects of the chemical synthesis of peptides from which acylaminoacids are obtained, is fairly widely represented in the literature.[1–11] However, there is at present only isolated information about the methods of synthesis of acylaminoacids suitable for industrial application, their properties, and their practical applications.[12–15] The large number of continuously appearing publications on this topic has necessitated a survey of the accumulated information.

This review gives a systematic account and discusses the methods of synthesis of *N*-acyl-α-aminoacids having the general structure $R^1C(O)NR^2[CH(R^3)CO]_nOH$ and the relation between their structure and their physicochemical properties and surface and biological activities.

Since the methods for the acylation of aminoacids by higher carboxylic acids have been described in fair detail in the literature, we shall deal in detail with certain data concerning the kinetics and general mechanisms of acylation by the Schotten–Baumann method and of the activated esters method, which are fairly widely used for the synthesis of the above compounds.

A P Mikhalkin Laboratory for the Synthesis and Physicochemical Properties of Surfactants, Protein Surfactant Research and Manufacturing Company, Oktyabr'skii prosp. 259, 140000 Lyubertsy, Moscow Region, Russian Federation. Fax (7-095) 554 41 63

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II. Methods for the acylation of aminoacids

Detailed analysis of the formation of the peptide linkage, carried out, for example, in the monograph of Gershkovich and Kibirev,[16] showed that as a rule the carboxy-group is initially activated in order to increase the electron density on the carbonyl carbon atom of the higher carboxylic acid and this is followed by nucleophilic attack, in the given instance by the amino-group of the aminoacid. Nowadays methods such as the carbodiimide, azide, mixed anhydride, activated esters, and carboxy-anhydride procedures are most widely used for the formation of the peptide linkage. However, these methods are not always effective in the development of a technology for the manufacture of acylaminoacids.

The ability of aminoacids to be acylated is in many respects determined by the nucleophilicity ($pK_a = 2.23 - 4.43$) of the amino groups,[1,7] steric factors, and the acylating capacity of the carboxylic acid derivatives RCOX, which is in its turn determined by the stability of the anion X^-. In terms of their reactivity, the principal types of acylating agents are equivalent to the acidity series (the stability of the anion X^-) and the series based on the rates of their hydrolysis and can be represented by the following sequence:

$$R^1COHal > (R^1CO)_2O \approx R^1COOR^2 > R^1CONR^2_2 > R^1COOH.$$

Hence it is seen that the most effective acylation of aminoacids requires the activation of the carboxy-group in carboxylic acids, for example up to the formation of acid chlorides, anhydrides, activated esters, etc. The overall mechanisms of reactions involving acylation by carboxylic acids and their various derivatives have been investigated quite adequately.[1–8, 16, 17]

The principal methods of synthesis of acylaminoacids suitable for practical application known at the present time are considered below.

1. Acylation by the Schotten–Baumann method

Acylation of aminoacids by HCA chlorides is one of the commonest methods of synthesis of acylaminoacids. It constitutes the basis of the industrial manufacture of a whole series of

products, for example 'medialans' which are derivatives of sarcosine.[18-20] There are various modifications of this method:

$$R^1COCl + H_2NCHR^2COOH \xrightarrow{NaOH} \longrightarrow R^1C(O)NHCHR^2COONa.$$

HCA chlorides with various structures are used as the acylating agents. The reaction is carried out in aqueous solutions, in aqueous organic mixtures containing 30%–50% of an inert water-soluble organic solvent, and in systems comprising two immiscible solvents, one of which is water. It is noteworthy that in the last case, for example in the water–toluene system, the yield of the target product is appreciably reduced.[15]

In the study of the kinetics of the acylation of α-aminoacids by benzoyl chloride in aqueous solutions, it has been shown[21] that the amino-group in the aminoacids investigated has a high reactivity, which is determined by the form in which the acid exists in solution. The forms having free amino-groups, $H_2NCHRCOO^-$ (A) and $H_2NCHRCOOH$ (B), are the most reactive, the activity of form A being higher. The rate of change of the concentration of benzoyl chloride, for example in the acylation of glycine in a water–dioxane mixture (298 K, $c_{H^+} = 1.17 \times 10^{-7}$ M), is described by the following equation when account is taken of its hydrolysis:

$$\frac{dc_b}{d\tau} = k_h c_b + \frac{kK_a}{c_{H^+}} c_b c ,$$

where k_h and k are the hydrolysis rate constant and the rate constant for the acylation of the α-aminoacid in form A by benzoyl chloride, K_a is the acid ionisation constant of the protonated amino-group of the aminoacid, c_b and c are the benzoyl chloride and aminoacid concentrations, and c_{H^+} is the concentration of hydrogen ions. Subject to the conditions $c \gg c_b$ and a constant pH of the reaction medium (the use of a buffer), the observed rate constant (k_o) for the given first-order reaction is calculated by the equation

$$k_o = k_h + \frac{kK_a}{c_{H^+}} c .$$

The constants, calculated by the least squares method (Table 1), show that under the experimental conditions the α-aminoacids do not catalyse the hydrolysis of benzoyl chloride; this is confirmed by the similar rate constants for the hydrolysis of the latter in reactions with various α-aminoacids. The reactivities of the amino-groups of α-aminoacids are analysed in terms of the quantity K_1, which includes the product of k and K_a. The reactivities of the amino-groups of the α-aminoacids investigated are approximately the same with the exception of L-proline and L-glutamine. The study of the hydrolysis kinetics of the chloride of lauric acid under conditions of aminoacid acylation has shown[22] that this reaction proceeds in the kinetic region with $E_a = 12.8 \pm 0.5$ kcal mol^{-1} at temperatures below 30 °C. The kinetic parameters for the acylation of a series of α-aminoacids by benzoyl chloride in aqueous solutions, obtained by Babaev et al.,[23] describe the experimental data satisfactorily (the error does not exceed 5%). However, there is no rigorous correlation between the reactivity of α-aminoacids and their structure.

The methods of synthesis of acylaminoacids via HCA chlorides proved to be effective not only for natural α-aminoacids but also for many others,[20,24] for example for α- and ε-aminohexanoic, α-aminobutyric, α-aminoisobutyric, and iminodiacetic acids as well as *N*-ethyl, *N*-propyl-, and *N*-butylglycine, *N*-methylalanine, and β-alanine.

In the acylation of sarcosine by HCA chlorides, it was found[25] that, in order to increase the quality of the product, it is necessary to maintain rigorously a series of technological process parameters (pH 10.5 ± 0.3, temperature below 30 °C, vigorous stirring during the addition of the acid chloride). In order to isolate the pure substances, the reaction mixture is extracted with ether, washed with water until neutral, dried over sodium sulfate, the solvent is distilled away, and the residue is recrystallised from hexane or petroleum ether.[24] It is recommended that acylsarcosine be neutralised by washing with hot water for 3 h at a temperature 10 °C below its melting point. More prolonged washing of the product under these conditions leads to the hydrolysis of the peptide linkage.

Table 1. The rate constants for the hydrolysis of benzoyl chloride (k_h) and the acylation of α-aminoacids (k_1 and k) and the acid dissociation constants (K) of α-aminoacids at 298 K and $c_{H^+} = 1.17 \times 10^{-7}$ mol litre^{-1}.[21]

α-Aminoacid (pK_a)[a]	$10^3 k_h$/s^{-1}	$k_1 = 10^7(kK_a)$/ s^{-1}	10^{-4} k/litre mol^{-1} s^{-1}
Gly (11.28)	1.93 ± 0.18	4.01 ± 0.23	7.64
DL-Ala (11.46)	1.69 ± 0.09	0.817 ± 0.005	2.35
DL-Val (11.25)	1.89 ± 0.05	2.14 ± 0.02	3.81
DL-Leu (11.09)	1.46 ± 0.15	1.74 ± 0.06	2.14
L-Ile (11.26)	1.92 ± 0.19	2.33 ± 0.08	4.24
L-Pro (12.0)	3.80 ± 1.54	23.0 ± 0.7	230
DL-β-Phe (10.83)	1.66 ± 0.23	3.97 ± 0.08	2.68
L-Gln (10.78)	2.41 ± 0.39	6.45 ± 0.25	3.89

[a] The values of pK_a are quoted to within ±0.02.

Much attention has been devoted to questions of the purification of *N*-acyl-α-aminoacids. One of the effective ways of solving this problem involves the washing of the reaction mass with C_1–C_4 aliphatic alcohols with simultaneous reduction of pH and filtration of the precipitated deposit or the employment of an alcohol–water mixture in the acylation stage.[26,27] These procedures make it possible to obtain acylaminoacids with a purity of 98%–99%.[28] Further development of industrial methods of synthesis of acylaminoacids by the Schotten–Baumann method involves the optimisation of the process and the development of continuous technological production schemes.[29]

Together with the natural and synthetic aminoacids, hydrolysed proteins are an important raw material for the industrial production of acylaminoacids and oligopeptides.[1,18-20,25] The products of the cleavage of the waste from leather (in the tanning of leather) and food industries, products of plant origin (cereal fibrin), microorganism biomass, etc. are as a rule employed as the protein raw material. The protein is usually hydrolysed by boiling in an excess of concentrated hydrochloric acid or alkali.

The industrial manufacture of products based on hydrolysed proteins with the trade name 'Lamepons', and 'Meipons' have been organised using the chlorides of lauric, palmitic, stearic, and oleic acids, as well as mixtures of acids from coconut and tall oils, lipids, and phospholipids.[13,18,30] The industrial methods of synthesis of acylated hydrolysed proteins are based on the Schotten–Baumann reaction in accordance with the following scheme:

$$R^1COCl + H_2NCHR^2CO[NHCHR^3CO]_nNHCHR^4COOH \xrightarrow{NaOH} \longrightarrow R^1CONHCHR^2CO[NHCHR^3CO]_nNHCHR^4COONa,$$

where R^1 = alkylated HCA, and R^2, R^3, and R^4 are fragments present in the α-aminoacids of protein raw materials of different origin.

In practice, the reaction is usually carried out with the gradual addition of HCA chlorides and stirring. A constant pH (9.5) and temperature (20 ± 5 °C) are then maintained.[31,32]

A commercial product with the following composition (%) is obtained under these conditions: acyl derivatives (25.0), initial hydrolysed protein (3.5), HCA (6.0), NaCl (5.0), and water (60.5). The optimum process conditions, making it possible to attain the maximum conversion of HCA chlorides and to obtain a high quality target product in a high yield, have been determined in a number of studies.[29,33-37]

The acylation of aminoalkanesulfonic acids takes place similarly to the reactions with aminoacids. The best known of the industrially produced acylaminoalkanesulfonic acids are derivatives of methyltaurine with the commercial names 'Igepons', 'Metaupons', 'Hostapons', etc. The methods of synthesis of acylmethyltaurine (including the principal industrial method of its preparation) by the Schotten–Baumann reaction, have been described in fair detail in a monograph.[25]

In recent years, studies in this field have been directed to the synthesis of highly concentrated acyltaurines with an increased purity. For example, repeated heating (to 50–90 °C) of the reaction mass containing 30%–60% of moisture, up to 50% of acylmethyltaurine, and 6% of NaCl followed by cooling to 10–30 °C[38] makes it possible to eliminate up to 90% of water from it. Highly pure acyltaurines have been obtained in a high yield in the stoichiometric interaction of HCA chlorides with taurine in an aqueous alcoholic medium.[39] The product, free from the NaCl impurity, has been isolated on heating the reaction mass, from which the NaCl deposit was filtered off and the product was crystallised.[40] A continuous method of synthesis of acyltaurines involving the continuous introduction of measured amounts of HCA chlorides has been developed. The optimum parameters of the technological process (pH 9–10, T = 40–60 °C) make it possible to obtain a highly concentrated pure product with an impurity content < 3%.[29,41-44]

2. The anhydride method

Symmetrical organic acid anhydrides and mixed anhydrides of inorganic acids are used for the acylation of aminoacids. Despite the fact that they are all less reactive than HCA chlorides, their employment for the synthesis of acylaminoacids is fairly important. The amide linkage is formed in this case in accordance with the following scheme:

$$(R^1R^2CO)_2O + H_2NCHR^3COOH \longrightarrow$$
$$\longrightarrow R^1CONHCHR^3COOH + R^2COOH.$$

Symmetrical organic acid anhydrides are preferable to others because they make a wide variety of side reactions avoidable. However, it is not possible to avoid the formation of the corresponding acids from the anhydrides (in stoichiometric proportions). For this reason, mainly the anhydrides of lower carboxylic acids are used in this method. The employment of extremely reactive anhydrides of halogenated acids with electron-accepting substituents, for example trifluoroacetic acid anhydride, for the large-scale production of acylaminoacids is economically unsound.

Aminoacids are as a rule acetylated by acetic anhydride in water or in acetic acid. For glycine and racemic aminoacids,[45-47] the yield of the target product is 89%–92%. Acetylation by acetic anhydride in boiling glacial acetic acid afforded derivatives of DL-alanine,[48] DL-valine,[49] and 4-aminobutyric and 6-aminohexanoic acids.[50] *N*-Alkylaminoacids are acetylated similarly.[51,52] In order to improve the quality of the acetylaminoacids obtained, acetylation by acetic anhydride in ethyl acetate in the presence of the cation-exchange resin K in the H^+-form has been suggested.[53] Together with acetyl chloride, acetic anhydride is widely used for the preparation of acetyl derivatives of aminoalkanesulfonic acids.[54,55] A method for the acetylation of aminoalkanesulfonic acid in the solid phase has been proposed. It makes it possible to obtain extremely pure products in a high yield.[56] It has been demonstrated by liquid chromatography that the product is up to 97% pure and contains about 1.5% of the initial aminosulfonic acid.

A series of acyl derivatives have been obtained by acylating aspartic acid with the anhydrides of alkenyl(alkyl)succinic acids[57] and by acylating taurine with the anhydrides of propionic and butyric acids.[58] HCA (C_8–C_{22}) anhydrides have been used in a series of syntheses.[59]

Mixed HCA anhydrides with sulfuric and carbonic acids are included among effective acylating agents despite the fact that in this case there is a possibility of side reactions. When mixed anhydrides of HCA and sulfuric acid were used at −5 to 40 °C in a water–acetone mixture, acyl derivatives of alanine, lysine, glutamic acid, and peptides were obtained.[60] The products of the acylation of aminoacids by mixed anhydrides of HCA and alkylcarbonic acids [alkyl carbonates? (Translator)] are the corresponding alcohols and carbonic acid together with the acylaminoacids.[61]

3. Method employing esters

Despite the fact that only the activated esters method has found extensive application in the synthesis of peptides, in practice both HCA esters and their activated forms are used to synthesise acylaminoacids. As a rule activated esters are obtained from nitro-, chloro-, and fluoro-phenols. The acylation of aminoacids by HCA esters leads to the simultaneous formation of acylaminoacids and alcohols in accordance with the scheme:

$$R^1COOR^2 + H_2NCHR^3COOH \longrightarrow$$
$$\longrightarrow R^1CONHCHR^3COOH + R^2OH.$$

This reaction is usually catalysed by an equimolar amount of a strong base, for example sodium alkoxide, sodium and lithium tetrahydroaluminates, etc. When this method of acylation of aminoacids or their salts was used, the yield of the target product reached 90%–95%.[62] The yield of the product decreases appreciably in the presence of traces of moisture. Acyl derivatives of α-aminoacids,[63] oligopeptides,[64-66] hydrolysed proteins,[67] and methylpurine[68,69] have been obtained by this method.

Nitrophenyl derivatives have been used to isolate α-aminoacids.[63,70,71] Pentafluorophenyl esters have been used successfully to acylate iminoacids despite the fact that *N*-alkyl substitution and branching at the α- and β-carbon atoms of the aminoacids interfere with the reaction.[72]

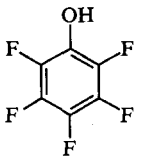
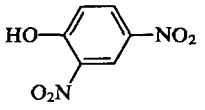
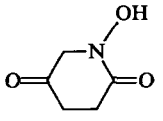
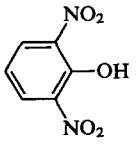
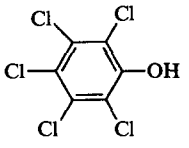
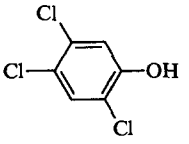
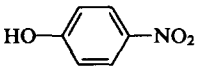
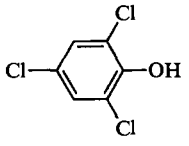
The reagents proposed nowadays for the activation of the carboxy-group and the subsequent formation of the peptide linkage by the activated esters method are as a rule stable during storage and exhibit a high reactivity, which in the case of substituted phenyl esters, for example, is determined by the acidity of their hydroxy-groups and by the type and position of the substituent and may differ by 2–3 orders of magnitude.[16] Pentafluorophenyl and nitrophenyl esters with a nitro-group which does not hinder the access of the amino-component to the electrophilic centre are the most reactive (Table 2, see over). A lower rate of acylation is characteristic of polychlorophenyl esters, which is due to the steric shielding of the electrophilic centre by the chlorine atoms in the *ortho*-positions.

4. Acylation by carboxylic acids

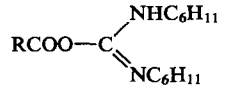
As a rule, aminoacids and their derivatives are not acylated by carboxylic acids at the usual temperatures. As stated above, the occurrence of such reactions under relatively mild conditions is possible only after the preliminary activation of the carboxy-group, for example by means of dicyclohexylcarbodiimide (DCHC).

$$R^1COOH + H_2NCHR^2COOH + C_6H_{11}N{=}C{=}NC_6H_{11} \longrightarrow$$
$$\longrightarrow R^1C(O)NHCHR^2COOH + C_6H_{11}NHC(O)NHC_6H_{11}.$$

Table 2. The rate constants (k) and the times (τ) required for 90% acylation by various activated esters.[16]

R^2	$10^2k/mol^{-1}\ s^{-1}$	τ/min
	40.4 ± 9	2.9
	18.4 ± 3	6.3
	5.4 ± 0.7	21
	1.73 ± 0.2	67
	1.72 ± 0.03	62
	0.3 ± 0.03	385
	0.1 ± 0.01	1088
	0.06 ± 0.002	1856

It has been suggested[73] that aminoacids are acylated in the presence of carbodiimides in accordance with a complex scheme involving the formation in the first stage of an adduct of the HCA and DCHC—*O*-acylurea.



This adduct, in which the carboxy-group is in an activated form, subsequently reacts with the aminoacid, forming an acylaminoacid. Acyl derivatives of glycine, alanine, leucine,[74] phenylalanine, lysine, methionine, glutamic acid,[75] and a number of other aminoacids[76] have been synthesised by this method in the presence of DCHC. It has been suggested that the acylation of HCA in an inert solvent with a calculated amount of carbonyldiimidazole be used to form the peptide linkage.[77] The imidazolide of the acid is formed as an intermediate in the reaction. It is subsequently transacylated to give the target products by reaction with the amino-group.

The synthesis of peptides, in particular of acylaminoacids, employing HCA as the acylating agent is favoured by the introduction into the reaction system of catalytic amounts of various phosphorus compounds: phosphorus chloride,[78] triphenyl phosphite,[79] the anhydrides of alkylphosphonic[80] and dialkylphosphinic[81] acids, derivatives of phenylphosphonic acid,[82] diethylphosphoryl cyanide,[83] diphenylphosphoryl azide,[84] and tetraethyl pyrophosphite.[1] Acylation by carboxylic acids in the presence of diethylphosphoryl cyanide is carried out in the presence of triethylamine.

$$R^1COOH + H_2NCHR^2COOH \xrightarrow[Et_3N]{NCP(O)(OEt)_2} R^1C(O)NHCHR^2COOH$$

The addition of tertiary amines promotes the formation of a carboxylate ion and the esterification reaction, increasing the yield of the target products. Acylaminoacids or peptides have been obtained in high yields (83%–94%) using carboxylic acids and diphenylphosphoryl azide.

$$R^1COOH + H_2NCHR^2COOH \xrightarrow[Et_3N]{N_3PO(OPh)_2} R^1C(O)NHCHR^2COOH$$

The effectiveness of the preliminary activation of the amino-group by tetraethyl pyrophosphite with formation of an amide has been demonstrated for the acylation of aminoacid esters with the aid of HCA.

$$R^1COOH + [(EtO)_2PNHCHR^2COOEt] \longrightarrow R^1C(O)NHCHR^2COOEt$$

The reaction with diethyl phosphorochloridite takes place in accordance with a similar mechanism.[1]

Despite the fact that the reactivity of carboxylic acids as acylating agents is extremely low without their preliminary activation, this method has found fairly extensive applications in practice in the development of technological processes. Acyl derivatives of glycine,[85] α-aminoacids, β-alanine, 6-aminohexanoic acid, and oligopeptides[86] have been obtained by this method. The reaction is carried out as a rule at 160–200 °C under an inert gas atmosphere. Depending on the type of the starting material, the yield of the target product can reach 40%–90% of the theoretical value. Under these conditions, acylaminoacids can be dehydrated with formation of oxazolones.

$$R^1C(O)NHCHR^2COOH \xrightarrow[-H_2O]{\Delta} R^1C\!=\!N\!-\!CHR^2 \;\; (O\!-\!C(O))$$

The method of synthesis of basic acylaminoacids, developed by the Ajinomoto Company,[87] involves the interaction of aminoacids with HCA at 100–250 °C in an organic solvent immiscible with water and forming an 'azeotrope with water' under the reaction conditions. The method of synthesis of acylaminoacids proposed by the Dynamit Nobel AG Company has effective technological parameters.[62] The experimental industrial technology for the production of acylaminoacids is based on the acylation of 6-aminohexanoic acid, obtained by the alkaline hydrolysis of ε-caprolactam,[88] and its amination and subsequent acylation by acrylic acid.[89,90] Acyl derivatives of peptides with valuable operating properties have been obtained by the reaction of HCA at 210–250 °C with oligopeptides obtained by

hydrolysing protein materials, in particular leather, bristle, hooves, animal hair, bird feathers, plant proteins, fish waste, and purified proteins such as collagen, casein, and elastin.[91]

Together with the traditional industrial methods for the synthesis of acyltaurides by the Schotten–Baumann acylation, a procedure involving the acylation of a methyltaurine salt by carboxylic acids has been proposed for commercial use.[92]

$$RCOOH + HN(CH_3)CH_2CH_2SO_3Na \xrightarrow[-H_2O]{\Delta} RC(O)N(CH_3)CH_2CH_2SO_3Na$$

A characteristic feature of this method is a higher content of the initial carboxylic acids in the reaction mass. The process is carried out at reduced pressure under inert gases. The corresponding acyl derivatives based on HCA have also been obtained for the sodium salts of *N*-cyclohexyltaurine,[93] *N*-2-hydroxypropyltaurine,[94,95] and methyltaurine.[96]

5. Other methods

Amides and carbon monoxide belong to the class of acylating agents which are rarely used in the synthesis of acylaminoacids but are potentially of practical value. The reaction of an amide with carbon monoxide and an aldehyde or a compound giving rise to an aldehyde takes place in the presence of a catalyst (Cat) in accordance with the scheme

$$R^1C(O)NH_2 + CO + R^2CHO \xrightarrow{Cat} R^1C(O)NHCHR^2COOH.$$

Group VIII transition metals (cobalt is the best) in the form of carbonyls, carboxylates, and various complexes have been proposed as catalysts.[97–100] The reaction is carried out at 50–150 °C, at a carbon monoxide partial pressure of 50–500 atm, in the presence of solvents, preferably alcohols, ethers, and ethyl acetate. The best results in the carbonylation reaction have been achieved with the aid of aliphatic aldehydes and primary amides.[99] As nucleophiles, amides add to the carbonyl group of aldehydes over a wide pH range and the initial product is usually an *N*-acylcarbinolamine $R^1C(O)NHCR^2R^3OH$.[17] When this reaction is carried out at an elevated temperature, the O → N rearrangement is facilitated. Under these conditions, ketones are as a rule less reactive.

A modified version of the above method, involving the replacement of the aldehyde by compounds containing double bonds, has been proposed.[101,102] The reaction is carried out in one stage, which increases its selectivity and rate. Ethers, ketones, and sulfoxides have been proposed as solvents. The highly nucleophilic amide anion, formed under these conditions on treatment with a strong base, undergoes Michael addition to the substituted alkene.

$$R^1C(O)NHR^2 \underset{}{\overset{OH^-}{\rightleftharpoons}} R^1C(O)\bar{N}R^2 \xrightarrow{R^3CH=CHCOOH} R^1C(O)NR^2CHR^3CH_2COOH$$

In practice, acylaminoacids are obtained under these conditions from alcohols and organic halo-derivatives.[103–105] The hydroformylation of an alcohol or halide in the presence of an amide and a catalyst (a Group VIII transition metal) is carried out at 50–200 °C and a pressure of 10–500 atm (a mixture of CO and H_2); the yield of the target product is up to 69%.

The method of synthesis of acylaminoacids by the reactions of oxiranes with amides, carbon monoxide, and hydrogen in the presence of cobalt-containing catalysts and promoting agents is of considerable interest.[106–109] Compounds containing Group I–V metals are employed as promoting agents. Among the diverse methods of synthesis of acyl aminoacids, the hydrogenation of an azlactone by *N*-acetylaminocinnamic acid in the presence of Raney nickel,[110] reactions of aliphatic nitriles with glyoxylic acid,[111] the interaction of an aminoacid salt with gaseous ketene,[112] and the acylation of the aminoacid by the succinimidine ester of the HCA[113] have been mentioned. In the last case, acyl derivatives of glycine, α- and β-alanines, and aspartic acid were obtained. The constant growth of the number of studies published on this topic shows that the methods are extremely promising.[114–118]

The processes based on the interaction of amides with chloro- and hydroxy-alkane sulfonates,[25] for example

$$R^1C(O)NHR^2 + HOCH_2CH_2SO_3Na \xrightarrow{\Delta} R^1C(O)NR^2CH_2CH_2SO_3Na + H_2$$

can also be included among the traditional methods of synthesis of acylaminoalkanesulfonic acids. Derivatives of aminomethanesulfonic[119,120] and aminoethanesulfonic[121–124] acids have been obtained in this way. For example, acylaminoethanesulfonates have been synthesised by the interaction of HCA, urea, and hydroxyethanesulfonates in the presence of an excess of the latter at 180–240 °C.[95,122] The process is distinguished by a high degree of conversion of the starting materials (92%–98%). HCA, amines, and hydroxyalkanesulfonates interact under virtually identical conditions.[125]

It has been suggested that, instead of amides, nitriles should be employed in the synthesis of acylaminoalkanesulfonates.[126–128] Acylaminoalkanesulfonic acids can also be obtained by aminating hydroxyethanesulfonates with subsequent acetylation[129,130] or activation of the aminoalcohols and the sulfonyl chlorination of the amidoalcohols obtained.[131]

One of the possible ways of obtaining acylaminoacids and their derivatives involves the interaction of lactams with HCA and their derivatives such as acid chlorides, anhydrides, esters, etc.[20] The acylation of lactams, for example of ε-caprolactam, by carboxylic acids is carried out at 240–250 °C and a pressure of 16 atm,[132] the target product being obtained with different degrees of oligomerisation of 6-aminohexanoic acid, depending on the ratio of the lactam and the acid taken for the reaction. The interaction of lactams with carboxylic acid esters leads to the formation of the corresponding acylaminoacids in fairly high yields (68%–71%).[133]

It follows from the foregoing that, for the industrial production of acylaminoacids, one may use (together with the acid chloride method, on the basis of which the technologies for the synthesis of virtually all the products of this kind have been developed by foreign companies) methods for their synthesis by the direct condensation of aminoacids with HCA, via carboxylic acid anhydrides, and by the reaction of amides, carbon monoxide, and an alkene (aldehydes, alcohols, and organic halides) are of considerable interest. The disadvantages of each of these procedures were noted above.

III. Properties of acylaminoacids

The properties of acylaminoacids are determined by the presence in the latter of peptide and carboxy-groups and by the conjugation of the lone pair of the nitrogen atom with the π-electrons of the carbonyl group, which leads to the manifestation by the peptide group of the properties of a double bond. The salts of these compounds in highly dilute aqueous solutions (below 10^{-3} M) tend to form micelles. Information about the properties of acylaminoacids has scarcely been treated systematically hitherto and is sometimes published in sources which are not readily available. The individual properties and constants of some of these compounds can be found in a number of communications.[11,14,15,24,25,68,134–140]

The solubility in water of *N*-acylaminoacids, forming colloidal solutions at low concentrations, is in many respects

Table 3. The dissociation constants (pK') and solubilities (P_s) of a series of aminoacids.[1]

Aminoacid	Chemical formula	pK'_1 (α-COOH)	pK'_2 (α-NH_3^+)	pH_i[a]	P_s/g[b]
Glycine	$CH_2(NH_2)COOH$	2.34	9.6	5.97	25.0
α-Alanine	$CH_3(NH_2)COOH$	2.34	9.69	6.00	16.6
Valine	$(CH_3)_2CHCH(NH_2)COOH$	2.32	9.62	5.96	8.8
Leucine	$(CH_3)_2CHCH_2CH(NH_2)COOH$	2.36	9.60	5.98	2.2
Sarcosine	CH_3NHCH_2COOH	2.23	10.01	6.12	
Aspartic acid	$HOOCCH_2CH(NH_2)COOH$	1.88[c]	9.60	2.77	0.5
Glutamic acid	$HOOC(CH_2)_2CH(NH_2)COOH$	2.19[d]	9.67	3.22	0.9
Lysine	$H_2N(CH_2)_4CH(NH_2)COOH$	2.18	8.95[e]	9.59	73.3
β-Alanine	$H_2N(CH_2)_2COOH$	3.60	10.19	6.90	16.6
γ-Aminobutyric acid	$H_2N(CH_2)_3COOH$	4.02	10.40	7.21	6.7
ε-Aminocaproic acid	$H_2N(CH_2)_5COOH$	4.43	10.75	7.60	

[a] pH at the isoelectric point. [b] Solubility in 100 g of water at 25 °C. [c] $pK''_1 = 3.65$. [d] $pK''_1 = 4.25$. [e] $pK''_2 = 10.53$.

Table 4. The solubilities of the sodium salts of certain *N*-acylated aminoacids (determined at the Krafft point).[140]

Aminoacid	Acyl group[a]				
	C_{10}	C_{12}	C_{14}	C_{16}	C_{18}
Glycine	(+) (40)	36 (65)	47 (93)	55 (−)	66 (−)
α-Alanine	(+) (154)	18 (666)	32 (523)	45 (301)	56 (−)
Valine	(+) (109)	(+) (372)	(+) (400)	8 (330)	36 (229)
Leucine	(+) (94)	(+) (299)	(+) (243)	(+) (236)	46 (−)
Sarcosine	(+) (109)	(+) (258)	(+) (273)	2 (229)	33 (229)
Aspartic acid	(+) (47)	(+) (78)	(+) (109)	(+) (169)	46 (154)
Lysine	8 (184)	34 (229)	61 (−)	84 (−)	

[a] The numbers in brackets are concentrations of Ca^{2+} ions in $CaCO_3$ in ppm; (+) indicates that the solutions remain clear at 0 °C; (−) indicates that the solutions become cloudy at 0 °C.

determined by the acid–base properties and structural characteristics of the initial aminoacids $R^1C(O)NR^2(CH_2)_nX$, such as the number and ratio of the polar groups (carboxy- and amino-groups), and the polar and nonpolar R^1 groups. The dissociation constants and solubilities of a number of aminoacids, the *N*-acyl derivatives of which are considered in the present review, are presented in Table 3. In the aminoacid series glycine–α-alanine–valine–leucine, the solubility in water decreases by an order of magnitude with increase in the size of the nonpolar R^1 group, i.e. with increase in their hydrophobicity. Thus, leucine, which contains the relatively large hydrophobic fragment Pr^iCH_2CH, can be extracted by hot n-butanol from its mixture with glycine. The solubilities of the basic α-aminoacids are much higher than those of the mono-carboxylic and acid α-aminoacids. Similar behaviour may also be traced for *N*-acyl derivatives of the same α-aminoacids (Table 4). The Krafft point for ionogenic surfactants characterises the lower temperature limit for the formation of micelles by the latter, because at lower temperatures the solubility of the surfactants is insufficient for the formation of micelles. The data in Table 4 show that the principal factors which determine the Krafft point are the size of the acyl group and the degree of branching of the aminoacid fragment.

The phase transitions from the solid to the liquid state (320–400 K) in acylaminoacids differing in the size of the acyl group have been investigated by IR spectroscopy.[141] It has been shown that, with increase in the number of methylene fragments and with the appearance of side chains in the aminoacid, ΔH_m and ΔS_m† both increase. Thus, for glycine and L-alanine derivatives the appearance of each additional CH_2 group entails an increase in ΔH_m and ΔS_m by 3–5 and 7 kJ mol^{-1} and by 8–10 and 18 J mol^{-1} K^{-1} respectively. Studies on solutions of acylaminoacid esters by spectroscopic methods have shown that they exist in the form of dimeric complexes[142] formed on associative interaction as a result of the formation of hydrogen bonds between the NH and ester CO groups.

† Enthalpy and entropy of fusion (Translator).

1. Spectroscopic properties

The UV spectra of acyl aminoacids are not of special interest to organic chemists because, like the UV spectra of the initial aminoacids and the HCA, they contain weak absorption bands in the region below 215 nm. The presence of a peptide group does not introduce a significant change into the UV spectra of acylaminoacids in this absorption region either.[143]

The IR spectra of acylaminoacids contain characteristic absorption bands of the functional groups C=O and OH (carboxyl), C=O and NH (amide bands I and II), and CH_3-, $-CH_2-$, and =CH– (the hydrocarbon skeleton). The range of the absorption frequencies of these compounds is determined by a number of factors (solvent, suspension medium, possibility of association, etc.) and for this reason Table 5 lists their average

Table 5. Characteristic vibration frequencies of the functional groups in the IR spectra of acylaminoacids.[14,15,144–146]

Functional group	Frequency/cm^{-1}	Type of vibrations
OH	3550–3000	stretching
NH	3460–3350	"
CH_3 and CH_2	2940–2870	"
C=O	1730–1710	"
C=O (amide I)	1685–1645	"
NH (amide II)	1550–1530	deformation

values. It is difficult to make reliable assignments in the high-frequency region of the IR spectra of acylaminoacids because the υ_{NH} and υ_{OH} bands of the corresponding groups in the free and associated states are as a rule observed simultaneously in this region.

^1H and ^{13}C NMR spectroscopy is one of the most important methods for the identification of acylaminoacids, which are polyfunctional compounds.

The ^1H NMR spectra of acylsarcosinate salts have been described in the literature. It has been shown that in aqueous solution acylsarcosinates exist as *cis*- and *trans*-isomers.[147] The presence of an intramolecular hydrogen bond between the amide carbonyl groups and the carboxyl in the *trans*-conformer has been established by NMR spectroscopy. On the basis of the spectra of certain acylaminoacids, general information has been obtained concerning the dependence of the chemical shifts of the amide protons on the dissociation constants of the carboxylic acid (the acylating agent)[148,149] and of the α-protons of the acylaminoacid on the nature of the solvent.[150] ^{13}C NMR spectroscopy has been more vigorously resorted to in recent years in order to investigate acylaminoacids containing long hydrocarbon groups. Thus Bouloussa and Dizabo[151] presented the ^{13}C NMR spectra of the palmitoyl derivatives of glycine, alanine, and glutamic acid, while Newmark and Hill[152] and Gunston[153] described a method for the assignment of the carbon atoms in the α-, β-, and γ-positions relative to the amide carbonyl group

Table 6. The chemical shifts of the signals in the ^1H NMR spectra (400 MHz) of the acylaminoacids $R^1C(O)NR^2(CH_2)_nX$.

Compound	$R^1C(O)-$	R^2	n	X	Solvent	Chemical shift/ppm (rel. to TMS)		
						$CH_2C(O)$	NCH_2	CH_2X
1	$C_{18:1}$	H	1	COOH	$CDCl_3$	2.35 (m)	4.05[a] (m)	4.05[a] (m)
1	$C_{18:1}$	H	1	COOH	CD_3OD	2.77 (m)	4.11[a] (m)	4.11[a] (m)
2	C_{18}	CH_3	1	COOH	$CDCl_3$	2.33 (m)	3.88[a] (s)[b]	3.88[a] (s)
3	$C_{18:1}$	H	2	COOH	$CDCl_3$	2.15 (m)	3.51 (m)	2.56 (m)
3	$C_{18:1}$	H	2	COOH	CD_3OD	2.15 (m)	3.39 (m)	2.47 (m)
4	C_{16}	H	3	COOH	$CDCl_3$	2.34 (t)	3.38 (br.t)	2.25 (t)
5	C_{11}[e]	H	5	COOH	$CDCl_3$	2.32 (m)	3.28 (m)	2.32 (m)
6	C_{12}	H	5	COOH	CD_3OD	2.15 (t)	3.15 (t)	2.28 (t)
7	$C_{18:1}$	H	5	COOH	$CDCl_3$	2.15 (t)	3.15 (t)	2.28 (t)
8	C_{12}	H	5[d]	COOH	CD_3OD	2.15, 2.17 (t)	3.14, 3.15 (t)	2.28 (t)
9	$C_{18:1}$	H	5[d]	COOH	$CDCl_3$	2.16	3.17, 3.19 (br.t)	2.31 (t)
10	$C_{18:1}$	H	5[d]	COOH	$CDCl_3$	2.16 (br.m)	3.19 (br.m)	2.31 (br.m)
11	C_{10}	H	2	SO_3Na	CD_3OD	2.17 (t)	3.58 (t)	2.95 (t)
12	C_{12}	H	2	SO_3Na	CD_3OD	2.15, 2.17 (t)	3.58 (t)	2.95 (t)
13	C_{14}	H	2	SO_3Na	CD_3OD	2.15, 2.17 (t)	3.57 (t)	2.95 (t)
14	C_{16}	H	2	SO_3Na	CD_3OD	2.15, 2.17 (t)	3.57 (t)	2.95 (t)
15	C_{18}	H	2	SO_3Na	CD_3OD	2.15, 2.17 (t)	3.58 (t)	2.95 (t)
16	$C_{18:1}$	H	2	SO_3Na	CD_3OD	2.15, 2.17 (t)	3.58 (t)	2.95 (t)
17	$C_{16}-C_{18:1}$	CH_3	2	SO_3Na	CD_3OD	2.34, 2.44 (t)	3.75 (m)	3.0 (m)

Remarks. The following notation has been adopted: m = multiplet, s = singlet, br.t = broadened triplet, br.m = broadened multiplet, t = triplet. [a]The same methylene group. [b]The chemical shift of the NCH_3 group is 3.02 ppm (s). [c]Undecenoyl. [d]For the compounds $R^1C(O)[NR^2(CH_2)_n]_mX$ (m = 2, 2, and 3) **8**, **9**, and **10**.

Table 7. The chemical shifts (δ) of the signals in the ^{13}C NMR spectra (20 MHz) of the acylaminoacids $R^1C(O)NR^2(CH_2)_nX$.

Compound	$R^1C(O)-$	R^2	n	X	Solvent	δ/ppm (rel. to TMS; the values of $^1J_{CH}$/Hz are given in brackets)				
						$CH_2C(O)$	CH_2X	NCH_2	C(O)	COOH
18	C_{12}	H	1	COOH	CD_3OD	36.8	41.7	41.6	173.1	176.3
19	C_{16}	H	1	COOH	CD_3OD	36.8	41.8[a]	41.8[a]	173.2	176.6
20	C_{18}	H	1	COOH	CD_3OD	36.7	41.7[a]	41.7[a]	173.1	176.5
2	C_{18}	CH_3[b]	1	COOH	CD_3OD	35.1	53.8	53.8 (J = 146)	171.0	177.0
21	$C_{18:1}$	CH_3	1	COOH	$CDCl_3$	35.4	51.9[a]	51.9[a]	176.0	178.0
22	CH_3	$C_{18:1}$	2	COOH	CD_3OD	7	34.6 (J = 127)	36.5, 36.4 (J = 139)	173.3 173.4	175.0
3	$C_{18:1}$	H	2	COOH	CD_3OD	36.5[a]	35.2[a]	37.1	175.1	176.1
7	$C_{18:1}$	H	5	COOH	CD_3OD	37.2	34.8	40.1	176.0	177.3
9	$C_{18:1}$	H	2[c]	COOH	$CD_3OD/CDCl_3$ 1:1	36.0, 36.4	33.7	38.9, 39.0	–	–
23	[d]	H	2	SO_3Na	CD_3OD/D_2O	35.6–35.9	50.4–50.9 (J = 137)	36.6–36.9 (J = 146)	176.0 176.4	
17	$C_{16}-C_{18:1}$	CH_3[e]	2	SO_3Na	CD_3OD/D_2O	33.9	48.6	44.6	175.0	

[a] The same carbon atom. [b]The chemical shift of the CH_3 group is 37.2 ppm (J = 144 Hz). [c]Here the compound is $R^1C(O)[NR_2(CH_2)_n]_mX$ (m = 5). [d] The range of chemical shifts for individual compounds is quoted. [e]The chemical shift of the NCH_3 group is 36.5 ppm.

involving the use of deuterium exchange. NMR spectroscopy has made it possible to establish the nature of the associated species of acylaminoacids in aqueous systems and to show that the formation of their micelles is accompanied by an upfield displacement of the chemical shift for the hydrophilic part of the molecule as a result of conformational rearrangements around the C(O)–N and N–CH_2 bonds.[154]

Measurement of the ^1H and ^{13}C NMR spectra (400 and 20 mHz) for a series of acylaminoacids with long hydrocarbon groups, involving the use of spectrometers with superconducting magnets, which increased the chemical shift resolution, has made it possible to make a reliable assignment of the majority of the signals due to the functional groups of individual compounds and to identify them readily in technical products constituting multicomponent mixtures.[155–165] Typical chemical shifts for certain functional groups in the ^1H and ^{13}C NMR spectra of acylaminoacids are presented in Tables 6 and 7.

2. Chromatographic separation

Despite the fact that the separation of acylaminoacids by gas–liquid chromatography is extremely difficult owing to their relatively high molecular masses and extremely low volatility, the application of this method for the separation of acyl derivatives of, for example, glycine, alanine, α-aminohexanoic and α-aminoheptanoic acids, β-alanine, and the mixture of α-aminoacids produced by the hydrolysis of natural protein materials have been described in the literature.[166–172] High performance liquid chromatography has been very widely used to separate acylaminoacids (see for example, Refs 173–177). The order in which acylaminoacids are eluted is determined both by the nature of the aminoacids and by the structure of the acyl group.

3. Surface-active and bulk-phase properties

Like other anionic surfactants, acylaminoacids form micelles, by virtue of their diphilic structure, over a narrow temperature range exceeding the Krafft point, i.e. the temperature below which micelles are insoluble. The structures of the aminoacids differ from those of the traditional surfactants, for example HCA soaps, by the presence of the peptide groups, which impart to them a number of specific properties. In particular, they exhibit an increased resistance to acids and salts, a greater rigidity, lower pH values of their aqueous solutions, lower critical concentrations for micelle formation (CCM) and Krafft points, and a lower surface activity (G_m), but they have higher minimum surface tensions (σ_{min}).[25,140,178,179] Certain colloidal-chemical properties of acylaminoacids are presented in Table 8.

The available data show that the principal factors determining the Krafft points and CCM are the size of the acyl group and the degree of branching of the aminoacid fragment. The salts of acylaminoacids are less active at the liquid–gas interface than the corresponding HCA salts, where the nature of the formation of their micelles is largely determined by the enhancement of the hydrophobic properties of the molecule owing to the lateral branching at the C_α atom of the aminoacid fragment. This has been confirmed by the minimum surface tensions and the CCM. The CCM for acyl derivatives of α-aminoacids diminishes with increase in the hydrophobicity of the molecules in the following sequence; glycine > α-alanine > valine > leucine.[179–181] The hydrophobicity increases sharply for salts of acyl derivatives of lysine. On the other hand, the salts of acyl derivatives of aspartic acid (a dicarboxylic acid) are more hydrophilic. The contribution of aminoacid side chains to the relative hydrophobicity has been estimated from the CCM for the salts of the lauroyl derivatives of a series of α-aminoacids in a study of the formation of their micelles in various media[182,183] and the authors suggested that the CCM be used as a characteristic of a surfactant, reflecting its hydrophile-lypophile balance (HLB).

The formation of micelles by acylaminoacids is accompanied by a change in certain physical parameters of their molecules, for example by a displacement of the chemical shift of the nuclei of the nucleophilic fragment, which is a consequence of the conformational rearrangements about the C(O)–N and N–CH_2 bonds.[184] It is noteworthy that the mechanisms of micelle formation are very significantly influenced by the type and number of impurities. Thus it has been shown[185] that values of CCM_1–CCM_4 in the range 0.026%–0.12% have been found in a technical product—sodium oleoylmethyltaurinate containing NaCl and NaOH as the main impurities—from the points of inflexion in the isotherm and from the solubilisation of a dye. The different micellar structures, characterised by the four typical concentrations for micelle formation, correspond to spherical and non-spherical (cylindrical) micelles and their aggregates.

The influence of the structure of the acylaminoacid molecules on their surface and bulk-phase properties has been estimated quantitatively by calculation and by correlating the values of σ_{min} derived from experimental σ isotherms.[179] It was shown that this parameter increases steadily with increase in the size of the acyl group, obeying the familiar Duclos–Traube rule, and decreases with increase in the size of the carbon skeleton of the molecule of the initial aminoacid.

Adsorption in a layer with participation of the carboxy- and peptide-groups is characteristic of acylaminoacids. This increases the surface area per molecule in the monomeric layer of the surfactant and decreases its limiting adsorption.[198] It has been shown for acyl derivatives of glycine and alanine[199] that they form a condensed monolayer over the entire range of surface pressures at temperatures of 283.2–308.2 K. Under these conditions, an increase in the size of the side group of aminoacid entails an increase in the area of the monolayer.

4. Hydrophobicity

The hydrophobicity of the molecules of organic compounds is an important property which determines the effectiveness of their activity. In view of this, constant attention has been devoted to the development of methods for the quantitative estimation of hydrophobicity or the HLB. The hydrophobicity of molecules is determined by their structure (each functional group makes a definite contribution in accordance with the values of the fragment constants).[200] Thus the introduction of a hydrocarbon group into the molecule makes it more hydrophobic, whilst the presence in the molecule of a double or triple bond as well as the lone pairs of the oxygen and nitrogen atoms make the compound hydrophilic. Recently it has been suggested that, together with the traditional methods for the instrumental estimation of the HLB, one should employ reversed-phase high performance liquid chromatography.[177] The hydrophobicities of the dodecanoyl derivatives of 17 most important aminoacids have been estimated from their measured chromatographic capacity coefficients and the results have been correlated with calculated data. It was shown that the correlation coefficients for structurally similar acylaminoacids are extremely high (0.978–0.999).

It has been found that the hydrophobic parameters of acylaminoacids determine the colloidal-chemical properties of these compounds and their fungicidal activity. The correlation between the hydrophobic and colloidal parameters for the dodecanoyl derivatives of a series of α-aminoacids[181] is entirely satisfactory, particularly for the CCM and σ_{min}. The results of in vitro tests on acylaminoacids by a standard method in a medium with toxicants acting against agents inducing fungal diseases showed[201] that the fungicidal activity of these compounds is satisfactorily correlated with their hydrophobic parameters, particularly in the case of structurally similar derivatives of α-aminoacids.

Table 8. The melting points (T_m), the Krafft points, CCM, and σ_{min} for aqueous solutions of the sodium salts of the acyl derivatives of a series of aminoacids $R^1C(O)NR^2(CHX)_nY$.[13,20,25,140,156,178–197]

No. of compound	$R^1C(O)$	R^2	X	*n*	Y	T_m/°C[a]	Krafft point/°C[b]	σ (60°C)/ mN m^{-1}	10^{-3} CCM (30 °C)/k mol^{-3}
24	C_{10}	H	H	1	COONa	113	+ (40)	34.5	45.72
18	C_{12}	H	H	1	COONa	117	36 (65)	35.6	12.66
25	C_{14}	H	H	1	COONa	121	47 (93)	35.6	4.30
19	C_{16}	H	H	1	COONa	121	55 (–)	35.4	1.25
20	C_{18}	H	H	1	COONa	127	66 (–)	36.1	0.44
26	C_{10}	H	CH_3	1	COONa	97	+ (154)	33.8	38.60
27	C_{12}	H	CH_3	1	COONa	104	18 (666)	34.5	11.53
28	C_{14}	H	CH_3	1	COONa	109	32 (523)	34.7	3.80
29	C_{16}	H	CH_3	1	COONa	114	45 (301)	34.3	1.23
30	C_{18}	H	CH_3	1	COONa	116	56 (–)	35.0	0.40
31	C_{10}	CH_3	H	1	COONa	36.5	+ (109)	33.8	53.08
32	C_{12}	CH_3	H	1	COONa	45.6	+ (258)	34.0	14.57
33	C_{14}	CH_3	H	1	COONa	52.0	+ (273)	34.2	3.99
34	C_{16}	CH_3	H	1	COONa	60.0	2 (229)	34.2	1.12
2	C_{18}	CH_3	H	1	COONa	71.5	33 (229)	34.1	0.32
35	C_{10}	H	$CH(CH_3)_2$	1	COONa	90	+ (109)	30.0	32.22
36	C_{12}	H	$CH(CH_3)_2$	1	COONa	92	+ (372)	31.0	9.97
37	C_{14}	H	$CH(CH_3)_2$	1	COONa	97	+ (400)	33.3	3.24
38	C_{16}	H	$CH(CH_3)_2$	1	COONa	99	8 (330)	32.1	0.82
39	C_{18}	H	$CH(CH_3)_2$	1	COONa	100	36 (229)	32.4	0.25
40	C_{10}	H	$CH_2CH(CH_3)_2$	1	COONa	109	+ (94)	28.6	19.09
41	C_{12}	H	$CH_2CH(CH_3)_2$	1	COONa	107	+ (229)	29.0	6.09
42	C_{14}	H	$CH_2CH(CH_3)_2$	1	COONa	101	+ (243)	30.0	2.04
43	C_{16}	H	$CH_2CH(CH_3)_2$	1	COONa	91	+ (236)	30.3	0.67
44	C_{18}	H	$CH_2CH(CH_3)_2$	1	COONa	65	46 (–)	29.9	0.22
45	C_{10}	H	$(CH_2)_4NH_2$	1	COONa	113	8 (184)	21.7	1.74
46	C_{12}	H	$(CH_2)_4NH_2$	1	COONa	117	34 (229)	23.8	0.90
47	C_{14}	H	$(CH_2)_4NH_2$	1	COONa	119	61 (–)	22.5	0.27
48	C_{16}	H	$(CH_2)_4NH_2$	1	COONa	122	84 (–)	23.6	0.17
49	C_{10}	H	CH_2COOH	1	COONa	103	+ (47)	39.6	112.20
50	C_{12}	H	CH_2COOH	1	COONa	109	+ (78)	39.3	33.56
51	C_{14}	H	CH_2COOH	1	COONa	115	+ (109)	40.1	13.02
52	C_{16}	H	CH_2COOH	1	COONa	118	+ (169)	40.6	3.69
53	C_{18}	H	CH_2COOH	1	COONa	119	46 (154)	40.8	1.33
54	C_{10}	H	H	5	COONa	58–60	18	44.8	13.0
6	C_{12}	H	H	5	COONa	85–86	29	42.4	6.0
55	C_{14}	H	H	5	COONa	90–91	39	39.6	2.0
56	C_{16}	H	H	5	COONa	99–101	49	38.2	0.6
57	C_{18}	H	H	5	COONa	105–107	61	36.7	0.2
7	$C_{18:1}$	H	H	5	COONa	–	5	32.0	0.3
58	C_{10}	CH_3	H	2	SO_3Na	224–225	0	61.0	–
59	C_{12}	CH_3	H	2	SO_3Na	207–208	1	49.6	8.7
60	C_{14}	CH_3	H	2	SO_3Na	201–203	23	41.4	1.82
61	C_{16}	CH_3	H	2	SO_3Na	187–188	43	40.4	0.43
62	C_{18}	CH_3	H	2	SO_3Na	171–173	58	37.8	–
63	$C_{18:1}$	CH_3	H	2	SO_3Na	162–164	0	39.3	0.29
11	C_{10}	H	H	2	SO_3Na	–	0	61.7	33.0
12	C_{12}	H	H	2	SO_3Na	–	14	50.9	10.1
13	C_{14}	H	H	2	SO_3Na	–	29	42.9	2.1
14	C_{16}	H	H	2	SO_3Na	–	46	41.4	0.55
15	C_{18}	H	H	2	SO_3Na	–	60	39.5	–
16	$C_{18:1}$	H	H	2	SO_3Na	–	0	39.1	0.40

[a] The melting points T_m were taken from Refs 14, 15, 24, 25, 135, 139, 180, 187, 189, 191, and 193. [b] The following notation has been adopted: (+) — pure solutions at 0 °C; the numerals in brackets denote the concentrations of the Ca^{2+} ions in $CaCO_3$ (10^{-4} %).

IV. Practical applications

There are almost no literature data on the practical applications of acylaminoacids, especially on their use as biologically and surface-active substances. A need for such a survey has arisen as a result of the continuous growth in the number of publications devoted to the study of the properties of acylaminoacids and especially their practical applications. Acylaminoacids exhibit different physiological and biological activities and are employed widely in various investigations in biology and biochemistry.[202] The latter include the study of complex membrane proteins, the preparation of liposomal systems, the crystallisation and study of the structures of proteins, etc. The uses of acylaminoacids associated with human vital activity are presented below.

1. Physiologically active agents

The search for new physiologically active agents among acylaminoacids embraces a wide range of compounds, for example acetylenic[203] and fluorine-containing[204–206] aminoacids, and phosphorus analogues of aminoacids.[207] The last exhibit an appreciable biological activity.[208]

Acylaminoacids, in particular derivatives of glycine, ornithine, and aspartic and glutamic acids have been detected in the organisms of certain warm-blooded animals and man.[1] This is due to the fact that they are the final products of the metabolism of proteins or are intermediates in the interconversions of aminoacids and proteins. It has been established experimentally that certain acyl derivatives are metabolised by the intestinal microflora under anaerobic conditions in vitro[209] and in animal tissues,[210] which leads to their deacylation.

The medical industry imposes very rigorous requirements on the chemical compounds employed. In this respect, acylaminoacids are favourable substances because their toxicity is extremely low. For example, LD_{50} = 5000 mg kg^{-1} (rats, administration via the stomach)[211] or 260–460 mg kg^{-1} (mice, intraabdominal administration)[212] for certain acylaminoacids. It was shown experimentally that acylaminoacids can be assimilated by the organism, since they are the starting materials for the synthesis of the organism's lipids and biologically active metabolites, for example arachidonic acid, the principal precursor of prostaglandins.[213]

Acetylcysteine, an active mucolytic agent which is indicated in the treatment of diseases of the respiratory organs, when there is a tendency toward lung haemorrhages, and in bronchial asthma, occupies an important place in the assortment of medicinal drugs.[214–216] Together with the mucolytic activity, acetylcysteine exhibits also an antibiotic activity.[217] The use of this preparation in the treatment of the diseases of the eye cornea[218] and for detoxication in cases of poisoning with methylmercury[219] in combination with haemodialysis has been described.

Effective preparations influencing the central nervous system have been discovered among acylaminoacids. These are derivatives of DL-aspartic[220] and 4-aminobutyric[221] acids, asparagine,[222] and the amides of acylaminoacids.[223] Their effect on the central blood circulation and the systemic arterial pressure, on the content of acetylcholine in various regions of the cerebral cortex, and on the functional disorders of the brain has been noted.

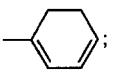
Acylaminoacids occupy a notable place among the rheumatological antiinflammatory and antiulcer preparations.[224–231] They are designed for the treatment of patients for whom the employment of traditional agents is contraindicated. Acylaminoacids do not as a rule induce undesirable side effects. A series of acylaminoacids are the active principles of antihypertonic[232–240] and therapeutic,[61,242] agents, inhibitors of enzymes with angiotensive activity,[235,243–246] and other preparations with many-sided activity.[247–252] The main principles of the selectivity and mechanisms of the action of medicinal drugs, including acylaminoacids, have been described in a monograph.[246] Thus certain acylaminoacids, for example benzoylglycine, are formed as metabolites when benzoic acid is eliminated from the kidneys. A series of benzoyl derivatives of aminoacids and oligopeptides have been used as anions in the study of a model of their transport through membranes.

Acylaminoacids with a complex structure which are the active principles of many medicinal drugs (ampicillin, oxacillin, carbenicillin, ceflorin, folic acid, levomycetin succinate, methotrexate, pantogam, picamilon, phenoxymethylpenicillin, cefazolin, cephalexin, and cephalothin) are included in a handbook.[253] These compounds are antibacterial, neotropic, and antitumour agents which are components of the Group B vitamin complex and participate in the carbohydrate and fat metabolism.

Table 9. Certain medicinal preparations based on *N*-acylaminoacids.

Compound	Chemical formula	Applications	Ref.
Acetylcysteine	$CH_3C(O)NHCHCOOH$ $\quad\quad\quad

Table 9 (continued)

Compound	Chemical formula	Applications	Ref.
Acylglutamine	$ABCC(O)NHCH(CH_2)_2CONH_2$ (R; $COOR^1$) A — Ph, cyclo-C_6H_{12}; B —  ; R — H, CH_3, C_6H_6; R^1 — H, M	Antiinflammatory agent and preparation for the treatment of diseases of the eye	225
6-(*N*-Acetyl)amino-hexanoic acid	$CH_3C(O)NH(CH_2)_5COOH$	Stimulation of the reparative processes in the healing of wounds and in the knitting of bones	248
Zn salt of 6-(*N*-acetyl)-aminohexanoic acid	$[CH_3C(O)NH(CH_2)_5COO]I_2Zn$	Therapeutic preparation with antiinflammatory and antirheumatic activities.	226
N-Acylaminoacids	$RC(O)NHCHCOOH$ (R^1) R — Alk (C_1-C_5); R^1 — $(CH_2)_4NH_2$, $-(CH_2)_3NHC(=NH)NH_2$	Antitumour and antiviral agent	249
Acylaminoacid derivatives	$RC(O)XC(O)NR^1CHR^2COOR^3$ R — Ar; R^1, R^2, R^3 — H, Alk (C_1-C_4); X — $-CH(SR^4)CHR^5-$; R^4, R^5 — H, Ac	Hypertonic preparations	232
Sulfur-containing acylaminoacids	$CH(2\text{-}HOC_6H_4)(CH)_2NC(O)ASR$ ($SCH_2CHCONHCHR^1COR^2$) R — H, Ac; R^1 — H, Alk, NH_2, COOH, H, S, RS; R^2 — OH, OAlk; A — $-(CH_2)_n-$, $n = 1-3$	Antihypertensive agents	233
N-(Thiopropanoyl)-aminoacids	$C(O)R^1CHCH_2SR$ ($NR^2CR^3R^4COOH$) R — Ac; R^1, R^2 — H, Alk; R^3, R^4 — Alk	Preparations with hypertonic activity	234
N-Acylaminoacid amides	$CH(YXR^2)(CH_2)_nSR^1$ ($CONR^3CHR^4COR^5$) R^1 — H, Bz, Ac; R^2 — H, Alk, Ac; R^3-R^5 — H, Alk, Ar; R^3, R^4 — $(CH_2)_m$, $m = 3, 4$; X — O, S; Y — (CHR)	Anticonvulsant and soporific agents and depressants of the central nervous system	223
N-(Mercaptoacyl)-aminoacids	$C(O)(CH_2)_nSH$ ($N(R)CHCOOH(R^1)$) R, R^1 — $(CH_2)_3$, $(CH_2)_4$, CH_2SCH_2; $n = 1-3$	Hypotensive preparation, in particular in the treatment of liver hypertonicity	236
N-(Carboxyacyl)-aminoacid derivatives	$C(O)CH_2XC(COR^3)R^1R^2$ ($N(COR^5)CH(CH_2)_m(CH_2)_nCHR^4$) R^1 — Alk, Ar; R^2 — H, Alk, Ar; R^3, R^5 — OH, OAlk, OAr, NH_2 R^4 — OAlk, SAlk; X — CHR, NR $n, m = 0-3$	Preparation for the treatment of hypertonicity	237
N-(Carboxyacyl)-aminoacids	$CHR^3(CH_2)_nC(O)R^4$ ($C(O)NR^2CHR^1COOH$) R^1 — H, Alk, Ph, HOC_6H_4, NH_2, HS; R^2, R^3 — H, Alk; n — 1, 2; R^4 — OAlk, OH	Inhibitors of the angiotensive transformation of enzymes	239

Acylaminoacids exhibit antimicrobial and antifungal activities and are used as disinfectants and antiseptic agents in toothpaste, tooth powders, and toilet requisites. These include acyl derivatives of glycine,[254] sarcosine,[13] arginine, histidine, lysine, diaminobutyric acid,[255] and their peptides.[256] The highest activity against Gram-negative bacteria among the homologous acyl derivatives has been discovered for caproylglycine[257] at the pH characteristic of the surface of the skin. Acyl derivatives of glutamic acid and glutamine have been proposed for the inhibition for the activity of bacteriophages[13,258] and are used in the preparation of antibiotics, enzymes, aminoacids, and nucleotides. The ability of acylsarcosinates to inhibit bacterial hexokinase and other acid forming enzymes, protecting thereby the tooth enamel, is widely used for commercial purposes in the manufacture of toothpaste.[20,259,260]

Table 9 presents a list of the medicinal preparations based on *N*-acylaminoacids.

2. Pesticides

Together with natural α-aminoacids and their alkyl derivatives, acylaminoacids exhibit a fairly broad spectrum of biological activity.[261]

Acylaminoacids manifest a fungicidal activity[254,262,263] and regulate the formation of ethene in plants, permitting an increase in the lifetime of cut flowers.[264] These products are effective as preparations against the tobacco mosaic virus and fungal and bacterial diseases of plants.[13,265–267] The stimulation of the growth of the central stem and of the flowering of carnations may be included among the advantages of the compounds indicated.[265–267] They are also capable of destroying the eggs of lice.[268–270] The highest biological activity has been noted for α-alanine derivatives.[261] The esters of acyl derivatives of alanine have found an application as herbicides against wild oats in spring and winter wheat, barley, rape, and pulses,[271–277] and as fungicides against phytophthorosis on tomatoes and potatoes,[278] peronosporosis on tobacco and hops, mildew on grape vine shoots, false mildew on onions,[279] root rot on beetroot, false mildew on potatoes,[280] and phytopathogenic fungi of the class of oomycetes.[281] Acylalanines act selectively on groups of peronosporaceous fungi.[279]

A large series of acylaminoacids with fungicidal activity have been synthesised from glycine, sarcosine, alanine, phenylalanine, valine, norvaline, leucine, proline, threonine, methionine, and α-aminobutyric acid.[13,265–267] Acylaminoacids are active against the diseases of rice (*Piricularia oryzae*)[12,282] and the radiating mildew on cucumbers and are used to combat *Bacterium oryzae, Diaporthe citri,* and *Spraerotheca fuliginca.*[283] Whilst exhibiting effective protecting properties in tests on plants in vivo, their toxicity to warm-blooded animals is low. They are nonphytotoxic and they accelerate the growth of plants. Studies on the mechanisms of the action of acylalanines on the fungal cell have shown that in most cases the synthesis of nucleic acid is retarded. The inhibition of the synthesis of RNA is the primary result of the attack by acylalanines, which has been confirmed by the retardation of the formation of RNA in a number of fungi.[279] The dodecanoyl derivatives of 15 α-aminoacids exhibit a fungicidal activity against fungi giving rise to fungal diseases: *Acterharia solani, Helmirtosporium sativum, Fusarium graminea-kum,* and *Fusarium nivali.*[201] The usual dose of the above preparations is 0.5–10 kg ha^{-1}.[284]

The benzoyl derivatives of alanine, valine, aspartic acid, and other acylaminoacids are effective herbicides.[13,285–287] These compounds proved to be effective in vivo against pathological fungi on plants, whilst they had no in vitro fungicidal activity.[288]

3. Cosmetic and hygienic preparations

The inclusion of acylaminoacids in cosmetic and hygienic preparations is due to their effective dermatological properties, biological compatibility, a low level of the irritant and allergenic activities on the skin, and the manifestation of specific types of biological activity. The use of acylaminoacids as polyfunctional surfactants in cosmetic and hygienic preparations has been described in a number of studies.[12,25,211,289,290]

The specific biological activity of acylaminoacids in cosmetic preparations is manifested by the regulation of the blood circulation in the skin. They are employed in moisturising creams for the treatment of dry skin[292] and for the retention of biologically active substances on the surface of the skin.[293] Acylaminoacids possess an antimicrobial activity against Gram-negative bacteria.[257] Acyl derivatives of a mixture of α-aminoacids have been proposed as a means of stimulating the growth of hair and promoting an increase in the content of soluble protein in the latter.[294] The preparation increases the diameter of growing hair by a factor of 2–3 and has a positive effect on the protein metabolism in the skin, increasing the content of soluble proteins by 25%–50%, which promotes a sharp decrease in defatting and irritant action. The biological activity was estimated from the total amount of soluble proteins (Bailey's method), hair being subjected under these conditions to trichlonometric monitoring by Khrunova's method.[295]

It has been demonstrated experimentally[296] that acyl derivatives of elastin are capable of penetrating deeper into the human skin epidermis compared with other agents, improving the tone and structure of the skin and eliminating fine wrinkles. The introduction of acylaminoacids combined with oligopeptides into a cream[297] has a moisturising and protecting effect on the hair and skin, limits the swellability of hair, reduces the level of irritant action in the presence of surfactants and alkalies, and makes it possible to restore damaged hair.

One of the principal requirements which must be met by modern cosmetics as regards skin care is the prevention of the premature ageing of the skin. For this purpose, deeper studies are necessary on the mechanisms of the ageing and moisturising of the skin and on the metabolic processes occurring in the latter. As a rule, acyl derivatives of hydrolysed protein,[298–300] glutamic acid,[301] and a number of other α-aminoacids[302,303] are included in such preparations in order to impart to them effective moisturising properties, to stimulate metabolic processes, and to maintain the normal water balance in the skin. As substances with a low primary toxicity and a weak side effect on the skin,[304] acylaminoacids have been proposed in recipes for decorative[305] and cleansing cosmetics.[306] They hinder the total removal of fat deposits during the washing of the skin and hair. This is important, since the secretions of the sebaceous glands have a protecting function while increased defatting of hair makes it dry and brittle and leads to the loss of its lustre and silky appearance.

Liquid detergents, shampoos, and gels occupy a leading place in the market of personal hygiene preparations. These preparations contain aminoacids and their derivatives, including acylaminoacids, as the most valuable additives.[13,307,308] In terms of a series of parameters such as the effectiveness of detergent action, degree of elution of aminoacids from the skin during washing, and the solubilisation of the defatting agent, acylaminoacids have a clear advantage over traditional surfactants such as HAC soaps, alkyl sulfates, and alkyl sulfonates.

A series of recipes for shampoos with a low irritant action and improved detergent and foam-forming properties, liquid and solid detergents, and gels incorporating acyl derivatives of β-alanine and acylglutamic acid have been developed.[309–326] Mild shampoos, which cause almost no irritation to the eyes and the skin on the head, for improving the state of hair have been created on the basis of acyl derivatives of hydrolysed proteins.[327–330] The introduction of the latter into recipes for shampoos eliminates the hardness and dullness of hair caused by the deposition of $CaCO_3$ from tap water.[331,332] Dermatologically mild detergents and shampoos with a wide variety of valuable properties from the consumer's point of view contain acyl derivatives of various α-aminoacids.[333–350]

When hair is washed, up to 50% of natural lipids are removed, as a result of which it becomes dry, loses its lustre, and

Table 10. Brief characteristics of certain recipes for cosmetic and hygienic preparations based on *N*-acylaminoacids.

Type of preparation	*N*-Acyl derivatives of aminoacids (mass %)	Consumption properties	Ref.
Shampoo	of glutamic acid		
	(1 – 10)	Preparations with a low irritant activity and improved detergent and foam-forming properties	309, 317, 318
	(20 – 25)	Transparent creamy detergents	310, 320
	or β-alanine		
	(0.5 – 10)	Preparations with improved detergent, foam-forming, and softening properties, which readily wash away fatty dirt, assist in feeding and strengthening hair, and do not irritate the skin and the mucous membranes around the eyes	325, 338
	(25 – 35)	In combination with acylsarcosinates, an effective preparation in the form of a transparent gel	326
	of hydrolysed proteins (3 – 30)	Dermatologically soft preparations for dry and sensitive skin, improving the state of hair, and possessing excellent foam-forming properties and increased stability during storage. These preparations exhibit a satisfactory affinity for the skin and hair, and improve the state of hair, rendering it pleasant to the touch, and preventing its entanglement during drying. They counteract the deposition on hair of water-insoluble salts, preventing the hardness and dullness of hair, and form on the damaged ends of hair a protective film which promotes softening and regenerative properties	327 – 332
	of sarcosine		
	(1 – 10)	Dermatologically soft preparations with high foam-forming and detergent capacities	336 – 338
	(30 – 50)	Transparent gel-like preparations, which do not irritate the skin and eyes	340
	of an aminoacid mixture (5 – 20)	Preparations with high foam-forming and detergent capacities. Therapeutic and healing agents with a low irritant activity containing biologically active additives, for example derivatives of α-pyridone	334, 335 333, 345
Cream	of oligopeptides (0.5 – 8)	Preparations improving the structure of the skin, influencing metabolic processes, promoting a better permeation through the corneous layer of the skin, and smoothing away fine wrinkles	296, 300
	of glutamic acid (0.1 – 12)	Effective preparations with biological activity for the care of ageing skin, improving its moisture-retaining capacity, and stimulating metabolic processes	301 – 303
Cream	of aminoacids (0.1 – 5)	Preparations promoting the restoration of damaged hair, increasing the affinity for the skin and softening and feeding the latter	297, 305
Preparations for hair care	of oligopeptides (0.1 – 3)	Effective preparations for the improvement of the state of hair by restoring its lipid balance, rendering it soft, improving its capacity for being set, and reducing the damage to hair after dyeing and the application of a chemical permanent wave	351, 356, 369
	of aminoacids (0.1 – 10)	Preparations softening leather and hair, imparting lustre to the latter and making it manageable, smooth, fluffy, and elastic. These preparations feed hair effectively, stimulate the occurrence of metabolic processes in it, exert an antistatic effect, improve the setting of hair, promote its growth, and prevent its falling out.	352, 354 – 359, 362 – 366
		The *N*-acylaminoacids in these preparations promote the retention of biologically active substances in hair and enhance blood circulation, thus preventing dandruff and loss of hair	291, 293

is difficult to set. The loss of lipids may be made good with the aid of cosmetics containing various plant extracts, natural lipids, and acyl derivatives of a series of α-aminoacids.[351] Cosmetics for skin and hair care in the form of lotions and sprays containing acyl derivatives of aminoacids and hydrolysed proteins soften hair,[352–362] strengthen it,[363,364] promote its growth,[365] feed it and stimulate metabolic processes in it,[366,367] improve its moisture retaining properties,[360,368] and reduce damage to hair and improve its structure.[369]

N-Acylaminoacids are a valuable cosmetic raw material for effective preparations with a broad spectrum of cosmetic and therapeutic and healing activities on skin and hair (Table 10).

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Adducts of proteins and water-soluble poly(alkylene oxides)

I N Topchieva, N V Efremova, B I Kurganov

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Abstract. The review is devoted to methods for the modification of proteins by water-soluble diphilic block-copolymers of ethylene and propylene oxides and also to the properties of the resulting polymer–protein adducts. Two principal classes of such adducts are examined: conjugates obtained by forming covalent bonds between the protein and the polymer and noncovalent complexes. It is shown that the amphiphilic nature of the polymer chains gives rise to a series of new properties of the conjugates with the block-copolymers, such as the ability to be translocated into cells, the ability to solubilise insoluble biologically active compounds, the ability to serve as agents transporting the latter, and also the ability to interact with surfactants of different chemical nature. The bibliography includes 50 references.

I. Introduction

A vigorous development of a new aspect of protein engineering, involving the specific alteration of the properties of protein molecules as a result of their chemical modification by water-soluble polymers, began since the beginning of the 1970s. The conjugate obtained by means of such modification consists of two macromolecular fragments — the protein and polymer fragments — and combines the properties of each of them. Dextran,[1] poly-*N*-vinylpyrrolidinone,[2] and poly(ethylene oxide) (PEO)[3–5] are usually employed as the polymer fragments. Among the polymers listed above, PEO is most widely used. It is a nontoxic, nonimmunogenic synthetic polymer, which is available with a wide range of molecular masses.[6] The poly(ethylene oxide)– protein conjugates are characterised by weaker immunogenic and antigenic properties, an increased circulation period in the blood circulation system, and in many instances an increased stability.[7] These properties are to a large extent determined by the effect of the steric stabilisation of the protein globule resulting from the creation around the latter of a shell comprising attached polymer chains.

An important property of the PEO–protein conjugates is their ability to dissolve in organic solvents. This makes it possible to employ such conjugates as biocatalysts for peptide synthesis,[8] transesterification,[9] and amination of esters.[10]

The next stage in the construction of polymer–protein conjugates is the introduction of additional fragments (blocks) into the polymer chain in the stage involving the synthesis of polymeric reagents. This approach led to the formation of conjugates of proteins with block-copolymers of ethylene and propylene oxides, namely proxanols (Pro) and pluronics. These copolymers are nonionogenic surfactants in which the PEO and poly(propylene oxide) (PPO) blocks are respectively the hydrophilic and hydrophobic parts of the molecule.[11] Compared with the PEO–protein conjugates, the conjugates of proteins with the block-copolymers are characterised by a greater structural variety, manifested, firstly, by the possibility of attaching copolymers to different numbers, compositions, and arrangements of the blocks and, secondly, by the possibility of different arrangements of the polymer chains on the surface of the protein globule. The amphiphilic nature of the attached polymer chains gives rise to new properties of the conjugates, such as the ability to be transported into the cell,[12,13] the ability to solubilise effectively insoluble biologically active compounds,[14,15] the ability to serve as agents transporting the latter, as well as the ability to interact with surfactants of different chemical nature.[16] In the present review, we shall examine the methods of synthesis and characteristics of the protein–Pro conjugates as well as their physico-chemical and biological properties. Together with the traditional methods of synthesis of polymer–protein conjugates, effected via the covalent interaction of the polymer with the protein, new approaches to the synthesis of structures of this type, based on the formation of noncovalent complexes between the protein and Pro, will be considered.

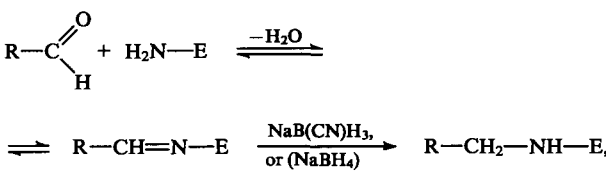
I N Topchieva Department of Macromolecular Compounds, Faculty of Chemistry, Lomonosov Moscow State University, Leninskie gory, 119899 Moscow, Russian Federation.
Fax (7-095) 939 01 74. Tel. (7-095) 939 31 27
N V Efremova, B I Kurganov Enzyme Systems Laboratory, Bakh Institute of Biochemistry, Russian Academy of Sciences, Leninskii prosp. 33, 117071 Moscow, Russian Federation.
Fax (7-095) 954 27 32

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II. Synthesis, isolation, and characteristics of the conjugates

1. Synthesis of the conjugates

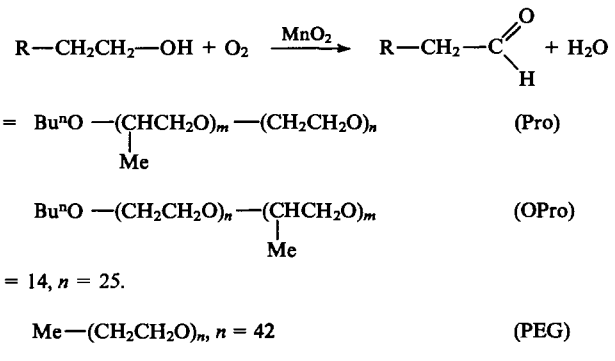
The conjugates of proteins with proxanols are synthesised by the reductive alkylation of the primary surface amino-groups of the protein by polymeric monoaldehydes,



where R is the polymer chain and E is the protein molecule.

Conjugates based on the following proteins have been obtained similarly: bovine serum albumin (BSA),[14] α-chymotrypsin (CT),[17] pyruvate kinase from the rabbit skeletal muscle, ricin from the castor bean, viscumin from the mistletoe,[18] the classical proteinase inhibitor of the Bauman–Birk type from the soya beans (BBI),[19] and cytrochrome *c*.[12] The conjugates based on CT and BBI have been obtained in the presence of reversible inhibitors of the active centres of enzymes. For example, in the synthesis of conjugates based on CT, we employed for this purpose *N*-benzoyl- or *N*-acetyl-L-tyrosine.[16] Sodium cyanohydroborate is a more convenient reducing agent for the preparation of the conjugates than sodium tetrahydroborate, which leads to the reduction of the disulfide bonds between polypeptide chains as a side reaction.

The monoaldehyde derivatives of PEO and Pro are obtained by oxidising the corresponding monofunctional polymers by atmospheric oxygen in solution in chloroform in the presence of manganese(IV) oxide as the catalyst.[20]



Evidently the only difference between the Pro and OPro (reversed proxanol) polymers consists in the position of the hydrophobic PPO block relative to the terminal aldehyde group. The use of these polymeric reagents makes it possible to synthesise conjugates with different sequences in the attachment of the polymeric blocks to the protein. The number of polymer chains in the conjugate may be regulated by varying the polymer/protein ratio in the reaction mixture.

The molecular models of the conjugates described in this review are presented in Fig. 1. Evidently the conjugates are star-shaped structures with a protein globule in the centre, the polymer chain being bound covalently to the globule. When polymeric reagents with a number-average molecular mass of 2000 are employed, the length of the polymer chains is 20.7 nm for PEO (Fig. 1, type *I*), and 21.6 nm for Pro and OPro (Fig. 1, types *II* and *III*), which is significantly greater than the diameter of the protein globule (for example, the average length of the two globule half-axes for CT is 2.5 nm). Such a structure suggests that the polymer chains provide a steric shield to the protein, diminishing its binding to macromolecular substrates, antibodies,

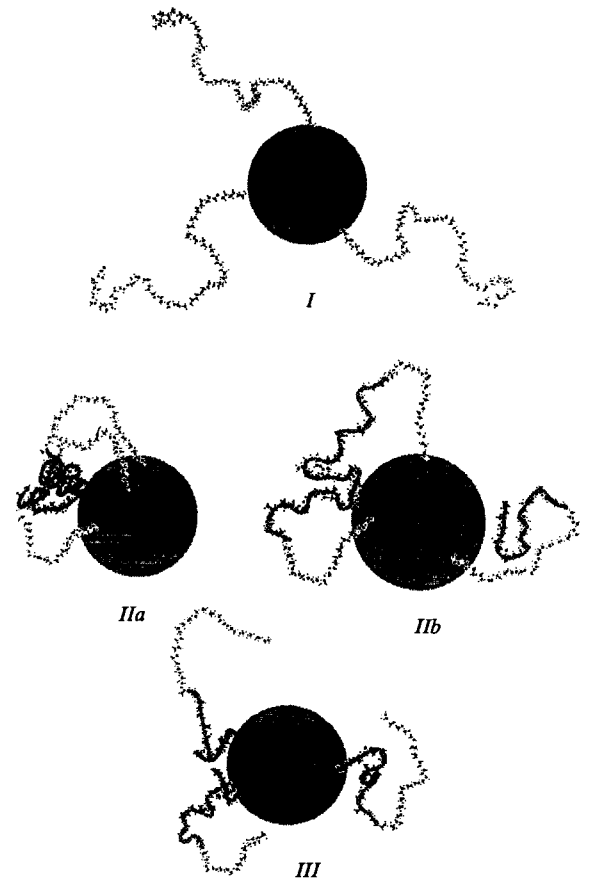


Figure 1. Molecular models of protein conjugates: (*I*) with PEO ($M = 2000$); (*IIa*) with Pro having a nonuniform distribution of polymer chains; (*IIb*) with Pro having a uniform distribution of polymer chains; (*III*) with OPro. The PPO blocks of the polymer chains of the proxanols are shown shaded; the radius of the protein globule is 25 Å (the average length of the two half-axes of the CT globule).[21]

and proteolytic enzymes. Evidently this effect of the polymer chains should depend on their number and on the nature of their distribution on the surface of the protein in the conjugate.

Since the polymer chains in the conjugates are attached only to a proportion of the surface amino-groups of the protein, a possibility arises of their different relative dispositions. Thus the polymer chains may be uniformly distributed on the surface of the protein (Fig. 1, *IIb*) or may be concentrated in one place with formation of domains (Fig. 1, *IIa*). Naturally, the formation of structures of a particular type is specified in the stage involving the synthesis of the conjugate. During the synthesis in aqueous buffer media, where proxanols manifest a capacity for self-association due to their diphilic nature,[22] conditions arise for their nonuniform distribution on the surface of the protein globule. The conjugates thus obtained may be regarded as a kind of intramolecular micelle, stabilised by the hydrophobic interaction between the polymer chains attached to the protein. On the other hand, when the conjugates are synthesised in aqueous organic media, where the hydrophobic interactions between the proxanol molecules are suppressed,[23] their more uniform distribution on the surface of the protein globule should be promoted. Taking these considerations into account, two series of conjugates were synthesised and will be designated below as nonuniform (nonun.) and uniform (un.). It is noteworthy that the concentrations of the organic solvent in the reaction mixture in the synthesis of the uniform conjugates were much lower than the threshold concentrations inducing the denaturation of the protein.[24]

In order to make sure that the above postulates are valid, it was necessary to estimate the differences between the distributions of the polymer chains on the surface of the protein globule in conjugates synthesised under different conditions. Use was made for this purpose of the ability of the polymer chains of poly(alkylene oxides) to interact with a bulky cyclic ligand — β-cyclodextrin (β-CD). We had shown earlier[25] that β-CD forms clathrate complexes with proxanols, the number of β-CD molecules 'threaded' onto the polymer chains being determined by the number of propylene oxide units entering into the composition of the proxanol. Naturally, the interactions of the polymer chains of the conjugates with this ligand depend on the nature of the distribution of the polymer chains on the protein surface. A uniform distribution of the polymer chains should not prevent the formation of complexes with β-CD, whereas for a nonuniform distribution the interactions are hindered for steric reasons. Indeed, it has been shown that only conjugates for which a uniform distribution of the polymer chains has been postulated (Fig. 1, *IIb*), form, like the free proxanols, crystalline clathrate complexes with β-CD which are insoluble in water. On the other hand, the conjugates with a tentatively nonuniform distribution of the chains do not form complexes with β-CD.[16] Thus it has been confirmed that the conjugates synthesised in an aqueous medium are characterised by a nonuniform (domain) type of distribution of the polymer chains, in contrast to the conjugates synthesised in an aqueous organic medium and characterised by a more uniform distribution. The differences between the structures of such conjugates are responsible also for a series of differences between their physicochemical properties and biological behaviour.

2. Purification of the conjugates

The purification of the conjugates based on proxanols in order to remove the excess polymeric reagent is a more difficult problem than in the case of the PEO – protein conjugates. This is due to the amphiphilic properties of the proxanols, which are capable of forming associated species with the polymer chains entering into the composition of the conjugate. Taking this into account, two purification methods have been proposed which make it possible to suppress the hydrophobic interactions between the polymeric reagent and the polymer chains of the conjugate: precipitation of the conjugate with acetone;[17] gel-permeation chromatography involving the use of the 1:4 ethanol – water mixture as the eluent.[12] Thin-layer chromatography has been used to demonstrate the absence of a free polymer impurity in the conjugate.

3. Characteristics of the conjugates

Tables 1 and 2 present the characteristics of the conjugates obtained: composition, degree of modification (average number of polymer molecules attached to one protein molecule), and the number of primary, i.e. unmodified, amino-groups in the protein component of the conjugate.

Table 1. Characteristics of the conjugates of α-chymotrypsin with poly(ethylene oxide) and proxanols.

Polymer	Type of conjugate[a]	Designation	Degree of modification (*n*)	CT content (mass%)[b]	No. of unsubstituted NH_2 groups (*m*)
PEO	*I*	$(PEO)_3$–CT	3	81.0 (80.5)	12
PEO	*I*	$(PEO)_9$–CT	9	58.1 (58.8)	5
Pro	*IIa*	$(Pro)_2$–CT(nonun.)	2	86.2 (86.1)	13
Pro	*IIa*	$(Pro)_3$–CT(nonun.)	3	82.1 (79.8)	12
Pro	*IIa*	$(Pro)_6$–CT(nonun.)	6	67.5 (66.7)	8
Pro	*IIa*	$(Pro)_7$–CT(nonun.)	7	64.0 (64.1)	–
Pro	*IIa*	$(Pro)_{10}$–CT(nonun.)	10	55.6	4
Pro	*IIb*	$(Pro)_3$–CT(un.)	3	80.6	11
Pro	*IIb*	$(Pro)_5$–CT(un.)	5	71.5 (71.0)	9
Pro	*IIb*	$(Pro)_6$–CT(un.)	6	67.4 (67.5)	–
Pro	*IIb*	$(Pro)_{11}$–CT(un.)	11	45.5 (46.0)	–
OPro	*III*	$(OPro)_3$–CT	3	80.6 (80.7)	12
OPro	*III*	$(OPro)_7$–CT	7	64.2 (64.0)	–

[a] Here and henceforth the designations *I*, *IIa*, *IIb*, and *III* correspond to the structures presented in Fig. 1.
[b] The protein content in the conjugates was determined spectrophotometrically and also with the aid of the biuret reaction (values in brackets).

Table 2. Characteristics of the conjugates of bovine serum albumin with poly(ethylene oxide) and proxanols.

Polymer	Type of conjugate	Designation	Degree of modification	BSA content (mass%)		
				biuret reaction[a]	UV (280 nm)[a]	^{13}C NMR
PEO	*I*	$(PEO)_5$–BSA	5	87	87	–
PEO	*I*	$(PEO)_{14}$–BSA	14	70	71	–
Pro	*IIa*	$(Pro)_5$–BSA(nonun.)	5	87	87	–
Pro	*IIa*	$(Pro)_8$–BSA(nonun.)	8	81	80	78
Pro	*IIb*	$(Pro)_{15}$–BSA(un.)	15	70	69	70
OPro	*III*	$(OPro)_6$–BSA	6	85	84	–
OPro	*III*	$(OPro)_{11}$–BSA	11	75	75	–

[a] The method for the determination of the protein content in the conjugate.

The protein content in the conjugate was determined spectrophotometrically (λ = 280 nm) and also with the aid of the biuret reaction.[26] In all cases, the initial proteins were employed as the standard. It had been shown previously[3,4] that the presence of poly(alkylene oxide) does not affect the results of the assay of the protein by means of the biuret reaction. The composition was determined by the ^{13}C NMR method, which permits independent measurements of the contents of the protein and polymeric components. Such measurements have been carried out for two conjugates of BSA with Pro (Table 2). The regions where the signals of the protein and the polymer do not overlap were found from the spectra of the individual components in a preliminary experiment. For BSA, this is the 172–180 ppm region corresponding to the carbon atoms of the carboxy-groups, while for Pro this is the 70–77 ppm region corresponding to the carbon atoms of the methylene groups of the main chain. The integral intensities of selected analytical signals of the protein and the polymer were determined from the spectra of specially prepared solutions containing mixtures of the protein and Pro in specified mass proportions. The dependence of the integral intensities on the polymer/protein mass ratio for these solutions proved to be linear. The mass compositions of the polymer synthesised were determined from the integral intensities in their spectra by means of a calibration plot. It was found that the results obtained agree, within the limits of the error of the measurement, with data obtained by the spectrophotometric and chemical methods (Table 2). Subsequently we assumed that the use of only the spectrophotometric and (or) chemical methods which do not require large amounts of the test substance, was sufficient for the determination of the composition of the conjugate. In this case, the content of the polymer [m_{Po} (mass%)] in the conjugate was assumed to be

$$m_{Po} = 100 - m_{Pr}, \quad (1)$$

where m_{Pr} is the content of the protein (mol%). The degree of modification (n) was calculated from the composition of the conjugate as the average number of polymer molecules attached to one protein molecule:

$$n = \frac{m_{Po}/\bar{M}_{Po}}{m_{Pr}/M_{Pr}},$$

where $\bar{M}_{Po}$ is the number-average molecular mass of the polymer and M_{Pr} is the molecular mass of the protein.

In addition, the degree of modification was determined independently by titrating the residual unsubstituted primary amino-groups of the protein. For proteins where the total number of the primary surface amino-groups is known, the degree of modification n may be determined as the difference

$$n = r - m, \quad (2)$$

where r is the total number of surface NH_2 groups and m is the number of unsubstituted NH_2 groups.

It is noteworthy that the number of unsubstituted surface NH_2 groups in proteins is usually determined by titrating a solution of the protein with 2,4,6-trinitrobenzenesulfonic acid (TNBS).[27] However, in our case this procedure is inapplicable, since both the remaining unsubstituted NH_2 groups of the conjugates and the substituted, secondary amino-groups react with TNBS.[28] The number of surface amino-groups in the conjugates determined by the reaction with TNBS therefore remains the same as in the initial protein. In order to determine the number of residual unsubstituted amino-groups of the protein after conjugation, we resorted to Ruff's method[28] based on the interaction of the primary amino-groups with *o*-phthalic dialdehyde in the presence of mercaptosuccinic acid. The number of primary NH_2 groups was determined by this method in a series of CT conjugates. The degree of modification calculated by Eqn (2), taking into account the fact that the total number of primary amino-groups with CT is 15, proved to be close to the value calculated by Eqn (1) from the protein content in the conjugate.

A satisfactory agreement between the results obtained by the two methods confirms the fact that only the primary amino-groups of the protein are modified and that the other aminoacid residues are unaffected.

4. Catalytic properties of the conjugates

The catalytic properties of the CT-based conjugates are presented in Table 3, from which it is seen that:

1. The conjugates retain a high enzyme activity in relation to both substrates employed — the low-molecular-mass substrate [the ethyl ester of *N*-benzoyl-L-tyrosine (BTEE)] and the high-molecular-mass substrate (casein).

2. The kinetic constants of the hydrolysis of the low-molecular-mass substrate (BTEE) by the enzyme forming part of the composition of the conjugates changed only slightly compared with the native enzyme. Similar results were obtained also in the study of the hydrolysis of the high-molecular-mass substrate (casein). This is apparently associated with the fact that the active centre of α-chymotrypsin was protected in the conjugate synthesis stage by the inhibitor bound reversibly to it and so the polymer chains were unable to be bound in the immediate vicinity of the active centre of the enzyme.

3. A significant loss of enzyme activity was observed only after the attainment of high degrees of modification (11 and more attached polymer chains). A similar trend has been described by Chiu et al.[30] for conjugates based on CT and PEO. Evidently the decrease in activity in this case is not a consequence of the decrease in k_{cat} but occurs as a result of the decrease in the number of active centres in the conjugates [Table 3, $(Pro)_{11}$–CT(un.)].

5. Thermal inactivation of the conjugates

An important practical consequence of the modification of proteins by polymers is a change in the resistance of the protein globule to the effect of elevated temperatures.[31] The thermal stabilities of the conjugates between proteins and proxanols have

Table 3. The enzyme properties of the conjugates of α-chymotrypsin with poly(ethylene oxide) and proxanols.

Protein, conjugate	Activity in enzymic hydrolysis of casein (%)	Enzymic hydrolysis of BTEE			Content of active centres (%)
		activity (%)	k_{cat}/s^{-1}	10^5 K_m/mol litre^{-1}	
CT	100	100	31.2 ± 0.5	6.27 ± 0.94	80
$(Pro)_5$–CT(nonun.)	102	97	42.4 ± 2.8	13.0 ± 2.9	61
$(Pro)_3$–CT(un.)	103	115	–	–	80
$(Pro)_6$–CT(un.)	96	98	32.5 ± 1.2	6.18 ± 0.82	67
$(Pro)_{11}$–CT(un.)	50	57	37.0 ± 0.4	21.7 ± 3.5	40
$(PEO)_6$–CT	97	98	40.4 ± 0.8	9.3 ± 1.5	80
$(OPro)_3$–CT	98	100	–	–	80

been investigated by a method involving the kinetic study of the enzyme properties of the conjugates at the elevated temperature.[17] The corresponding kinetic curves (the time variations of the activity) are presented in Fig. 2. Evidently the rate of the thermal inactivation of CT diminishes significantly even after the addition of only three polymer chains (curves *2* and *3* in Fig. 2). With increase in the degree of modification of the conjugate, this effect becomes more pronounced (curves *4*–*6* in Fig. 2), i.e. the thermal stability of the conjugates increases in parallel with the increase in the degree of modification. The modification of the enzyme by PEO has the greatest stabilising effect (curve *6* in Fig. 2; the conjugate contains nine polymer chains), the specimen retains 80% of the initial activity after heating for 3 h at 45 °C.

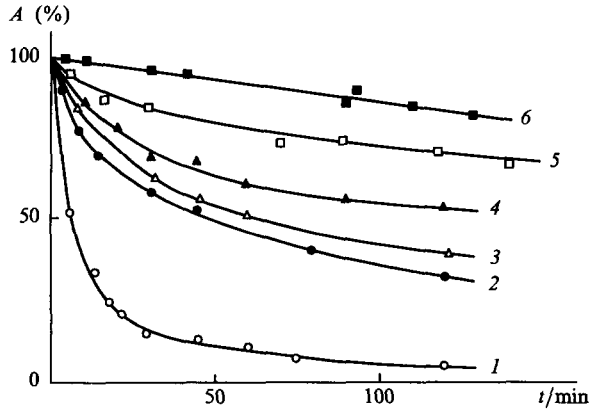


Figure 2. Kinetic curves for the thermal inactivation of CT and its conjugates with poly(alkylene oxides): (*1*) CT; (*2*) $(OPro)_3$–CT; (*3*) $(Pro)_3$–CT(nonun.); (*4*) $(Pro)_6$–CT(nonun.); (*5*) $(Pro)_5$–CT(un.); (*6*) $(PEO)_9$–CT. The thermal inactivation conditions here and in Figs 3 and 4 were as follows: 0.2 M tris.HCl, pH 8.0, 45 °C; the enzyme concentration in each specimen was 0.1 μM.

It was shown in a specially formulated experiment that simple addition of poly(alkylene oxides) to a solution of CT does not affect its thermal stability.

The difference between the shapes of the kinetic thermal inactivation curves for the CT–PEO conjugate (curve *6* in Fig. 2) and three conjugates with block-copolymers (curves *2*–*4*) is striking. In all cases, the curves were treated mathematically in terms of the variables of a first-order reaction. The kinetic data for the inactivation of the $(PEO)_9$–CT conjugate in terms of such variables can be described by a linear relation. The rate constant calculated from these data is $k = (2.3 \pm 0.1) \times 10^{-5}$ s^{-1}.

These relations for the remaining conjugates are represented by curves consisting of two or more regions with different shapes. The molecular causes of such heterogeneity in the case of native CT were discussed previously.[32] It is most likely that in the case of the conjugates this is also associated with their inhomogeneity as regards both structure and composition, which may be manifested both by a distribution with respect to the degrees of modification of different protein globules and by a nonuniform arrangement of the chains on the surface of an individual protein globule. Such inhomogeneity has a particularly notable effect on the properties of the $(OPro)_3$–CT(nonun.), $(Pro)_3$–CT(nonun.), and $(Pro)_6$–CT(nonun.) conjugates synthesised under conditions such that the polymeric reagents are in the micellar form, which promotes a nonuniform filling of the surface of the protein globule by the polymer (Fig. 1, *IIa*). On the other hand, the $(PEO)_9$–CT conjugate, containing polymer chains incapable of forming micellar structures,[33] should be characterised by a much more uniform distribution of the polymer chains. It may be that this is in fact one of the causes of the high thermal stability of the $(PEO)_9$–CT conjugate.

The thermal stability of the $(Pro)_5$–CT(un.) conjugate, synthesised under conditions which rule out the possibility of a micelle formation reaction between the molecules of the block-copolymers, approaches (curve *5* in Fig. 2) the thermal stability of the $(PEO)_9$–CT conjugate. This effect is particularly pronounced, since the degree of modification in the $(Pro)_5$–CT conjugate is smaller almost by a factor of two than in $(PEO)_9$–CT.

Thus the thermal stability of the conjugates increases in parallel with the increase in their content of polymer chains. For the same number of polymer chains, the thermal stability of conjugates with a uniform distribution of the chains is higher than that of the conjugates with a nonuniform distribution (curves *5* and *4* in Fig. 2). On the other hand, the stability of the conjugates in which the hydrophobic block is on the periphery is higher than that of the conjugates with the reverse order in the arrangement of the blocks. The results can be explained in terms of the ideas, being developed in the literature, according to which the modification of the protein surface by hydrophilic reagents should stabilise the protein molecule, since it makes it possible to shield the surface hydrophobic groups of the protein from unfavourable contact with water.[34,35] Indeed, as can be seen from Fig. 1 in the case of a nonuniform distribution of the polymer chains in the conjugate, a considerable proportion of the protein surface remains unprotected, whereas for a uniform distribution there is a greater possibility of the shielding of the protein globule. This in fact leads to an increase in the thermal stability of the conjugates with a uniform distribution of the chains compared with those having a nonuniform distribution.

6. Interaction of the conjugates with diphilic compounds

One of the remarkable properties of the conjugates of proteins with proxanols is their ability to interact with both synthetic and natural diphilic compounds.[17,36] The polymer chains then play the role of a reinforcing construction, organising around themselves assemblies of other diphilic compounds. In supramolecular structures of this kind, diphilic substances may have an indirect effect on the properties of the protein globule forming part of the composition of the conjugate. For example, we may quote the increase in the thermal stability of the conjugate following the introduction of the free proxanol (Fig. 3). This is apparently due to the binding of the polymer chains of the conjugate to the additionally introduced polymer with formation of a more compact polymer shell around the protein, which leads to the shielding of the hydrophobic domains on its surface.

Another picture is observed when β-CD, capable of forming clatrate complexes with proxanols, is introduced as a diphilic additive into the system. As shown previously, in the interaction with β-CD the polymer chains of the proxanols assume a more

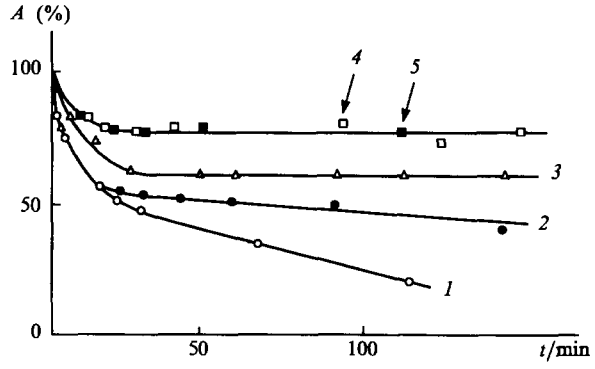


Figure 3. Kinetic curves for the thermal inactivation of the pure $(Pro)_4$–CT(un.) conjugate (curve *1*) and the conjugate with added Pro (curves *2*–*5*). Molar excess of Pro relative to the conjugate: (*2*) 50; (*3*) 100; (*4*) 500; (*5*) 750. For thermal inactivation conditions, see Fig. 2.

extended conformation.[37] Such chains are apparently no longer able to shield the hydrophobic sections of the protein and hence the thermal stability of the protein in the conjugate is somewhat reduced (Fig. 4), although it still remains higher than that of the native protein. It is noteworthy that β-CD affects only the thermal stability of the conjugates with a uniform distribution of the polymer chains on the protein surface (Fig. 1, *IIb*), but does not influence at all the thermal stability of the conjugates with a nonuniform distribution of the chains, with which it does not interact for the reasons stated previously.[16]

Thus the study of the thermal stability of the conjugates may constitute in many instances an extremely informative method, whereby complex formation reactions between the conjugates and diphilic substances may be discovered.

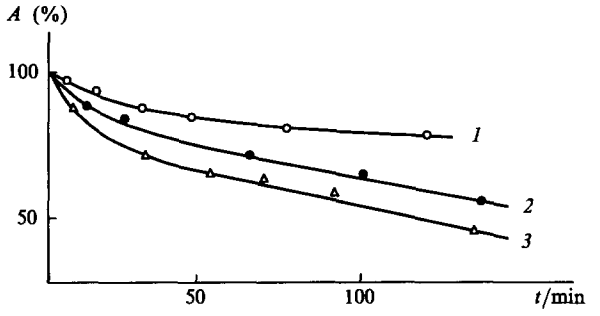


Figure 4. Kinetic curves for the thermal inactivation of the $(Pro)_3$–CT(un.) conjugate (curve *1*) and the same conjugate in the presence of β-CD (curve *2*) and egg lecithin (curve *3*) (Molar ratio conjugate : additive = 1 : 50). For thermal inactivation conditions, see Fig. 2.

III. Physicochemical properties of the conjugates

1. Differential scanning calorimetry

The data on the thermal stability of the conjugates obtained by the kinetic method have been supplemented by the results of the study of the thermal denaturation of the conjugates by differential scanning calorimetry (DSC). Fig. 5 presents heat absorption curves for aqueous solutions of CT and its conjugates. Evidently a significant alteration of the shape of the heat absorption peak is observed for the conjugates. Apart from the first maximum, located in the temperature range 47.6 – 49.6 °C as in the initial CT, a second maximum appears on the thermograms for the conjugates in the region of higher temperatures (54.5 – 55.5 °C), while for the $(OPro)_3$–CT and $(Pro)_7$–CT(un.) conjugates there is a shoulder in the same temperature range. Thus the appearance of an additional thermal transition is characteristic of all the conjugates. The most trivial explanation of this phenomenon is that the appearance of additional transitions is associated with the heterogeneity of the conjugates: the first maximum on the heat absorption curve corresponds to the fraction of the conjugate with a low degree of modification, while the second maximum corresponds to the fraction with a high degree of modification. However, this hypothesis conflicts with the DSC data for the conjugates with a higher degree of modification — $(Pro)_7$–CT(un.) (curve *6* in Fig. 5). As can be seen from the figure, there is only one maximum on the heat absorption curve for this conjugate (T_{max} = 51.2 °C) and there is a shoulder in the range 54.5 – 55.5 °C.

During the denaturation of the protein globule, the hydrophobic sections of the polypeptide chains are exposed to the solvent, becoming accessible to the hydrophobic units of the polymer chains entering into the composition of the conjugate. The appearance of a second maximum on the heat absorption curves for the conjugates is apparently due to the fusion of such a polymer – protein complex.

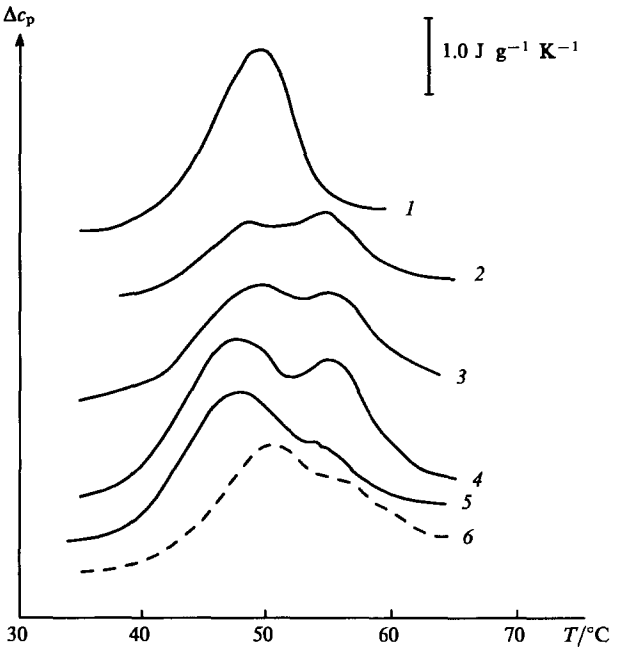


Figure 5. Heat absorption curves for CT (curve *1*) and its conjugates $(PEO)_3$–CT (curve *2*), $(Pro)_3$–CT(un.) (curve *3*), $(Pro)_3$–CT(nonun.) (curve *4*), $(OPro)_3$–CT (curve *5*), and $(Pro)_7$–CT(un.) (curve *6*). Buffer — 0.02 M sodium phosphate, pH 7.0; concentration of preparations 1 mg ml^{-1}; heating rate 1 K min^{-1} (c_p = heat capacity at constant pressure).

In order to demonstrate the validity of this hypothesis, additional studies were made. These confirmed the ability of proxanol to interact with CT at an elevated temperature. It was shown that:

1. During the scan heating from 20 to 60 °C (1 K per minute) of the solution of CT containing Pro (molar ratio 1 : 20), this protein does not aggregate.

2. Similar heating of a solution containing a mixture of CT and PEG leads to the aggregation of the enzyme similar to that occurring in the solution of CT under the same conditions.

3. The product of the interaction, obtained as a result of the heating of a mixture of CT with Pro to 60 °C and separated from the excess of the free proxanols, contains only 50% of the protein. According to ^1H NMR data, the remainder comprises the bound proxanol.

4. A peak whose maximum is close to the second maximum on the thermograms of the conjugate (T_{max} = 54.5 °C) is observed on the heat absorption curve for the solution containing a CT – Pro mixture.

The facts listed above show that the polymer – protein complex is formed at elevated temperatures. The complex has a fusion peak located in the same temperature range as the second maximum on the heat absorption curves for the conjugates.

Thus the DSC study of the conjugates showed that (a) the conjugates are thermally more stable than the initial protein, (b) that the thermal stability of the conjugates based on proxanol is comparable to that of the PEO – protein conjugates, and (c) that the appearance of the second maximum on the heat absorption curves for the conjugates is probably associated with the formation of intramolecular polymer – protein complexes.

2. Sedimentation of the conjugates

The hydrodynamic properties of the conjugates have been investigated by the high-speed sedimentation method. The sedimentation coefficients of the conjugates and the initial proteins are listed in Table 4, which shows that the modification of the proteins by polymers does not alter appreciably the sedimentation coefficient. This permits the conclusion that

Table 4. Sedimentation coefficients of proteins (s_{20}) and their conjugates with poly(ethylene oxide) and proxanols (T = 20 °C, 48 000 rev min^{-1}, 0.02 M phosphate buffer, pH 7.0).

Protein, conjugate	Concentration/mg ml^{-1}	s_{20}/Sv
BSA	1	4.3 ± 0.2
$(PEO)_{15}$–BSA	1	4.2 ± 0.2
$(Pro)_8$–BSA(nonun.)	1	4.5 ± 0.3
	2	4.0 ± 0.2
	4	4.0 ± 0.2
	6	4.2 ± 0.2
	10	4.6 ± 0.2
$(OPro)_6$–BSA	1	4.1 ± 0.2
CT	1	2.0 ± 0.15
	4	2.02 ± 0.15
	8	2.2 ± 0.17
	10	2.45 ± 0.12
$(Pro)_3$–CT(nonun.)	1	2.3 ± 0.1
	3	2.42 ± 0.15
	5	2.51 ± 0.16
	6	2.61 ± 0.21
	7	2.60 ± 0.18
$(Pro)_3$–CT(un.)	1	1.91 ± 0.13
	3	1.99 ± 0.15
	5	2.11 ± 0.08
	10	2.25 ± 0.13

solutions of the conjugates do not contain aggregates or products of intermolecular interaction in the experimental concentration range.

It might have been expected that, even in the absence of intermolecular interactions, the covalent attachment of polymer chains to the protein should have affected its sedimentation coefficient. The fact that significant changes in the sedimentation coefficients of the conjugates compared with those of the initial proteins were not observed apparently means that the increase in molecular mass in the modified protein is compensated by the flotation effect due to the polymer chain. It is noteworthy that the poly(alkylene oxides) used to modify the protein have a density close to that of water and they do not therefore undergo sedimentation in the ultracentrifuge.[38]

3. Hydrophobic chromatography

The hydrophobicity of the conjugates has been estimated with the aid of reversed-phase hydrophobic high-performance liquid chromatography (HPLC). Fig. 6 illustrates chromatograms of the native BBI and the $(Pro)_5$–BBI conjugate.[18] Evidently the retention volume of the conjugate is smaller than that of the native protein. This indicates its lower affinity for the hydrophobic carrier. The same trend has been observed also for the conjugates of CT with proxanol. At first sight, these results may appear surprising, since the modification by diphilic proxanols should impart an additional hydrophobicity to the protein. However, they can be accounted for by assuming that the hydrophobic blocks of the proxanol participate in intramolecular interaction with the hydrophobic region on the protein surface, whereas the hydrophilic blocks of the polymer occur mainly on the periphery of the conjugate.

4. Conformational models of the proxanol–protein conjugates

The entire set of data obtained with the aid of hydrophobic chromatography, sedimentation, and DSC indicate the existence of common features in the formation of the structures of the conjugates synthesised by the attachment of Pro to the protein.

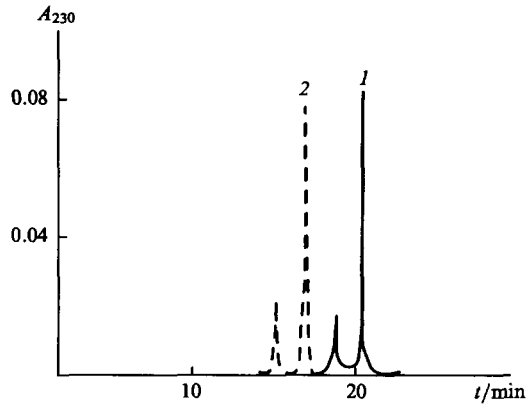


Figure 6. High performance liquid chromatography of native BBI (curve *1*) and of its conjugate $(Pro)_5$–BBI(nonun.) (curve *2*). The chromatography was carried out on a Zorbax C-8 column with 70% acetonitrile as the eluent; A_{230} = optical density at 230 nm.

These properties are manifested particularly strikingly for conjugates with a hydrophobic block on the periphery of the molecule (Fig. 1, structure *II*). The excess hydrophobicity introduced by the proxanols in such conjugates may be compensated either by the formation of intermolecular associated species or as a result of intramolecular interaction. Since associated species were not detected in dilute solutions of the conjugates, it is natural to postulate the formation of structures stabilised by intramolecular hydrophobic interactions. This hypothesis is confirmed by hydrophobic chromatographic data, indicating that the conjugates behave as substances which are more hydrophilic than the initial protein. Such structures are apparently constructed in the form of 'intramolecular micelles', in which the PPO blocks enter into the composition of the hydrophobic core, while the PEO blocks form part of the hydrophilic environment.

One can also postulate that the formation of such structures facilitates the complex formation reaction between the polymer chains of the proxanols and the protein occurring at elevated temperatures. It should be noted especially that the proposed structures have a definite conformational lability. This is manifested in the presence of hydrophobic or diphilic 'partners' such as lipids,[36] proxanol,[17] and cyclodextrins,[16] which are capable of interacting with the hydrophobic block of the polymer chains entering into the composition of the conjugates. There is probably in this case competition between the hydrophobic sections on the surface of the protein and the hydrophobic 'partners' for a chance to interact with the PPO block of the conjugate, as a result of which the 'intramolecular micelle' decomposes and mixed associated species or complexes are formed.

IV. Membranotropic properties of the conjugates

A fundamentally new property of the conjugates of proteins with proxanols is their ability to interact with biological membranes. Since the hydrophilic proteins forming part of their composition are not membranoactive, one can postulate that this property is due to the presence of the diphilic polymer chains of the proxanols. As shown previously, proxanols have the capacity to become incorporated in a biological membrane and to be translocated through it.[36]

In order to investigate the translocation of the conjugates through a biological membrane, use was made of the approach involving the study of the influence of these compounds on the rate of consumption of oxygen by liver mitochondria and the thymus lymphocytes.[12] It is known that the diphilic substances capable of being translocated through a cell membrane can

reach the NADH-dehydrogenase complex, located in the mitochondrion and responsible for cell respiration, and inhibit the NADH-dehydrogenase activity, which is manifested by a decrease in the rate of consumption of oxygen. When such experiments were carried out with the conjugates, it was found that some of them are capable of suppressing cell respiration of T-lymphocytes. This indicates their translocation to the cell. We investigated the dependence of the translocation of the conjugates on the nature of the attached chains and of their distribution relative to the protein globule.[13]

In order to elucidate the question of the influence of the nature of the arrangement of the hydrophilic and hydrophobic blocks in the proxanol chains in relation to the protein in the conjugate on its ability to suppress the respiration of T-lymphocytes, the effects of the type *II* and *III* conjugates based on CT and BSA were compared (Fig. 1): Fig. 7 shows that only type *II* conjugates, in which the hydrophobic block is on the periphery of the molecule, are able to suppress respiration in the lymphocytes. On the other hand, neither the PEO–protein conjugate, nor the conjugate with the hydrophilic block on the periphery of the molecule (type *III*), nor the initial CT affect respiration in the lymphocytes. The effectiveness of the influence of the type *II* conjugate on respiration is comparable to that of the pure proxanol. The concentrations which induce 50% suppression of the respiration were 9.8 ± 2.4 μg mol^{-1} for the proxanol and 30.0 ± 6.2 μg mol^{-1} for the conjugates (Table 5, A). Comparison of the corresponding concentrations of the free proxanol and the proxanol incorporated in the conjugates showed that they are similar (Table 5, B). Similar results were also obtained for the conjugates based on BSA and cytochrome *c*. This means that the capacity for translocation is determined by the polymer chains and depends little on the nature of the protein.

The conjugates of the three proteins investigated showed a similar effect also on respiration in isolated mitochondria (Table 5).

The dependence of the suppression of respiration on the number of polymer chains attached to the protein and needed to effect its translocation has been investigated in relation to the inhibiting effect of a number of CT conjugates with different contents of polymer chains. Fig. 8 shows that the suppression of cell respiration by the conjugates begins to be manifested to an appreciable extent in the presence of not less than three polymer chains per protein molecule.

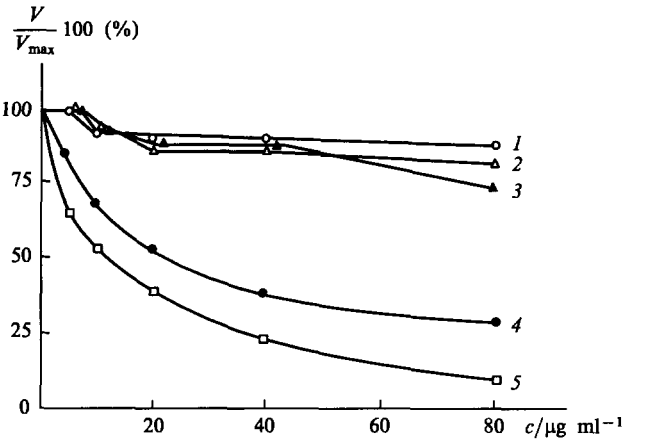


Figure 7. The influence of conjugates of proteins with various polymers on the rate of consumption of oxygen (V) by thymus lymphocytes: (*1*) initial CT; (*2*) $(PEO)_9$–CT; (*3*) $(OPro)_7$–CT; (*4*) $(Pro)_8$–BSA(nonun.); (*5*) $(Pro)_{10}$–CT(nonun.). The incubation medium for the lymphocytes contained (the concentrations are expressed as mM) NaCl (145), KCl (3.6), KH_2PO_4 (2), morpholinopropanesulfonic acid (8), and pyruvate (10); pH 7.4; T = 37 °C; the conjugates were added after oligomycin (0.2 μg ml^{-1}) and dinitrophenol (60 μM); in the control sample, the incubation medium was added instead of the conjugates to the lymphocytes; the concentration of lymphocytes in the cell was 10^8 cells in 1 ml.

Fig. 9 presents the results of a comparative study of the inhibiting effect of BSA-based conjugates, differing in the type of distribution of polymer chains on the surface of the protein globule, on the consumption of oxygen by T-lymphocytes. Evidently only the conjugates with a nonuniform distribution of chains cause a significant inhibition of respiration. CT conjugates with the corresponding structure exhibited the same effect.

As regards the mechanism of the action of conjugates on cell respiration, it is possible to examine several alternative versions: (1) the conjugates interact with the receptors located on the outer surface of the cell membrane and these receptors then transmit the signal to the cell; (2) the conjugates disrupt the cells; (3) the polymer chains are split off from the protein during the incubation of the conjugates with the lymphocytes and then

Table 5. The effectiveness of the suppression of the uncoupled respiration of lymphocytes and mitochondria by the Pro polymer and its conjugates with CT, cytochrome *c* (CYT), and BSA: $(Pro)_6$–CT(nonun.), $(Pro)_8$–CYT(nonun.), and $(Pro)_7$–BSA(nonun.).

Object of study	Pro	$(Pro)_6$–CT(nonun.)	$(Pro)_8$–CYT(nonun.)	$(Pro)_7$–BSA(nonun.)
	A. Concentration of Pro and the conjugates/μM (μg ml^{-1})			
Lymphocytes	4.9 ± 1.2 (9.8 ± 2.4)	0.66 ± 0.1 (30.6 ± 6.2)	1.1 ± 0.1 (33.0 ± 3.4)	0.75 ± 0.1 (61.0 ± 6.2)
Mitochondria	4.7 ± 1.2 (9.3 ± 2.4)	0.48 ± 0.06 (21.6 ± 4.7)	– –	– –
	B. Concentrations of free Pro and the Pro in the conjugates/μM			
Lymphocytes	4.9 ± 1.2	6.6 ± 1.9	3.3 ± 0.3	5.3 ± 0.5
Mitochondria	4.7 ± 1.2	4.8 ± 1.5	–	–

Remarks. The absorption of oxygen was recorded in the presence of 50–60 μM DNP, 4 mM glutamate, and 1 mM malate. The result was calculated as the arithmetical mean from 5–6 experiments. The table lists the concentrations of Pro and the conjugates inducing a 50% inhibition of the consumption of oxygen. The efficiencies of free Pro and the Pro in the conjugate are compared in Part B of the table.

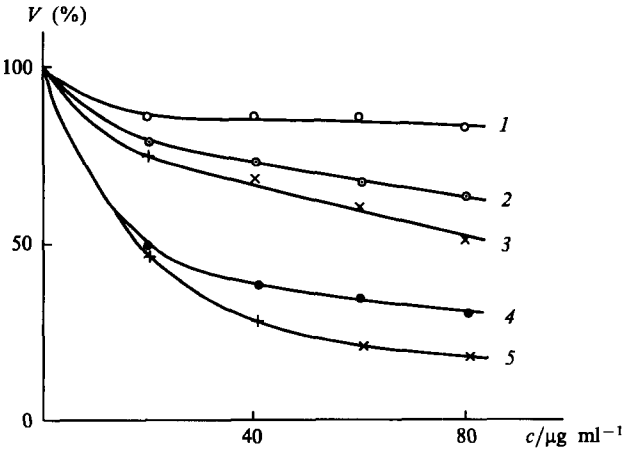


Figure 8. The influence of CT conjugates containing different numbers of Pro chains on the rate of consumption of oxygen by thymus lymphocytes: (*1*) $(Pro)_2$–CT(nonun.); (*2*) $(Pro)_3$–CT(nonun.); (*3*) $(Pro)_6$–CT(nonun.); (*4*) $(Pro)_{10}$–CT(nonun.); (*5*) $(Pro)_{15}$–CT(nonun.). For the experimental conditions, see Fig. 7.

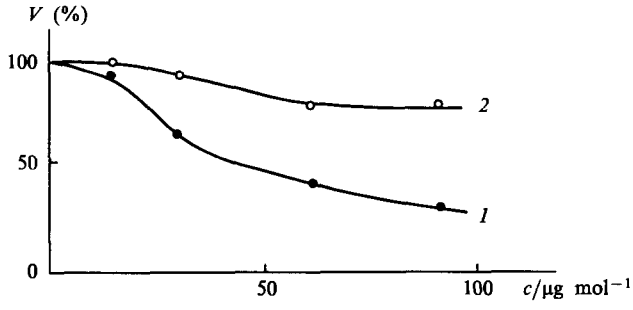


Figure 9. The influence of conjugates of BSA with a nonuniform (curve *1*) and uniform (curve *2*) arrangement of the Pro chains on the rate of consumption of oxygen by thymus lymphocytes: (*1*) $(Pro)_8$–BSA(nonun.); (*2*) $(Pro)_{15}$–BSA(un.). For the experimental conditions, see Fig. 7.

permeate through the cell membrane; (4) the conjugates permeate through the plasma membrane into the cell and reach the mitochondrial membranes.

The first hypothesis conflicts with the fact that the conjugates at virtually identical concentrations inhibit the separate respiration of both the cell as a whole and of an isolated mitochondrion. The substances capable of affecting the respiration of lymphocytes by interacting with the receptors on the outer surface of the plasma membranes, in particular with concanavalin A, increase the rate of their respiration only by 20% and do not affect the respiration of isolated mitochondria.[39]

It has been shown in special experiments that inhibition of the respiration of lymphocytes by proxanols and their conjugates is a reversible process and that it is fully restored after the cells have been washed. Consequently the inhibiting effects are not associated with the breakdown of the integrity of the plasma membranes of T-lymphocytes.

The separation of the polymer chains from the protein is also hardly likely to be the cause of the membrane activity of the conjugates. Indeed, on the basis of the idea that the $NH-CH_2$ bonds formed during the synthesis of the conjugate are hydrolytically stable and that their susceptibility to the action of hydrolytic enzymes is low, such separation appears fairly improbable. Nevertheless, in order to be able to reach the final conclusion that the polymer chains are not split off during the incubation of the conjugate with T-lymphocytes, an additional biological test of the ability of cells to cleave the conjugates has been carried out.[13] It confirmed with a high degree of reliability the absence of free proxanols in the supernatant after the separation of the cells. Thus one may conclude that the influence of the conjugates on the respiration of T-lymphocytes is the result of their permeation through the plasma membranes into the interior of the cells. Hydrophilic substances such as the proteins used to synthesise the conjugates are known to be incapable of permeating into the cells directly through the cell membranes. However, the same proteins acquire the capacity for translocation as a result of their being rendered hydrophobic by aliphatic acids.[40] The results permit the hypothesis that the modification of proteins by synthetic polymers (proxanols), capable of permeating through the cell membrane,[12] acts similarly to the addition of aliphatic acids. It must be emphasised that the necessary conditions for the translocation of such conjugates are the location of the hydrophobic blocks on the periphery of the conjugate molecule and also a nonuniform distribution of the polymer chains (Fig. 1, structure *IIa*). The type *IIb* and *III* conjugates of proteins with proxanols and the conjugates with PEO do not affect the respiration of cells. In certain cases, the PEO–protein conjugates may permeate into the cells via the endocytosis mechanism,[41] but the rate of this process is several orders of magnitude lower than that of the diffusion of the conjugate with membranotropic properties. Furthermore, endocytosis cannot occur in mitochondria.

Thus it has been shown that the covalent attachment of proxanols to hydrophilic proteins can serve as a method of imparting membranotropic properties to the latter.

V. Solubilising properties of the conjugates

1. The solubilisation of benzaflavin by conjugates of BSA with poly(alkylene oxides)

One of the important functions of serum albumins is their ability to transport nonpolar compounds of different chemical nature—aliphatic acids, hormones, and vitamins.[42] Bearing in mind the diphilic properties of proxanols described above, it might have been expected that their attachment to serum albumins would permit the creation of systems with an enhanced solubilising capacity in relation to water-insoluble biologically active substances. Such compounds include a dihydroriboflavin ester—5-acetyl-2′,3′,4′,5′-tetrabenzoyl-1,5-dihydroriboflavin [benzaflavin (BF)]. Dihydroriboflavin esters have a broad spectrum of biological activity and are of interest not only as long-acting vitamin B_2 preparations but also as medicinal drugs for metabolic therapy.[43]

The solubilisation of BF in aqueous solutions of BSA and its conjugates with poly(alkylene oxides) has been observed by UV spectroscopy at a wavelength of 306 nm, which corresponds to the BF absorption maximum. The extinction coefficients of the solubilised BF in a solution of pure BSA and of the $(PEO)_{14}$–BSA and $(Pro)_5$–BSA(nonun.) conjugates were determined from the dependence of the optical density on the concentration of the solubilised BF.

Protein, conjugate	BSA	$(PEO)_{14}$–BSA	$(Pro)_5$–BSA(nonun.)
10^{-3} ε/litre mol^{-1} cm^{-1}	4.9	4.7	3.5

The solubilisation limit (p), equal to the number of molecules of the solubilised substance per molecule of the solubilising agent, was determined by high-speed sedimentation in an analytical ultracentrifuge with an optical recording system. The use of the sedimentation method was based on the fact that the bound BF undergoes sedimentation together with the protein or the

conjugate.[13] The fact that the absorption by BF corresponds to a longer-wavelength part of the spectrum compared with BSA and the conjugates makes it possible to select a wavelength where only the bound ligand absorbs and its concentration can be determined.

In order to compare the solubilising capacities of BSA and the conjugates, a series of experiments were carried out in which the BF concentration was varied for a constant content of the protein or the conjugate. It is seen from the results that BSA has an appreciable solubilising capacity in relation to BF (Table 6). It was demonstrated by special experiments that proxanols do not solubilise BF. On the other hand, in all the systems containing the conjugates, the BF solubilisation limit proved to be higher than for BSA, the highest value corresponding to the $(Pro)_5$–BSA(nonun.) conjugate, in which the hydrophobic blocks are located on the periphery of the conjugate.

An increase in the number of polymer chains per protein molecule in the conjugate leads to a decrease in the solubilisation limit. This apparently occurs owing to the greater shielding of the regions responsible for the solubilisation of BF. Two procedures for the solubilisation of BF were used in the above investigation — by suspending BF and by introducing it into the above systems from an alcohol solution. The second procedure makes it possible to include a greater amount of BF, probably for kinetic reasons. The study by the nonelastic light scattering method of the system obtained by both procedures showed that, together with the particles whose size corresponded to the conjugate present in the system (less than 30 nm), larger particles with radii from 200 to 3000 nm (possibly BF aggregates) were observed when BF was introduced from an alcoholic solution. On solubilisation by the suspension method, only particles with radii less than 30 nm are formed.

In order to obtain systems with the optimum BF content, a study was made of the dependence of the solubilising capacities of BSA and the $(Pro)_5$–BSA(nonun.) conjugate on the pH of the medium (Fig. 10). The figure shows that the dependence is bell-shaped. The maximum solubilisation is observed in the pH range 7.6–9.0. Study of the dependence of the solubilisation limits on the phosphate buffer concentration (pH 6.2 and 7.2) showed that an increase in the buffer concentration impairs the solubilising

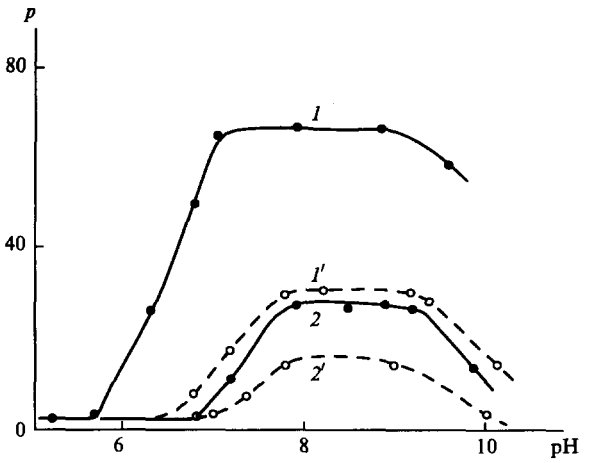


Figure 10. Dependence of the BF solubilisation limit on the pH of the medium: (*1*) visual method; (*2*) sedimentation method; BSA — dashed line; $(Pro)_5$–BSA(nonun.) conjugate — continuous lines.

capacities of both the protein and the conjugate. Thus, the attainment of the maximum solubilising effect requires the use of solutions in the pH range 7.6–9.0 at the lowest ionic strength.

Experiments in which the solubilisation of BF in solutions of BSA and the conjugates was investigated at an elevated temperature (40 °C) made it possible to observe an appreciable heterogeneity of such systems in contrast to the systems containing the pure solubilising agent (Table 6). A definite fraction of the substance undergoing sedimentation in such systems is characterised by a sedimentation coefficient exceeding by a factor of approximately two the corresponding sedimentation coefficients of the protein and the conjugates. It may be that the BF in such systems promotes the formation of 'bridges' between the protein molecules.

The results suggest that the BF molecules in the conjugates investigated are localised in the hydrophobic regions of the BSA

Table 6. The solubilising properties of BSA and its conjugates with poly(alkylene oxides) in relation to BF (0.02 M phosphate buffer, pH 7.2; the BF was introduced from alcoholic solution).

Solubilising agent	T/°C	p	s_{20}/Sv (solubilising agent)	s_{20}/Sv (complex with BF)	Fractions of different forms (%)
BSA	20	17	4.2	6.3	100
	40	17	6.7	11.0	47
				6.2	53
$(Pro)_5$–BSA(nonun.)	20	40	4.4	10.1	100
	40	40	6.8	14.2	21
				7.3	79
$(OPro)_{11}$–BSA	20	19	4.2	6.8	100
	40	19	6.6	13.2	47
				5.9	53
$(PEG)_{14}$–BSA	20	21	4.2	6.6	100
	40	21	6.5	10.5	49
				6.8	51
$(Pro)_{100}$–BSA[a]	20	18	2.9	6.2	100
	40	18	5.8	12.0	80
				6.6	20

[a] The solubilising agent was obtained from the conjugate $(Pro)_5$–BSA(nonun.) by adding free proxanol.

protein globule. This is also confirmed by the finding that the attachment of proxanol to other proteins, for example to class G immunoglobulins or to CT, which are unable to bind this ligand, has no effect on their solubilising properties.

2. The transfer of benzaflavin into mitochondria with the aid of BSA conjugates

The data presented in this Section presuppose the possibility of using the conjugates of proteins with poly(alkylene oxides) as agents transporting water-insoluble biologically active substances into the target cells. In order to test this hypothesis, a study was made of the transfer of benzaflavin into rat heart mitochondria.[15] This phenomenon was observed by studying the relation between the amount of BF bound by the mitochondria and the amount of BF present in solution in the solubilised form. The amount of BF bound by the mitochondria was determined from the difference between the total content of BF in solution and its content in the supernatant after incubation with the mitochondria. This quantity reaches a maximum after 1 min and remains constant on further incubation with the mitochondria.

It was observed that the BF solubilised by BSA and its conjugates with PEO and Pro is capable of being transported into the mitochondrial membranes. Quantitative data on the transfer of BF are presented by the binding isotherms in Fig. 11. In the BF concentration range investigated (up to 8×10^{-4} M), the dependences of the amount of bound BF on the concentration of free BF are linear:

$$\frac{[BF]_{bound}}{[MC]} = K[BF]_{free}, \quad (3)$$

where K is the proportionality coefficient, which depends on the nature of the solubilising agent, and [MC] is the concentration of the mitochondrial protein. The linearity of these relations showed that the experimental data correspond to the initial sections of the binding isotherms. It is important to emphasise that the experimental points obtained for different concentrations of the solubilising agent lie on the same isotherm characteristic of the given solubilising agent. Thus the proportionality coefficient in Eqn (3) is independent of the concentration of the solubilising agent.

It is of interest that BSA and its conjugate with PEO proved to have identical capacities to transport BF. Both solubilising agents may be characterised by the same proportionality coefficient $K = 0.31 \pm 0.01$ litre (g of mitochondrial protein)$^{-1}$. For the conjugate of BSA with proxanol, $K = 0.96 \pm 0.01$ litre (g of mito-chondrial protein)$^{-1}$. The higher capacity of the BSA–proxanol conjugate to transport BF can apparently be explained by the formation of a weaker complex between BF and this conjugate than the complex between BSA and its conjugate with PEO.

Thus the BSA–proxanol conjugates have definite advantages over other systems investigated as regards both their solubilising and transport capacities, which creates preconditions for their employment in the development of new medicinal preparations.

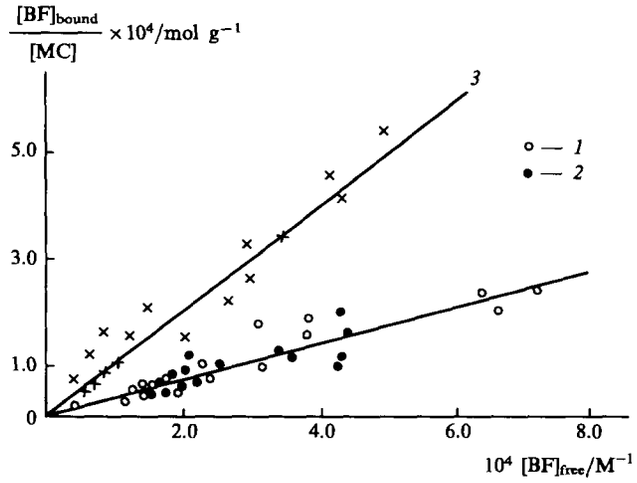


Figure 11. Dependence of the amount of bound BF [in moles per gram of the mitochondrial protein (MC)] on the concentration of free BF. Solubilising agent: (*1*) BSA; (*2*) $(PEO)_{14}$–BSA; (*3*) $(Pro)_5$–BSA(nonun.).

VI. Noncovalent complexes between α-chymotrypsin and the block-copolymer of ethylene and propylene oxides

The complex formation reactions between proteins and water-soluble proteins constitute one of the effective methods in protein engineering. Thus many synthetic linear polyelectrolytes form complexes with proteins.[44,45] Protein molecules are bound to polyions by electrostatic interaction, which may be accompanied by the formation of hydrogen bonds and hydrophobic contacts. In contrast to this, water-soluble polymers which contain no ionogenic group, for example PEO, do not form complexes with proteins.[46] When solutions of BSA or CT are mixed with solutions of proxanols at room temperature, complexes are not produced either.[21]

As mentioned above, we demonstrated in relation to CT that stable protein–proxanol complexes can nevertheless be obtained when their solutions are heated to temperatures corresponding to the onset of the thermal denaturation of the protein (this problem has been examined in greater detail elsewhere[46]).

The first results indicating the formation of mixed CT–Pro particles were obtained with the aid of a visual method for the observation of the turbidity of solutions of a protein and poly(alkylene oxide). The formation of such particles is also indicated by data obtained by the DSC method for aqueous solutions of CT, CT–PEG, and CT–Pro. Fig. 12 presents thermograms for the fusion of CT (curve *1*), CT in the presence of PEO (curve *2*), and CT in the presence of Pro (curve *3*). Evidently PEO does not affect the fusion of the protein globules: the fusion curves *1* and *2* virtually coincide (the heat of fusion is 1090 kJ mol^{-1} in the former case and 1080 kJ mol^{-1} in the latter). In contrast to this, in the presence of Pro, a shift of the fusion peak towards higher temperatures and an increase of its height (the heat of fusion is

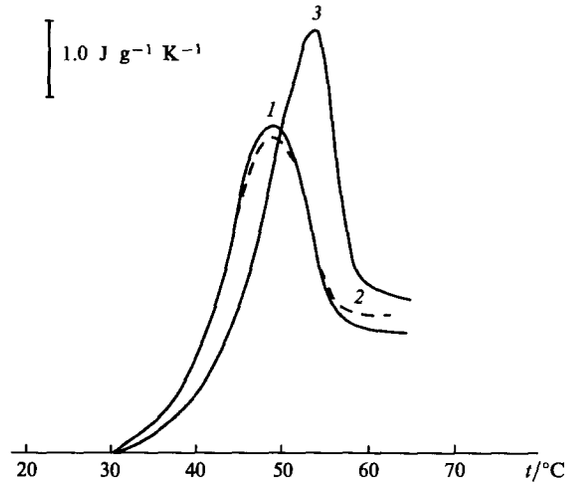


Figure 12. Heat absorption curves for CT (concentration 2 mg ml^{-1}, curve *1*), for a mixture of CT and PEO (2 mg mol^{-1} and 0.48 mg ml^{-1}, curve *2*), and for a mixture of CT and Pro (2 mg ml^{-1} and 0.48 mg ml^{-1}, curve *3*). Buffer—0.02 M sodium phosphate, pH 7.0; heating rate 1 K min^{-1}.

Table 7. Characteristics of the CT–Pro complexes (heating rate 1 K min^{-1}, initial temperature of the solution 20 °C, incubation time in the thermostat before the attainment of the upper limit in the heating process 5 min).

Complex	Preparation conditions		Content of polymer in complex/mol (mol of CT)$^{-1}$	Activity (% of initial protein)		Content of active centres (%)	10^5 K_m/M[a]	k_{cat}/s^{-1}
	upper limit in heating process/°C	CT:Pro molar ratio		before isolation	after isolation			
CT–$(Pro)_{3.5}$	44	1:2.5	3.5	–	50	–	–	–
CT–$(Pro)_5$	44	1:10	5	82	120	–	–	–
CT–$(Pro)_5$	44	1:20	5	87	125	82	7.1+0.8	25+3
CT–$(Pro)_5$[b]	44	1:20	5	76	118	83	9.5+0.7	27+1
CT–$(Pro)_6$	48	1:20	6	50	97	74	13.2+0.8	30+2
CT–$(Pro)_7$	48	1:20	7	45	92	57	16.7+0.8	32+2
CT–$(Pro)_{10}$[b]	48	1:20	10	34	79	–	–	–
CT–$(Pro)_{10}$	52	1:20	10	22	74	32	13.9+0.6	48+4
CT–$(Pro)_{13}$	52	1:20	13	26	51	14	18+2	166+19
CT–$(Pro)_{11}$	60	1:20	11	0	0	–	–	–
Native CT		0	–	100		92	5.6+0.4	24+2

[a]The kinetic constants were obtained by studying the enzymic hydrolysis of BTEE (pH 8.0; 25 °C). The errors were determined with a fiducial probability of 0.95.

[b]The complexes were cooled and isolated immediately after the attainment of the upper temperature limit of the heating process without subsequent incubation in a thermostat.

1250 kJ mol^{-1}) are observed. Hence it follows that during heating the CT and Pro are bound to one another in some way, giving rise to a new product, in which the protein component acquires a somewhat higher thermal stability. The thermally induced binding of CT and Pro is irreversible under the experimental conditions. After such solutions have been cooled, the mixed reaction product is preserved in them, which is indicated by the determinations of the protein content in the products isolated (Table 7) (the method of isolation of these products from the reaction mixture ensured the complete removal of the excess free polymer, which was checked by thin-layer chromatography.)

The question of the nature of the interactions between Pro and the protein is of fundamental importance. The hypothesis of the formation of a noncovalent complex is most natural. In order to determine the nature of the bonds between Pro and CT, we studied the dissociation of the complexes in the presence of urea by thin-layer chromatography (TLC). The method is based on the difference between the chromatographic mobilities of the dissociation products and the initial complex. The rate of dissociation of the complexes in aqueous solutions is low and the dissociation becomes appreciable only after 24 h. The process accelerates significantly in the presence of 8 M urea. These data show that the reaction products are noncovalent complexes between CT and Pro.

On the basis of ideas concerning the complex formation process, one may postulate that the composition of the complexes may be regulated in two ways: by varying the polymer/CT ratio at a fixed heating temperature and by varying the heating temperature for a fixed reactant ratio. Indeed, Table 7 shows that, for a fixed excess of Pro in the system, the number of polymer chains entering into the composition of the complex increases in parallel with the increase in the maximum heating temperature. For example, in the system with a 20-fold molar excess of Pro, the number of polymer chains entering into the composition of the complex increases from 5 to 11 when the upper temperature limit of the heating process rises from 44 to 60 °C. The same tendency towards an increase in the number of polymer chains in the complex is observed also with increase in the molar excess of the polymeric component for a fixed upper temperature limit of the heating process.

We may note that the protein fraction isolated from a mixture of CT and PEG after heating to 60 °C represents the pure protein, which indicates the absence of interaction between the components. This conclusion agrees well with the results of differential scanning calorimetry.

Fig. 13 presents the ^{1}H NMR spectra of pure CT and two of its complexes with Pro obtained by heating to 44 and 48 °C respectively. Evidently, with increase in the temperature of the formation of the complexes, the denaturation changes in the protein become more appreciable, although a complete breakdown of the native structure is not observed. On the other hand, the positions and width of the signals due to the polymeric component of the complex indicate a fairly high molecular mobility of the majority of the units of the polymer chains in the complex.

A notable feature of the complexes is that they retain enzyme properties. It was of interest to elucidate how the specific enzyme activity of the complexes depends on the conditions of their preparation and isolation. Table 7 presents data on the enzyme activity of the complexes directly after the completion of the heating process but before their isolation from the reaction mixture. They reflect the properties of the complexes closest to those at the instant of their formation. The enzyme activity of the complex was measured also after their isolation from the reaction mixture. Comparison of the activities of the complexes before and after their isolation shows that the activity of the isolated complexes was higher for all the systems investigated. It may be that this is associated with the fact that the molecules of the free Pro, present in excess, form micellar structures incorporating CT. As a result of this, the active centre of the enzyme becomes less accessible to the substrate. During the isolation of the complex from the solution, the micellar structures are disrupted, which leads to a greater accessibility of the enzyme active centre to the substrate. It is important to note that in certain cases an increase in the enzyme activity of the isolated complexes compared with the initial CT was actually observed. Similar superactivity phenomena had been observed earlier in a study of the enzymic hydrolysis of the ethyl ester of *N*-acetyl-L-tyrosine catalysed by CT in inverted micelles.[48–50]

It was therefore of interest to determine the kinetic constants for the hydrolysis of BTEE catalysed by the complexes and to compare them with the corresponding constants for the initial CT. The contents of the active centres in the complexes were determined simultaneously. The corresponding data are presented in Table 7. Evidently, with increase in the upper

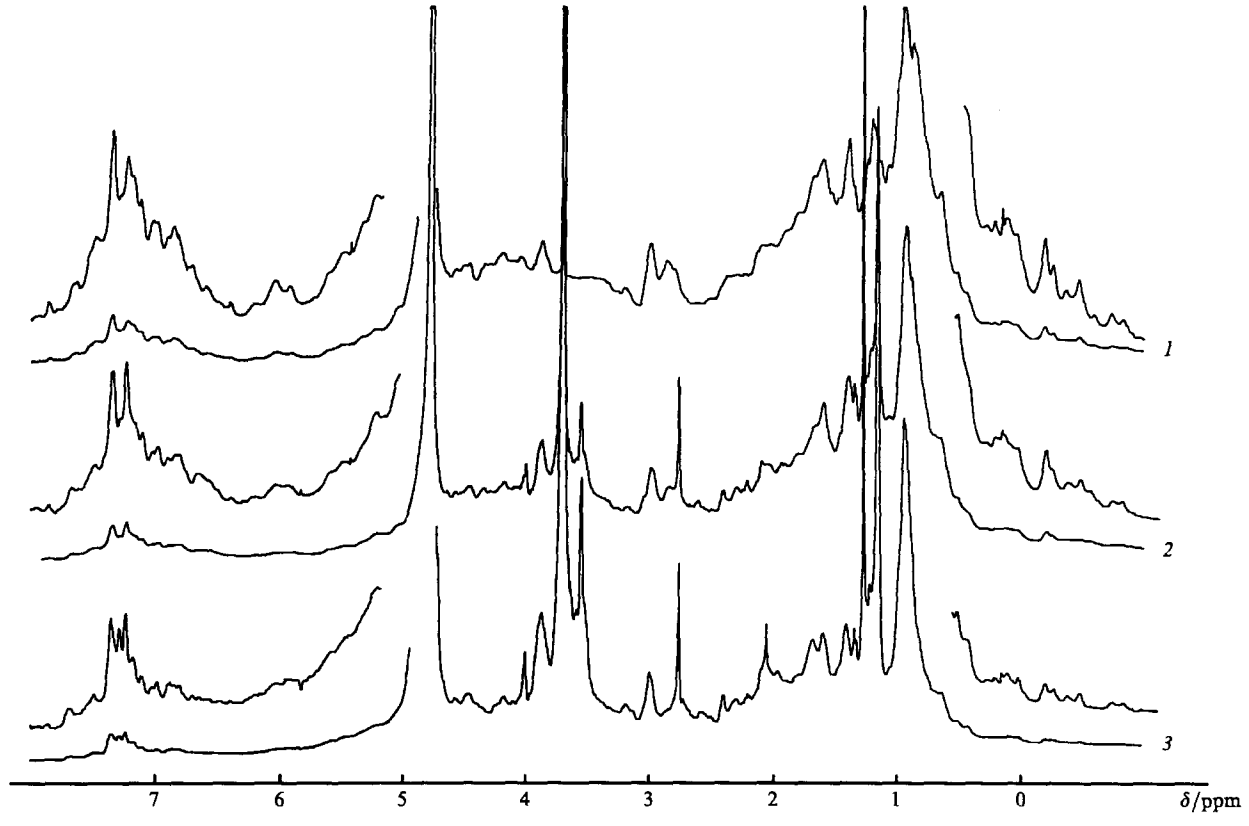


Figure 13. ^{1}H NMR spectra of solutions of CT (curve *1*), the CT–$(Pro)_5$ complex obtained by heating to 44 °C (curve *2*), and the CT–$(Pro)_7$ complex obtained by heating to 48 °C (curve *3*) in D_2O; concentration of protein in the specimen 2 mg ml^{-1}.

temperature limit in the heating of a mixture of CT and Pro and also in the incubation time for a fixed temperature limit in the heating process, the content of the active centres in the complex diminishes. The values of K_m increase steadily in the same sequence, which indicates a decrease in the affinity between the complex and the substrate. On the other hand, the increase in k_{cat} for the same series of catalysts indicates an increase in the catalytic effectiveness of the CT active centres entering into the composition of the complex.

On the basis of the overall results obtained, the mechanism of the formation of complexes between Pro and CT can be represented as follows. On heating, the protein globule uncoils, as a result of which the hydrophobic aminoacid residues appear on the surface of the protein. This is accompanied by the simultaneous dehydration of the hydrophobic Pro blocks, which promote the formation of compatible polymer–protein structures. During cooling and during the isolation of the complex from solution, sections of the hydrophobic Pro block are fixed near the protein globule via a multipoint interaction with the hydrophobic and polar groups located on the surface of the protein. The fact that the dissociation of the complex intensifies in the presence of a denaturing agent (urea) does not rule out the possibility that, together with the hydrophobic interactions, hydrogen bonds between Pro and the protein globule make a significant contribution to the stabilisation of the complex.

Thus the thermally induced interaction of Pro with CT leads to the formation of a new type of supermolecular structure—stable catalytically active complexes. The simplicity of the method of preparation of such structures and the retention of functional properties by the latter makes it possible to regard this procedure for the modification of proteins as one of promising methods in protein engineering.

VII. Conclusion

The methods developed for the preparation of conjugates of proteins and proxanols make it possible not only to vary within wide limits the structures and physicochemical properties of the products but also to simulate with their aid the biological functions of membranotropic proteins. The properties of the conjugates described above permit their use in enzyme therapy, in the creation of new therapeutic agents, and in the manufacture of biocatalysts for biotechnology soluble in organic media. Furthermore, these compounds may find applications in biochemical studies on water-insoluble biologically active compounds. The proposed alternative method for the modification of proteins by proxanols, based on the formation of nonvalence complexes between them, constitutes a new approach to the preparation of proteins modified by polymers. The set of covalent and noncovalent methods for the modification of proteins leads to extensive possibilities for the preparation of polymer–protein adducts with specified properties.

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Silicon nitride: synthesis and properties

R A Andrievskii¶

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Abstract. Methods of preparing silicon nitride and silicon nitride materials as powders and as materials consolidated from the powders, and also as films and coatings, are reviewed. Information on the structure and on the physicochemical properties of silicon nitride materials is analysed and discussed. The bibliography includes 172 references.

I. Introduction

The synthesis of silicon nitride by heating elemental silicon in an atmosphere of nitrogen generated by the decomposition of potassium cyanide was first reported by Balmen in the middle of the last century.[1] Thus, though first synthesised about 150 years ago, silicon nitride (like silicon carbide) has played a leading role among all known refractory compounds (judging by the number of publications, seminars, conferences, etc.) only during the last two decades. The most 'productive' period was the autumn of 1993, when a symposium on silicon ceramics was held in Tokyo in September, the conference 'Silicon nitride 93' was held in Stuttgart in October, and a symposium on silicon ceramics as construction materials was held in Hawaii in November, in spite of the authoritative symposia held in December 1992 and in April 1993 respectively, in the USA, by the Materials Research Society and by the Ceramics Society, aimed at the scientific and the technological aspects of silicon nitride materials. This sustained interest is not fortuitous: it can be attributed to at least two factors. Firstly, to the remarkable properties of silicon nitride (high hardness, good tribological and elastic characteristics, low density, adequate mechanical and thermal stability, inertness towards many aggressive media, unique electrical properties, and readily available starting materials). Secondly, it is stimulated by the relative complexity of silicon nitride as the object of physicochemical research and technological development.

† The author is also known as R A Andrievski. The name used here is a transliteration under the BSI/ANSI scheme adopted by this journal.

R A Andrievskii Institute of New Chemical Problems, Russian Academy of Sciences, 142432 Chernogolovka, Moscow Region. Fax (7-095) 292 65 11, Box 112 46. E-mail: ara@incp.ac.ru

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Whereas the first of these factors accounts for the wide range of possible applications of this compound (in structural, cutting tool, and tribotechnical materials, and also in materials with special physical and physicochemical properties), and therefore for the interest shown by specialists in different disciplines, the second factor explains the need for comprehensive investigations.

One of the most notable contributions was made in the 1950–1970s by Samsonov, who reported a comprehensive study of refractory compounds in general and silicon nitride in particular.[1,2] Monographs so far published on this topic are few,[3–5] and deal with aspects which are now obsolete: the more recent information is to be found in journals and in relatively obscure symposia.[6–9] The latest reviews[10–12] deal with specific aspects, and do not consider the overall problem. It should be noted that the chemical and physicochemical aspects are among the most important in the development of modern silicon nitride materials, and that their relevance is increasing continuously.

The aim of the present review is to discuss and generalise as fully as possible the most recent data on the synthesis and properties of silicon nitride in the form of powders and materials made from the powders, and also in the form of films.

II. Powders and their consolidation

1. Synthesis and thermal dissociation

Si_3N_4 powders can be prepared by many of the standard powder technology methods: direct synthesis in its numerous variants, carbothermic reduction, gas–phase synthesis and dissociation reactions, and mechanical comminution as an additional treatment. These methods are listed in Table 1 with some of their modifications.

The main methods of preparing Si_3N_4 powders used recently have relied on mechanosynthesis, now widely used in the preparation of powders of many refractory compounds and intermetallics.[13–15] It has been shown[16] that the use of ammonia during the milling of silicon is much more effective than the use of nitrogen. The hydrogen formed during the dissociation of ammonia reacts with oxygen impurities in the atmosphere and decreases the probability of forming oxynitride surface films, which suppress the nitridation of the silicon particles. Intensive milling of silicon in ammonia for 150 h, followed by vacuum treatment at 800 °C (τ = 8 h), produces α-Si_3N_4, but the product contains 14.22 at.% of oxygen, 1.28 at.% of iron, and 1.99 at.% of titanium. This result is undoubtedly encouraging, but it also makes clear the need for further optimisation of the regimes adopted in the preparation of Si_3N_4 by the mechanosynthesis method.

Table 1. Main methods of synthesis of silicon nitride powders and their variants.

Method	Main reactions	Main variants of the method
Direct synthesis of components	$3Si+2N_2 \rightarrow Si_3N_4$ $3Si+4NH_3 \rightarrow$ $\rightarrow Si_3N_4+6H_2$	Self-propagating high-temperature synthesis (SHS). Plasmachemical synthesis. Mechanosynthesis
Carbothermic reduction	$3SiO_2+6C+2N_2 \rightarrow$ $\rightarrow Si_3N_4+6CO$	–
Gas-phase synthesis	$3SiCl_4+16NH_3 \rightarrow$ $\rightarrow Si_3N_4+12NH_4Cl$ $3SiH_4+4NH_3 \rightarrow$ $\rightarrow Si_3N_4+12H_2$	Plasmachemical synthesis. Laser synthesis
Dissociation (pyrolysis)	$3Si(NH)_2 \rightarrow$ $\rightarrow Si_3N_4+2NH_3$ $(1/n)[SiR_2-NR]_n \rightarrow$ $\rightarrow Si_3N_4+RH+H_2$	Laser induced
Milling	–	–

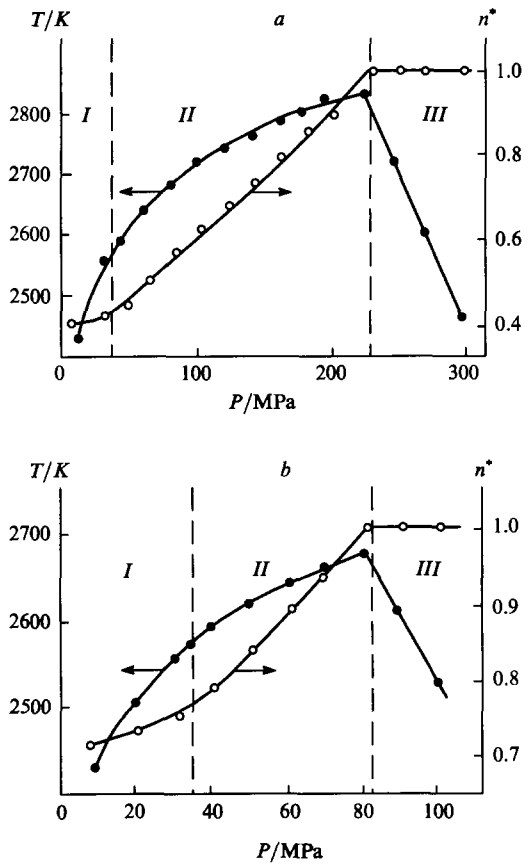


Figure 1. Effect of the nitrogen pressure on the adiabatic combustion temperature and on the extent of reaction of the silicon (n^*). (*a*) Si; (*b*) $Si:Si_3N_4 = 50:50$. Calculated for an assumed porosity of 65%. *I*–*III* see text.

The kinetics of the interaction of silicon with nitrogen are strongly influenced by the density of defects in the initial powders, as shown by X-ray structural analysis and by ESR and IR spectroscopy methods applied during the milling of silicon.[17] The mechanism of the reaction of silicon with nitrogen has been analysed in detail also by earlier workers,[4,10] and we shall not dwell upon it further here.

Detailed studies of the interaction of silicon with nitrogen during the self-propagating high-temperature synthesis (SHS) of the compound[18–21] have been reported. Fig. 1 shows the dependence on the nitrogen pressure of the calculated adiabatic combustion temperature of silicon and of the extent of reaction. The effect of diluting the initial silicon with silicon nitride, which lowers the nitrogen pressure and the combustion temperature, is also shown. Three regions of the reaction have been defined:[21] in the first (*I*) the rate of combustion is limited by the transport of nitrogen, in the second (*II*) the reaction is controlled by the high-temperature dissociation of the silicon nitride, and in the third region (*III*) rate limitation is provided by the reaction kinetics. In the latter region complete conversion of the silicon into the nitride is observed at the front of the combustion wave ($n^* = 1$).

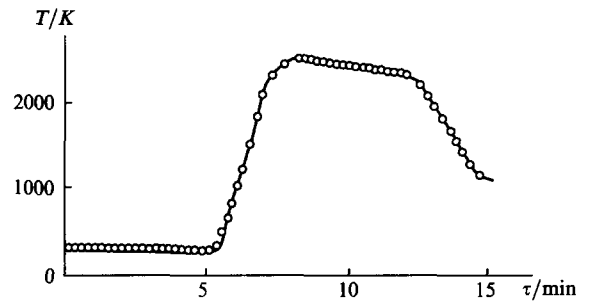


Figure 2. Typical thermogram for the combustion of a mixture of $Si:Si_3N_4 = 50:50$ in nitrogen at a pressure of 50 MPa (porosity 65%).[21]

On the whole these calculations are confirmed by experiment. Fig. 2 shows one of the thermograms obtained in the combustion of silicon (50 mass%) + Si_3N_4 (50 mass%) in nitrogen under a pressure of 50 MPa. The maximum combustion temperature recorded in these experiments (~2500 K) differs by approximately 100–150 K from the calculated values: in view of the approximate nature of the calculations this result can be accepted as fully satisfactory. However, at other temperatures the agreement between the experimental and the theoretical results was not so good.

One of the advantages of the silicon nitride powders prepared by the SHS method is their relatively low oxygen content (0.4%–0.6%).[22] This is due to the use of pure starting materials (semiconductor-grade silicon and thoroughly purified nitrogen). Commercial-grade powders prepared by the SHS method have a much higher content of impurities (for example, their oxygen content is between 1.5% and 2%). Some recent papers[23–25] describe their technological and other properties.

The favourable economic indicators of the SHS method have been discussed by Golubjatnikov et al.,[26] who calculated that for an annual production rate of 50 t by the SHS method the cost of 1 kg of Si_3N_4 powder would be ~US \$28, compared with ~US \$33.7 for material produced by the normal method. Characteristically, in both cases the main contribution to the cost comes from the economically inefficient milling operation.

The tempting idea of preparing silicon nitride powders by the self-propagating combustion of silane–ammonia mixtures without additions of oxygen has not so far been realised.[27] Only the synthesis of silicon oxynitride powders has been reported.

The carbothermic reduction of silicon oxide in a nitrogen atmosphere has long been of interest as a method of using widely available materials including waste products (for example rice husks[28]). However, the powders obtained by this method do not offer a high purity and require additional milling. Their purity can be improved by chemical purification (acid etching) of

the materials.[11] A detailed study of the mechanism of formation of Si_3N_4 under the conditions of carbothermic synthesis (T = 1400–1550 °C, p_N = 0.1–6 MPa) in relation to the properties of the carbon black and of the silicon has been carried out.[29] It was shown that at nitrogen pressures between 2 and 6 MPa the evaporation of the silicon monoxide and the formation of nonequilibrium phases can be largely suppressed, thus bringing the carbon and oxygen content of the reaction products under control. The special features of the carbothermic reduction of silica in nitrogen were discussed also by several contributors to the Stuttgart conference[9] in 1993. For example, it was reported that the well-known Dow Chemical Company (USA) had developed a technology for the carbothermic synthesis of Si_3N_4 which produced a powder of submicron particle size with a high content of the α-phase (>95%) and a relatively small content of oxygen (2%–2.5%) and of carbon (0.3%–0.5%).[30] The moderate cost and the useful technological characteristics of this powder were stressed.

Most of the work reported during the last few years relates to the gas-phase synthesis of silicon nitride, and is mainly aimed at the production of ultrafine powders (UFP) with a particle size of less than 100 nm (usually $d < 20$ nm).[15] The reactions between ammonia and the vapours of silicon tetrachloride or silane, or their derivatives, have been widely studied.[11,31–35] Work aimed at the preparation of carbide nitride powders should also be mentioned.[31,35]

Under appropriate conditions the gas-phase synthesis stimulates homogeneous nucleation, and thus allows silicon nitride to be prepared in the form of UFP. As has been pointed out,[11] the use of silicon tetrachloride or of silane as the starting materials involves some important considerations. On the one hand the low cost of $SiCl_4$ must be weighed against the need to take special steps to remove corrosive side products (NH_4Cl). On the other hand the less easily available silane, which also requires special precautions in handling, gives a better-quality product. Nevertheless silicon tetrachloride is widely used in the industrial production of silicon imide $Si(NH)_2$. This material decomposes at ~1000 °C with formation of amorphous Si_3N_4, which is then annealed to induce crystallisation at 1500 °C.[36]

The most significant results of the studies of gas-phase reactions include the recognition of the special features of the laser-assisted synthesis of silicon nitride as non-agglomerating UFP,[33] and also calculations of the thermodynamic equilibrium in the Si–H–Cl–N system in the temperature range 800 to 2600 K using SiH_4, $SiCl_4$, their many derivatives, and the imide.[37] The pyrolysis conditions in various media (argon, oxygen, nitrogen, helium) of crosslinked organosilicon polymers have also been analysed in detail.[38,39] The formation of various intermediates during these experiments was demonstrated by NMR and IR spectroscopy.

It should be noted that the use of organosilicon polymers of the polysilazane type $\{[SiR_2-NR]_n$ and $[SiR_2-SiR_2-N]_n\}$ as the precursors in the synthesis of UFP of silicon nitride and of its mixtures with silicon carbide is now being widely adopted.[40] Unfortunately, polymeric precursors of Si_3N_4 with the ideal atomic ratio Si : N : C = 3 : 4 : 0 cannot be prepared by the method used successfully for SiC. The traditional plasma methods of synthesising these products are still proving valuable.[31,32,41] Laser technology is used mainly on the laboratory scale. An increasing number of publications on the use of gas-phase reactions in thermal reactors of the flow type is now appearing. Thus, the thermal dissociation of hexamethyldisilazane $Me_3SiNHSiMe_3$ introduced in a stream of helium as the carrier gas (rate 8.55×10^{-3} mol min^{-1}, silazane concentration 16.5 mol%) has been described; some characteristics of the silicon nitride UFP thus obtained are listed in Table 2.[35]

The low density values (up to ~15% lower than in silicon nitride and carbide) and the acceptable agreement between the particle sizes calculated from measurements of the specific surface by the BET method and from transmission electron microscopy (TEM) data are noteworthy. However, the oxygen content of the powders was fairly high. The amorphous powders first obtained were then annealed. Annealing in an argon atmosphere caused crystallisation of cubic β-SiC ($T \approx$ 1300 °C), whereas α-Si_3N_4 was crystallised by an anneal at 1400 °C in a mixture of $NH_3 : H_2$ = 1 : 1.

The residence time of the precursor–gas mixture in a high-temperature reactor 25.4 mm in diameter and ~200 mm long was less than 0.1 s. The extent of conversion increased from 30% to 51% at temperatures between 1100 and 1400 °C. Approximately 2 g of the powder was deposited in 30 min on a rotating drum cooled in liquid nitrogen. It was noted that the preparation of nonagglomerating UFP required a low concentration of the precursor in the carrier gas (which minimises the probability of cluster coalescence in processes of short duration), a fast expansion of gas stream at the outlet from the high-temperature region into a low pressure of inert gas ($10^2 - 5 \times 10^3$ Pa), and rapid cooling of the particles. These assemblies also include special attachments for collecting the powder and for consolidating it in situ at high pressures with complete protection from the surrounding medium.

Studies of the milling of silicon nitride are still being reported.[42,43] Contamination of the product from the material of the milling balls and of the lining can be avoided by using piece parts made from silicon nitride, but milling is invariably accompanied by oxygen contamination. This effect is well illustrated by the milling of a powder of H1 grade (produced by H C Stark Co.) in a specially lined attrition mill (Table 3).[42]

Table 3. Some characteristics of a powder of H1 grade from the H C Stark company after milling for 4 h and 12 h.

Milling time/h	S/m^2 g^{-1}	d/nm	O (mass%)
0	8.4	220	0.9
4	20	95	2.1
12	30	60	3.0

Table 2. Effect of the dissociation temperature on the properties of an ultradispersed $SiC_xN_yO_z$ powder.

T/°C	γ/g cm^{-3}	S/m^2 g^{-1}	Particle size d/nm		Composition		
			from BET data	from TEM data	x	y	z
1100	2.614	568	4	10	1.26	0.35	0.61
1200	2.737	555	4	10	1.35	0.40	0.47
1300	2.781	360	6	8	1.45	0.48	0.29
1400	2.783	272	8	6	1.51	0.49	0.28

Notes. γ is the pyknometric density; S is the specific surface.

The use of milled powders increases the density of sintered and hot-pressed samples.

To conclude this section we shall list the various forms of commercially produced silicon nitride: fibres, monocrystals, and SiAlON ceramics. The production and properties of Si_3N_4 fibres have been discussed in recent reviews.[11,44] Almost all the chemical methods listed in Table 1 are applicable to the production of fibres, but they require an additional organisation of the crystallisation processes in the liquid–vapour–crystal or vapour–crystal systems for the successful growth of fibres or of filamentary crystals (whiskers). For example, the formation of fibres by heating silicon imide with small addition of iron or of silicon oxide in an oxygen-free atmosphere at 1200–1500 °C or by high-temperature treatment of polycarbosilane in ammonia has been reported. It has also been pointed out[35] that monocrystalline nanofibres (30–40 nm diameter, length to diameter ratio > 500) can be produced in a very perfect structural state. It was suggested that the growth of these fibres takes place by the formation of liquid microdrops of silicon during the reduction and decomposition of the ultrafine SiC_xN_y powder, followed by dissolution and subsequent crystallisation of the nitride. The formation of single crystals of the α phase (up to 1 μm in diameter, several micrometres in length) was observed also in the synthesis of silicon nitride in the SHS regime at pressures of 10–180 MPa.[21]

Single crystals of α-Si_3N_4 (1–3 μm diameter, 6–10 mm in length) have been obtained[45] by the gas-phase method using the reaction $SiH_x + N_2 \rightarrow Si_3N_4$ with iron as a catalyst: they were used in studies of the physicomechanical properties of these crystals. Crystals of α-Si_3N_4 several millimetres long were produced[46] in a graphite crucible 300 mm in diameter at 1300 °C by the reaction of $HSiCl_3 + N_2 + H_2$ (pressure ~65 Pa). Crystals were isolated from the polycrystalline sample with a diamond cutting tool. It was pointed out that single crystals grown in the $\langle 10\bar{1}0 \rangle$ direction contained far fewer defects (cracks) than monocrystals with a [0001] orientation, though the latter were larger.

The term SiAlON usually refers to compounds formed in the $Si_3N_4-SiO_2-AlN-Al_2O_3$ system and having the general formula $Si_{3-x}Al_xON_{4-x}$. An authoritative review of the properties of these ceramics has recently been published,[47] and we shall not dwell upon them further.

2. Properties of the powders

The compositions and particle sizes of most of the industrial silicon nitride powders and of some samples now being developed are shown in Table 4. These data, collected by the present writer from various publications,[11,22–25,36,48–50] are on the whole consistent with the considerations discussed above on the advantages and disadvantages of the different methods of synthesis. According to Cambier et al.[50] in the late 1980s 18 companies in the USA, Japan, and Western Europe produced ~40 grades of Si_3N_4 powder, of which 35 were made by the direct synthesis method, 3 by the dissociation of the imide, and only one by the carbothermic and one by the gas-phase synthesis method.

An additional comment should be made concerning the specifications placed on the powders. Thus, the content of free silicon, which can be as high as 1%–2%, has to be specified.[25] High concentrations of free silicon are usually found in the powders prepared by nitridation of the silicon. In the prospectuses of the H C Stark Co. the quantity of free silicon in the H1, LC10, and LC12 grades is stated to be not more than 0.1 mass%. The content of metallic impurities is controlled in order to avoid the formation of vitreous phases, which seriously lower the high-temperature strength of silicon nitride materials at the grain boundaries. An associated requirement is the control of the oxygen content, but this effect is also influenced by the activation of the agglomeration process caused by the formation of a liquid phase, which we shall examine below. As was recently pointed out,[51] halogen impurities can also degrade the properties of the powders. In most of the commercial grades of silicon nitride the content of fluorine and chlorine is claimed to be 0.001–0.009 mass%.[36] The phase composition of the powders

Table 4. Composition and size of silicon nitride powders.

Supplier	Grade of powder	Method of synthesis[a]	Composition (mass%)				α-Si_3N_4, (mass%)	S/m^2g^{-1}	$\bar{d}/\mu m$
			N	O	C	Fe+Al+Ca			
H C Stark, Germany	LC12	DS	38.2	1.8–2.1	< 0.2	< 0.015	> 92	19–22	0.6
	LC10	DS	38.2	1.7–2.0	< 0.2	< 0.1	> 94	13–16	0.8
	H1	DS	38.2	1.3–1.8	< 0.5	< 0.16	> 90	7–10	0.9
	GP	GS	38.5	1.1–1.6	< 0.05	< 0.016	> 90	10–13	0.5
Ube Ind., Japan	SN-E10	ID	38.6	1.3	0.1	0.008	97	11	0.55
	SN-A	ID	39.0	0.9	0.2	0.043	88	7	0.65
Toshiba Cer., Japan	A-200 (SN-D)	CS	37.5	2.0	0.9	0.217	98	10.2	0.9
	SN-B	DS	38.2	1.1	0.48	0.16	96	8.5	1.0
Denka, Japan	SN-P21B	DS	38.6	0.3		0.02	92	9	0.7
Institute of Inorganic Chemistry, Latvia	–	PCS (Si)	38	3.1	0.18	0.19	9130		
		PCS ($SiCl_4$)	38.5	1.6	0.07	0.08		45	
Institute of Structural Macrokinetics, Russia	–	SHS	38.8	1.5–2.2		0.14 Fe	75	3–6	
		SHS	39–39.3	0.4–0.6	< 0.05	< 0.08 Fe	80	1–4	

[a] Here and elsewhere the following symbols are used: DS direct synthesis, GS gas-phase synthesis, ID imide dissociation, CS carbothermic synthesis, PCS plasmachemical synthesis using silicon or silicon tetrachloride as the starting material.

has a marked influence on the microstructure of the sintered and hot-pressed materials. A predominance of the α-phase in the initial powders is thought to be the best composition.

Lastly, properties of UFP related to their agglomeration capacity have attracted special interest in recent development work on nanocrystalline materials.[15,35] The presence of agglomerates affects the formation in the structure of sintered materials of relatively large pores, which degrade the physicomechanical and other properties. More detailed formulations of the requirements on Si_3N_4 powders are continually being proposed, and therefore the data in Table 4 may have to be revised. We should also add that clear criteria for the agglomeration capacity of powders have not yet been formulated.

It follows from the above discussion that the chemical and the phase composition of silicon nitride powders possibly exert a dominant contribution to the final properties of the materials. Not surprisingly, therefore, the distribution of the components in the powders and the special properties of their surface layers continue to be studied in depth. We know that powder surfaces are usually enriched in oxygen; this effect is also seen[4] in Si_3N_4. The most successful recent studies of this type[48,51-57] used various methods of measurement: IR spectroscopy, X-ray photoelectron spectroscopy (XPES), Auger spectroscopy, and others. Szepvolgyi et al.[48] showed that no correlation existed between the overall chemical composition and the particle size of the powders (between 40 and 115 nm). The same workers observed an enrichment of the particle surface by carbon as well as by oxygen. The nitrogen was distributed more or less uniformly over the cross-section. The segregation of oxygen, fluorine, and carbon in the surface layer was observed also by other workers.[52,54-57]

Data on the oxygen content of the powders are of special interest. Possible sources of oxygen include the starting materials and substances specially added to facilitate the sintering process. The presence of oxygen can also be associated with special features of the preparation and pressing technology, and of the conditions under which the powders are stored and treated. In silicon nitride oxygen can be accommodated as so-called lattice oxygen (found in SiO_2 and in oxynitrides of variable composition, such as Si_2N_2O and complex SiAlON ceramics), and also in the composition of hydroxyl groups [$Si(OH)_x$ ($x > 2$)] with different degrees of hydration and of carbonate compounds. The presence of the last two forms was established by XPE spectroscopy.[54] The presence of oxygen in the adsorbed gases (CO, CO_2, water vapour) should also be noted. As reported,[48] the amount of oxygen in the surface layers is 2-20 times greater than in the bulk. According to chemical methods of analysis the oxygen content in the surface was 3-4 times greater than in the bulk.[57] According to calculations based on XPES data the N:Si ratio in the surface layers of powders supplied by the H C Stark company was 0.8-1.0, which differs markedly from the theoretical value of 1.63 but is almost indistinguishable from the value for the oxynitride Si_2N_2O.[58] The most uniform distribution of oxygen is found over the cross-section of carbothermic powders.[36,48]

The large segregations of carbon on the surface are also of interest: they can exceed the bulk content of carbon by a factor of several hundred.[48] The results of studies of the gas evolution during heating of the powders are of interest from this point of view.

The temperature and time dependences of the gas evolution from silicon nitride powders heated in high vacuum, prepared by the SHS method (with an oxygen content of 0.5%) are shown in Fig. 3. We note the dominant presence of carbon monoxide in the desorbed gases, whose evolution effectively ceases after 1.5 h annealing at 1000 °C. (The same treatment was applied to the Si_3N_4 powders to remove adsorbed and other gases before determining the dissociation pressure of the silicon nitride.) Gas evolution was studied also in other samples of Si_3N_4 powder (Table 5). As can be seen, the correlation between the total amount of adsorbed gases and the specific surface, though often observed, is not invariably followed. There is also no regularity in

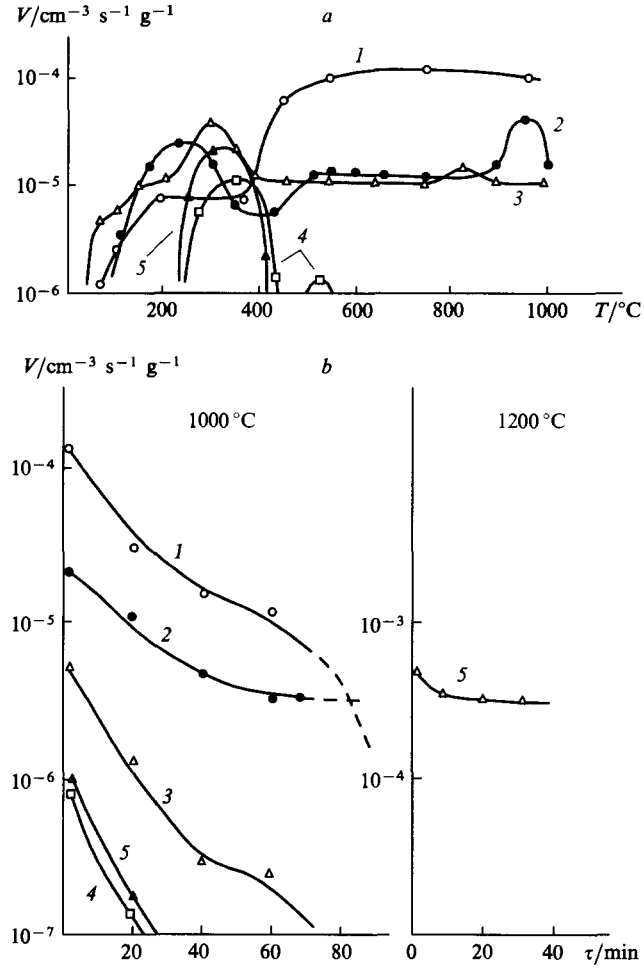


Figure 3. Temperature (*a*) and time dependence (*b*) of the rate of gas evolution during high-vacuum heating of a Si_3N_4 powder prepared by the SHS method.[59] (*1*) CO; (*2*) H_2; (*3*) N_2; (*4*) CO_2; (*5*) N_2.

the temperature at which the rate of gas evolution is a maximum. We know that silicon nitride undergoes hydrolysis when stored in insufficiently pure media. In powders heat treated in vacuum for 1 h at 1200 °C after brief exposure to the air a substantial decrease in the gas content was observed, the desorbed gases consisting mainly of CO.

Thus the results in Table 5 reflect not only the difference in grain size and in the general impurity level of the particles but also the difference between the storage conditions, which were markedly different in the powders listed in Table 4. The role of the storage conditions has been independently confirmed.[48] Whereas the overall level of impurity is determined mainly by the preparation technology, the distribution of the impurities over the cross-section of the particles is controlled by the conditions under which the powders are stored and subsequently handled.

It is important to note that in all the powders the predominant component of the desorbed gases is carbon monoxide (as was also observed, for example, in a study of the gas evolution from titanium nitride powders[63]). This effect can be correlated with the above mentioned segregation of carbon on the surface of the Si_3N_4 particles.[48,54,57] According to Vaivads et al.[54] the carbon can exist on the surface as carbonates and carboxyls.

Table 5 also shows that the temperature of the degassing heat treatment should be about 1000 °C for almost all the powders. However, it is not clear why the dominant species in the desorbed gas below 1000 °C is carbon monoxide, and not carbon dioxide, as could have been expected from the well known equilibrium of the Bell-Boudouard reaction.

Table 5. Parameters of the gas evolution during high-vacuum heat treatment of some silicon nitride powders.[59-62]

Method of preparation	$S/m^2 g^{-1}$	$Q/cm^3 g^{-1}$ (see [a])	Predominant gas concentration (mass%)				Temperature of maximum rate of gas evolution/°C				
			CO	H_2	N_2	H_2O	CO	H_2	N_2	H_2O	CO_2
SHS	0.7	0.9	65	21	10.5	–	500–1000	200–900	300–800	–	–
SHS	1.7	2	see [b]	see [b]	see [b]	–	300–1200	300–1200	300–1200	–	–
SHS	7.1	23.7	62	2.5	23	–	1000	1000	700	–	–
DS	2.5	3.5	see [b]	see [b]	see [b]	–	300	300	300	–	–
PCS	37.5	22.3	see [b]	see [b]	see [b]	–	800–1000	300	800–1000	–	–
PCS	109	263.7	see [b]	see [b]	see [b]	–	700	300	700	–	–
PCS[c]	125	625	59	11	21	7	500–900	500–900	500–900	300–400	300–400
PCS[c] (after annealing for 1 h at 1200 °C)	125	89	79	7	10	6	450–900	450–900	450–900	250–400	250–400

[a] Q is the amount of gas evolved. [b] In the earlier work[60,61] (in contrast to Refs 59, 62, and 63), carbon monoxide and nitrogen were not distinguished in the mass spectroscopy determination of mass number 28. [c] This writer's results, obtained with the help of R A Lyutikov and V I Chukalin.

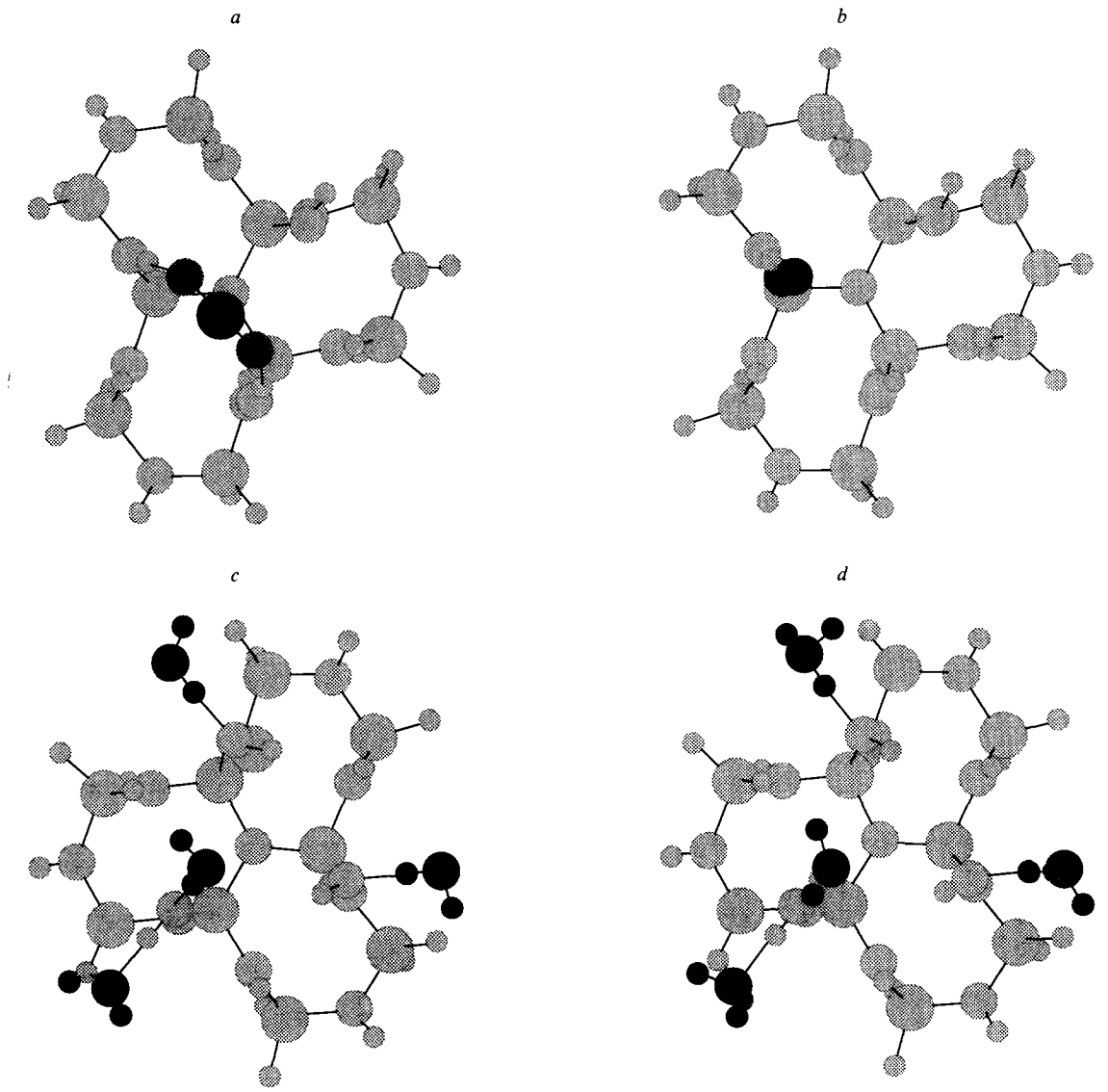


Figure 4. Schemes of the location (top view) of molecules of various adsorbates on the silicon nitride surface. (*a*) CO_2; (*b*) CO; (*c*) H_2O (4 molecules); (*d*) NH_3 (4 molecules). The adsorbate molecules are shown as filled circles. This figure was kindly supplied by N V Goncharova and E F Sheka.[66]

A complex picture of the structure of the surface layers of silicon nitride powders from different producers was observed in a study of these materials by the inelastic neutron scattering method.[64,65] An analysis of the spectra revealed the presence in the surface regions of the powders produced in a 'chlorine' plasma of adsorbed complexes of the NH_4Cl type, and also of NH_3 and HCl. In the case of powders produced by direct nitridation the presence of hydroxyl groups and water is suggested. Quantum-chemical calculations showed that silanol and silamine groups are the principal functional groups of the reaction centres on the surface.[66] Schemes of the proposed arrangement of CO_2, CO, H_2O, and NH_3 molecules on the silanol centres of the Si_3N_4 surface are shown in Fig. 4.

Other impurities also have been detected on the surface of Si_3N_4 and SiC particles: iron, aluminium, calcium, and sodium.[67] However, on the whole we must acknowledge the need for further systematic studies in this direction, using a range of modern methods and carefully standardised materials at all stages (preparation, storage, and applications of the powders).

We shall conclude our discussion of the powders by reexamining their relative costs. A figure of ~US $30 per 1 kg has been stated.[26] This was independently confirmed,[68] and a cost of $115 was quoted for 1 kg of UFP of Si_3N_4 ($d \approx 0.017$ μm) produced by laser synthesis. It was stressed that the main contribution (~96%) to the cost of the Si_3N_4 powders came from the cost of the silane. Thus the range $30–115 is typical of the cost of Si_3N_4 powders (including the UFP materials); for carbothermic powders it can be even lower than $30.

3. Consolidation

Consolidation processes (compaction, sintering, hot pressing, high-energy methods such as static or dynamic high pressures) are used to prepare silicon nitride materials having a prescribed density. In this context we must allow first of all for the covalent nature of the bonds in Si_3N_4, which accounts for the high brittleness, the high temperature of the brittle–ductile transition, and the low diffusional mobility of the material.

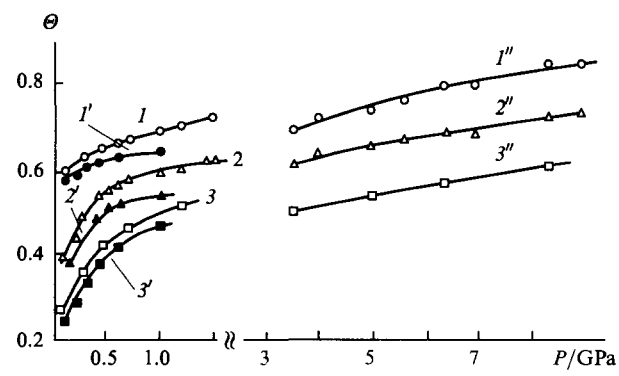


Figure 5. Pressure dependence of the relative density (Θ) in the compaction of Si_3N_4 samples of different granularity.[70] *1–3* compaction in the hydrostat; *1′–3′* compaction in standard dies; *1″–3″* compaction in high-pressure apparatus; *d*/μm: *1*, *1′*, *1″* 1; *2*, *2′*, *2″* 0.05; *3*, *3′*, *3″* 0.017.

Figs 5–7 show the results of a study of compaction over a wide range of pressure and temperature, and also of the sintering of Si_3N_4 powders.[61,69–73] As can be seen from Fig. 5, even at very high pressures (~9 GPa) samples with a relative density greater than 0.85 cannot be obtained at room temperature. The poor compressibility of Si_3N_4 is associated with a poor plasticity. In the case of UFP the limiting relative densities fall to 0.6–0.7 as a result of the negative effect of the interparticle friction. Only the use of combined high temperatures and pressures result in full densification, when the granularity effect of the powder is to a large extent suppressed (see Fig. 6). Sintering without the

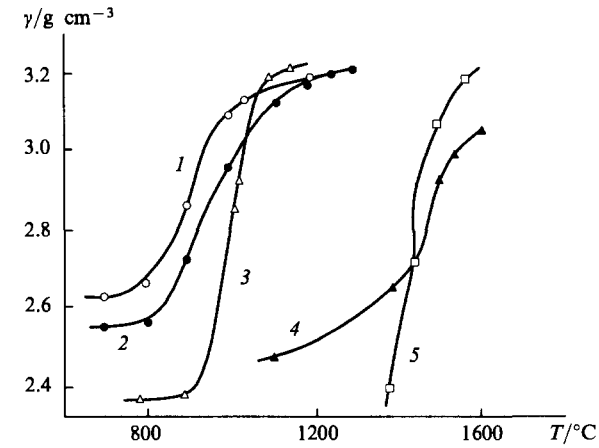


Figure 6. Effect of the compaction temperature and pressure on the density of Si_3N_4 powders of different granularity.[71–73] *d*/μm: (*1*) 1.1; (*2*) 0.75; (*3*) 0.05; (*4*) 0.45; (*5*) 0.08; *P*/GPa: (*1–3*) 8.5; (*4,5*) 3.

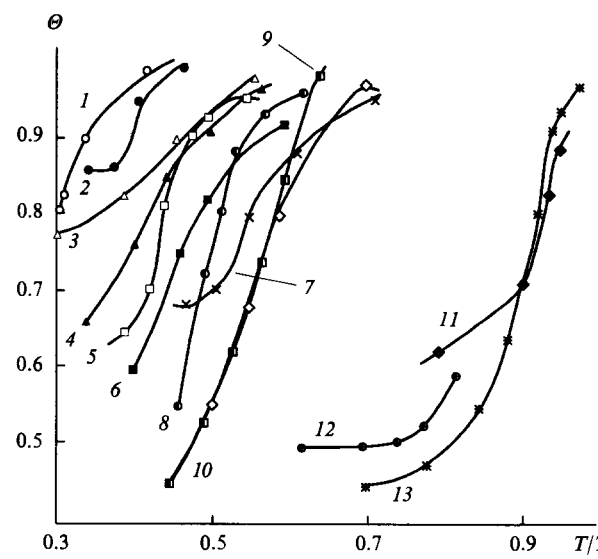


Figure 7. Temperature dependence of the densification during the sintering of various powders.[69,71,72] (*1*) ZrO_2; (*2*) TiN; (*3*) TiO_2; (*4*) Ni; (*5*) CaF_2; (*6*) Mo; (*7*) ZrC; (*8*) MgO; (*9*) WC; (*10*) AlN; (*11*) B; (*12*) Si_3N_4; (*13*) Si.

application of external pressure should produce a temperature of active densification greater than 0.85 T_m in silicon nitride as in other covalent solids (for example, boron and silicon) (see Fig. 7). This conclusion, previously formulated by me,[4,69,71] was recently confirmed by Kryl'.[74] It is interesting to note that whereas in powders of metals, alloys, intermetallics, and ionic compounds the transition to UFP is accompanied by a substantial lowering of the sintering temperature (see Fig. 7) in UFP with covalent bonds this effect is practically undetectable.

Because of the poor sintering properties of Si_3N_4 powders various oxides are added to them (Al_2O_3, MgO, Y_2O_3, singly or in combination) in order to form a liquid phase and thus to accelerate the sintering and hot pressing of the powders.[4] This artifice is used mainly in the hot isostatic pressing variant, which has been widely discussed (see, for example, Refs 69 and 75–79). The liquid phase is formed at high temperatures by the interaction between the added oxides and the films of silica and of oxynitrides present on the surface of the powder particles. The oxygen content of the initial powder plays a limiting role, and it is usually held at the 1%–2% level, though under these

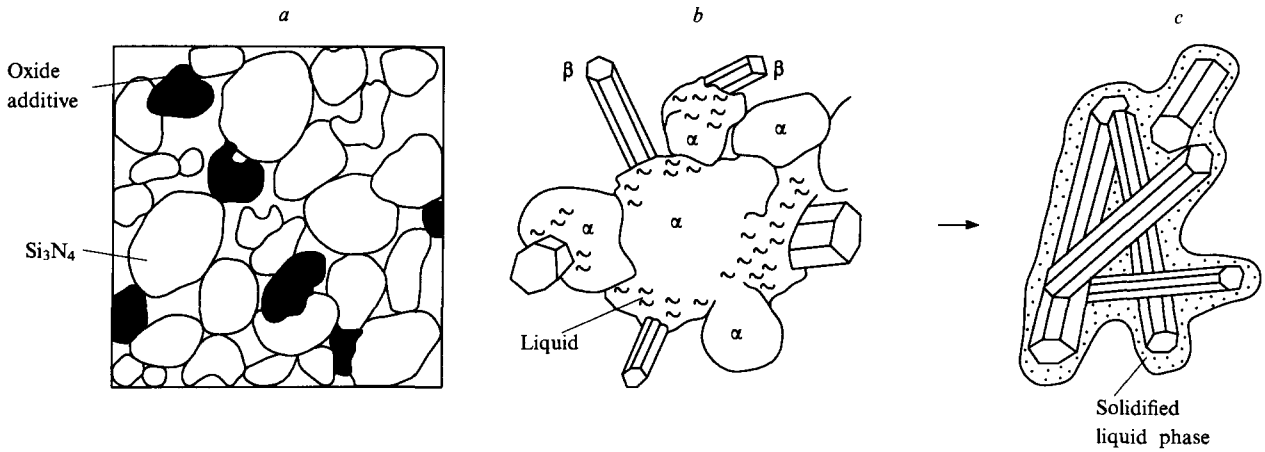


Figure 8. General scheme for the formation of a microstructure during the liquid-phase sintering of silicon nitride materials.[10] (*a*) initial powder; (*b*) α→β transformation; (*c*) microstructure of the densified sample.

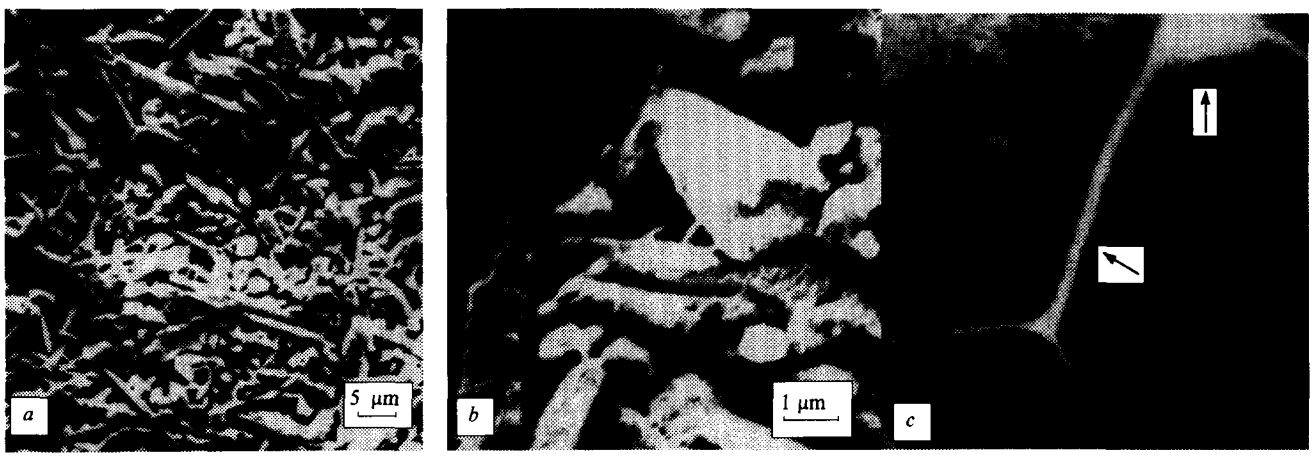


Figure 9. Microstructures of Si_3N_4 obtained in an optical (*a*), a scanning electron (*b*), and a transmission electron microscope (*c*).[10]

conditions the high-temperature strength and creep indices may undergo undesirable changes. Undoubtedly in this case the high-temperature consolidation is complicated by the dissociation of the silicon nitride. Consideration of the complex crystallographic processes associated with the crystallisation of the amorphous phases, the α→β transformation, and the crystallisation from the melts, and also for the normal shrinkage and recrystallisation during sintering and isostatic hot pressing, shows that the nature of the physicochemical mechanism of formation of the structure and properties of silicon nitride materials is far from being trivial.

The mechanism of the liquid-phase sintering and of the isostatic hot pressing has been analysed in many papers.[4,10,11,48,79–81] A general scheme of structure formation during liquid-phase sintering is shown in Fig. 8, while Fig. 9 shows real microstructures obtained by optical microscopy, scanning electron microscopy, and transmission electron microscopy.[10]

Suttor and Fischman[80] have quantified some features of the sintering mechanism. Fig. 10 shows the effect of temperature on the density and on the amount of β phase during the sintering of Si_3N_4 containing 10 mol% of (1:1) $Al_2O_3 + Y_2O_3$.[80] As can be seen from this figure, a significant change in density begins at 1400 °C (the temperature of the ternary eutectic in the $SiO_2-Al_2O_3-Y_2O_3$ system is 1350 °C). A relative density of 0.93 is reached at the temperature (T = 1650 °C), when the α→β transformation is only 23% complete. Microstructural studies of

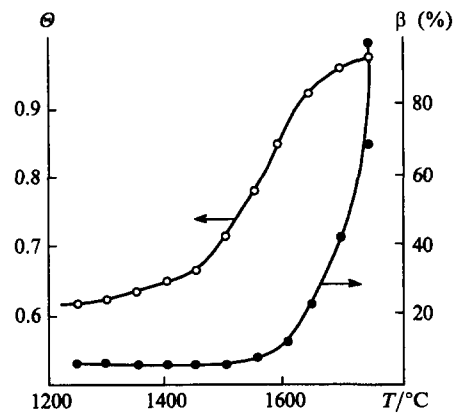


Figure 10. Effect of temperature on the relative density and on the content of β phase during the sintering of Si_3N_4 + 5% Al_2O_3 + 5% Y_2O_3 (see Ref. 80).

quenched samples showed that the characteristic columnar structure (elongated grains of the β phase, see Figs. 9*a* and 9*b*) is formed only during the closing stage of the sintering. Comparing the kinetic coefficients calculated from the experimental data with those of Kingery's theory of liquid-phase

sintering showed that under practical conditions a more complex mechanism must be postulated. NMR was used in a study[81] of the role of additives during sintering, which accounted for the distribution of the elements (^{29}Si, ^{27}Al, ^{25}Mg, ^{89}Y) in the different component phases.

The activating effect of additives of REE oxides (La_2O_3, CeO_2, and others) and of yttrium oxide drew attention to the possibility of finding an active influence on the formation of the so-called self-reinforced fibre structures and of increasing the strength and crack resistance parameters of the material at room temperature and above.[82-85] Thus, fracture toughness values K_{Ic} = 8–9 MPa $m^{1/2}$ have been obtained for the composition Si_3N_4 + 1% Al_2O_3 + 5% CeO_2, exceeding almost two-fold the normal values for silicon nitride materials.[82] The length of individual elongated grains in the structure of these compositions reached 40–50 μm. The bending strength (σ) at room temperature and at 1300 °C for the composition Si_3N_4 + 2% Al_2O_3 + 5% Y_2O_3, into which the additives were introduced by chemical mixing, was 1084 ± 49 and 722 ± 38 MPa respectively, which is also much higher than ordinary values. This effect is attributed to high-melting silicates, which are deposited at the grain boundaries in small quantities.[83] The following parameters have been reported[84] for hot-pressed Si_3N_4 + (8–10%) Y_2O_3 powders synthesised in a plasma: σ(20 °C) = 650–900 MPa, σ(1400 °C) = 550–780 MPa, K_{Ic} = 6–10 MPa $m^{1/2}$. Higher values were obtained for Si_3N_4 doped with oxides of the rare-earth metals: σ(~1500 °C) ≈ 800 MPa (see Takahashi et al.[85]).

Even from this brief survey it is clear that the concepts of grain boundary engineering are of great importance in the development of silicon nitride materials: this is a relatively new area in materials science,[86] which is only now beginning to be applied to silicon nitride. Some aspects of the recrystallisation of silicon nitride have been analysed in detail.[87,88] TEM was used[89] to examine the behaviour of the Si_3N_4 structure at high temperatures and pressures (T = 1300–2300 °C, p = 7.7 GPa). The development of plastic deformation with formation of a high density of dislocations and fragmentation of the larger grains was observed (at T = 1300–1500 °C), and also dynamic recrystallisation, produced both by the migration of grain boundaries and by the rotation of fragments (at T > 1500 °C). The formation of a microstructure is completed by collective recrystallisation, which proceeds rapidly at 2100–2300 °C.

Several studies of the crystallisation of amorphous Si_3N_4 have been published.[36,90-94] Fig. 11 shows the kinetic plots for the crystallisation of the α phase as equiaxial grains from an amorphous powder prepared by the ID method.[36] The calculated activation energy of the process was 890 kJ mol^{-1}. As can be seen from the figure, the crystallisation of Si_3N_4 is completed at 1440 °C. At higher temperatures we observe the formation of the α phase as needle-like grains, and carrying out the process under high nitrogen pressures (up to 100 MPa), at which gas-transport reactions are suppressed, shifts the temperature of the incipient formation of needle-like grains to the region of 1800–2000 °C.[91] Under high-pressure conditions the crystallisation of amorphous Si_3N_4 sets in at lower temperatures: ~800 °C at P = 5 GPa.[90] During sintering and hot pressing the amorphous powders are more inert than the crystalline powders: their active densification temperatures are shifted into even higher temperature ranges, but this effect is almost completely compensated by the use of activating oxide additives.[90,92] The crystallisation of a mixture of amorphous ultrafine powders of Si_3N_4 + SiC begins at 1500 °C and is completed at 1600–1700 °C, i.e. at higher temperatures than for the undoped silicon nitride.[94]

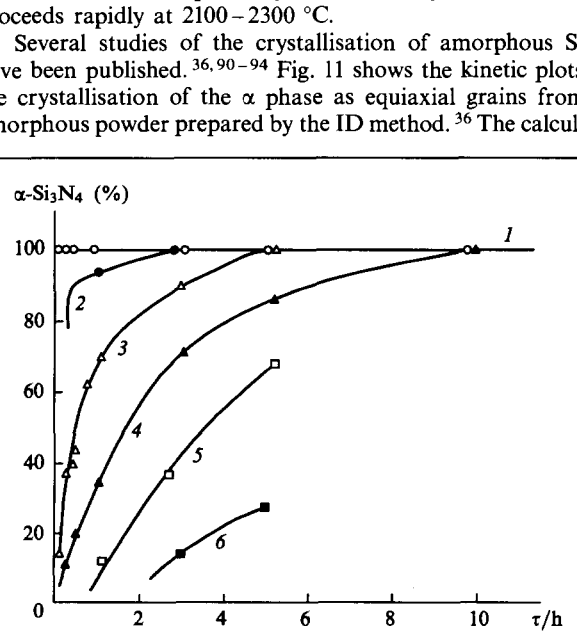


Figure 11. Kinetics of the crystallisation of α-Si_3N_4 from an amorphous powder prepared by the ID method.[36] T/°C: (*1*) 1440; (*2*) 1430; (*3*) 1420; (*4*) 1400; (*5*) 1385; (*6*) 1360.

Studies of the consolidation of Si_3N_4 by the shock compaction method have been reported.[95-97] It is claimed that samples with a relative density of 0.99 were obtained from powders of SN-E10 grade (see Table 3) at pressures of ~40 GPa and temperatures of ~1200 K; their hardness was H_V ~ 23 GPa, and their grain size (calculated from TEM data) was 50–60 nm.[97] The suggested densification mechanism includes plastic deformation and surface melting of the particles.

In conclusion we should note one of the earliest methods of consolidation of silicon nitride materials: reactive sintering. However, this method is rarely studied at present because it does not produce high-density articles. We shall only refer to one report[98] of the use in reactive sintering of fine silicon powders prepared by the laser treatment of silane, which markedly shortened the time of the process.

A relatively new method (infiltration by chemical deposition from the vapour phase, 'chemical vapour infiltration') has not yet found extensive application in the preparation of silicon nitride because of the presence of residual porosity in the final product and because of phase interactions. The use of this method to prepare composite materials of the graphite fibre–silicon nitride type has been reported.[99]

III. Films, coatings, and layers

Both chemical (CVD) and physical (PVD) methods of deposition from the gas phase are used, in different variants, to produce silicon nitride films, coatings, and layers. SiF_4 (or SiH_4, $SiCl_4$)–NH_3–H_2 mixtures are most commonly used. The thermodynamics and kinetics of the deposition of thin layers (up to ~1 μm) of Si_3N_4 have been discussed in monographs[3,5] from the standpoint of problems in microelectronics. Japanese workers[4,100] obtained coatings and layers of polycrystalline and of monocrystalline (as well as amorphous) Si_3N_4 up to 3–4.5 mm thick by deposition from $SiCl_4$–NH_3–H_2 mixtures onto graphite substrates at 1200–1500 °C. Fig. 12 shows the effect of the total gas pressure on the temperature limits of the deposition of the above forms of silicon nitride.

In recent years chemical deposition has been carried out mainly in a high-frequency plasma discharge: the main variants are called plasma assisted and plasma-enhanced CVD processes (PACVD and PECVD respectively). The effect of the power of the high-frequency (13.56 MHz) discharge on the thickness of the coating deposited from a SiF_4–NH_3–H_2 mixture has been studied.[101] The increase in thickness was substantial: at a power of 400 W the thickness increased by more than 50% and reached 700 μm. This result can be explained in terms of the increase in the electron temperature produced by the increased power of the plasma. A high electron temperature increases the rate of dissociation of the gas molecules characterised by a high bond energy, thus increasing the concentration of the corresponding free radicals. Since the bond energy of the SiF_4 molecule (~600 kJ mol^{-1}) is much higher than the bond

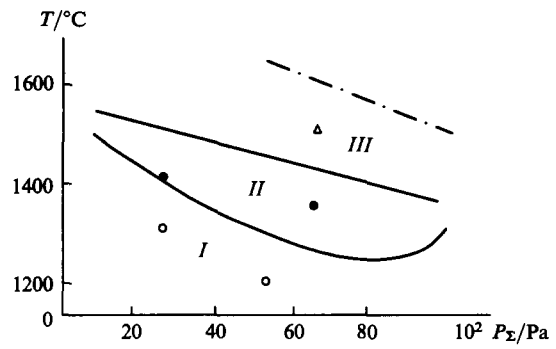


Figure 12. Regions of existence of amorphous (*I*), polycrystalline (*II*), and monocrystalline deposits (*III*) of Si_3N_4 (see Ref. 100). The points denote some specific regimes used to prepare amorphous or polycrystalline samples of size 10 × 40 × 1(3) mm and single crystals 2–3 mm long. The broken line shows the upper limit of the possible formation of deposits. P_Σ is the total pressure of the mixture of gases ($SiCl_4$ + NH_3 + H_2).

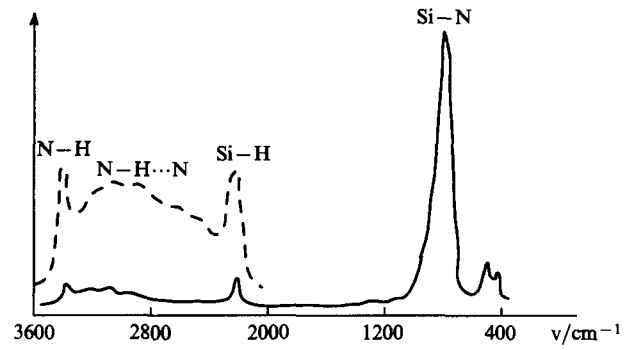


Figure 13. IR spectra of a film of Si_3N_4 0.8 μm thick prepared by PECVD at 293 K (see Ref. 105).

energy of NH_3 (~435 kJ mol^{-1}) it is assumed that the relative number of radicals containing silicon is higher in PECVD.

The optimisation of the regimes used in the deposition of Si_3N_4 films from SiH_4–NH_3–N_2–H_2 mixtures under PECVD conditions has been examined.[102,103] In particular, it was shown that when the power of the high-frequency discharge is increased the residual stresses in the films change sign and are converted from tensile (up to ~270 W) into compressive stresses (>270 W); hydrogen in the gas phase has a similar effect. Table 6 shows the results of an analysis of the composition of films prepared under different conditions.[103] The width of the forbidden gap (E_{gopt}), one of the most important characteristics of these films when used as isolating elements in semiconductor devices and in thin-film field effect transistors in liquid-crystal display systems, is also given in Table 6. As can be seen, the Si:N ratio, the concentration of hydrogen in the films, the presence of Si–Si bonds, and the E_{gopt} parameter show a complicated dependence on the power of the discharge and on the composition of the gas mixture. The use of stoichiometric nitride films, deposited under conditions of minimum residual compressive stress, is recommended.

Problems of hydrogen and other impurities in films of Si_3N_4 have a long history. Many different methods have been used to characterise the films: IR spectroscopy (in different variants), XPES, Auger spectroscopy, RBS, Raman spectroscopy, etc.[3,5,102–105] Fig. 13 shows the IR spectrum of a film of Si_3N_4 deposited from a SiH_4–NH_3–N_2 mixture at 293 K in the plasma of a high-frequency discharge (450 kHz).[105] The peaks at 825, 2215, 3000, and 3400 cm^{-1} correspond to the vibrations of the Si–N, Si–H, N–H...N, and N–H bonds. Traces of oxygen and carbon (~1 at.%) were detected in these films by Auger spectroscopy. IR and XPE spectroscopy methods were used to study the composition of SiN_xC_y coatings prepared by deposition from an $SiCl_4$–CCl_4–N_2–H_2 mixture at 1100–1700 °C onto a tungsten filament.[104] It was found that under these conditions (for example, at a deposition temperature of 1185 °C) the composition of the coatings corresponds to the formula $SiN_{0.8}C_{0.2}$, and that silicon carbide, silicon, and silicon nitride are undetectable.

The thermodynamics of the deposition of condensed phases in the Si–N–C–H system at temperatures up to 2800 K have been discussed by Varlamov et al.[106] It was shown that 'pure' silicon nitride (without codeposition of other condensed phases) is formed in the presence of an excess of nitrogen (N:Si>1.5) at relatively low temperatures ($T < 1100$ K). The regions of coexistence of different phases for C:Si = 4 and H:C = 225 are shown in Fig. 14. The thermodynamics of the formation of Si_3N_4 in the Si–N–Cl–H system have been analysed by Kruis et al.[37]

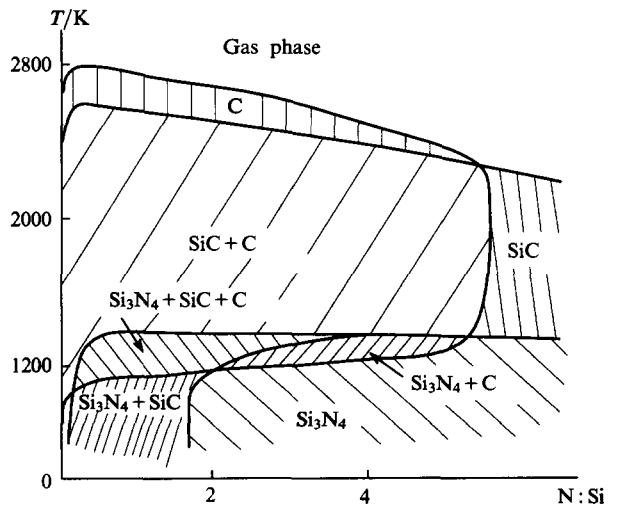


Figure 14. Regions of existence of condensed phases in the Si–N–C–H system with C:Si = 4 and H:C = 225 (total pressure 10^5 Pa).[106]

Table 6. Results of analyses of amorphous films of Si_3N_4 by Rutherford back scattering (RBS) and XPE spectroscopy methods.[103]

Deposition regime		E_{gopt}/eV	Si:N (from RBS data)	Concentration of components (XPES) (at.%)		
W/W	H_2:H_2+N_2 (%)			Si_3N_4	SiNH	Si–Si
100	100	4.1	0.98	76	13	11
400	100	5.6	0.78	76	15	9
300	50	5.3	0.90	85	5	10
300	0	5.3	0.75	90	0	10

Various PVD methods have also been actively applied to the preparation of silicon nitride films. They include a.c. and d.c. sputtering (in different variants), ion-beam deposition (including ion implantation), etc.[107-112] Si_3N_4 films prepared by d.c. sputtering have a columnar structure.[110] The effect of oxygen on the composition and properties of films prepared by r.f. sputtering was analysed by Volkov and Satunkina.[112] A new theory of ion-beam deposition (or ion beam assisted deposition, IBAD) identifies the effect of various technological factors on the composition and certain other properties of silicon nitride films prepared by evaporating silicon and bombarding the amorphous films with nitrogen ions.[109]

IV. Structure and properties

1. Crystal structure and nature of the bond

The crystal structure and the nature of the bond in silicon nitride have been discussed in detail by many workers (see, for example, Refs 3-5 and 10), and therefore we shall dwell on them only in the most general terms, mentioning some new results.

As we know, silicon forms only one chemical compound with nitrogen: Si_3N_4, which exists in two modifications (α and β). Silicon nitride crystallises in the trigonal (α) and the hexagonal crystal system (β). The crystals have identical structures of the Be_2SiO_4 type (phenacite). The main structural element in silicon nitride, as in many silicates, is the tetrahedron 'SiN_4'. A set of three of these tetrahedra share a common nitrogen atom, being arranged with angles of 120° between the tetrahedra. The structures of the α and β modification differ in the arrangement of the tetrahedra along the *c* axis, and therefore they contain different numbers of formula units in the unit cell. The structure of silicon nitride and its main parameters are shown in Fig. 15 and Table 7.

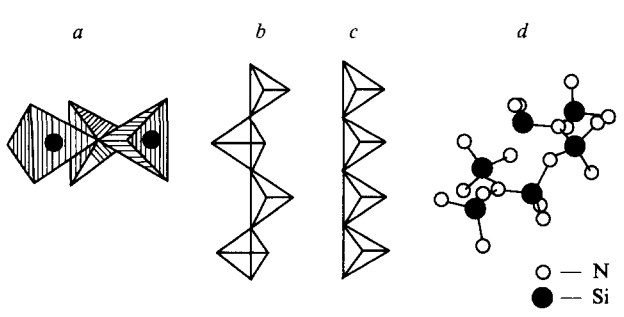


Figure 15. Structure of silicon nitride.[4] (*a*) group of three 'SiN_4' tetrahedra; (*b*) scheme of the arrangement of tetrahedra along the *c* axis in the α phase; (*c*) ditto in the β phase; (*d*) unit cell of β-Si_3N_4.

The special aspects and the mechanism of the α→β transformation have been widely discussed in the literature.[4,10,11,113] It was shown that only the α→β transition is possible: the reverse transition does not take place. This indicates a monotropic transition, and shows that the α→β transition can be classified as a transformation in the second coordination sphere, in which the mutual location of groups of atoms (tetrahedra) is changed but the structure within these groups stays unchanged. A calculation of the Madelung energy showed that above $T = 293$ K the β phase is more stable than the α, which again confirms the monotropic nature of the α→β transformation.[114]

The temperature and the detailed aspects of the α→β transition are still not entirely clear: we know, for example, that heating α-Si_3N_4 samples prepared by gas-phase deposition does not induce the transition at temperatures below 1800 °C.[4] It was pointed out[46] that hot isostatic pressing of the α single crystals at 1600 (P = 5 GPa) and at 2200 °C (P = 70 MPa) is also not accompanied by an α→β transformation. At the same time additions of oxides (MgO, Al_2O_3, Y_2O_3, and others) to activate the sintering and hot pressing processes (see Fig. 10) activate also this transformation as a result of liquid-phase crystallisation. An intensification of polymorphic transformations as a result of dissolution-deposition processes in the presence of a liquid phase is also characteristic of transitions of the rearrangement type in the second coordination sphere. Lastly, under high-pressure conditions (8.5 GPa) the α→β transformation begins at 800 °C and is completed at 1200 °C.[61,115] As was stated above, high pressures also lower the crystallisation temperature of amorphous silicon nitride.[90] However, on the whole we should stress the need for further studies in this area. The structure of amorphous films has been discussed in monographs.[3,5]

NMR is an effective method of localising various structural states and of producing a phase analysis of Si_3N_4, especially if the sample is rotated through the so-called magic angle.[81,116] Its main advantage over the traditional X-ray phase analysis (XPA) is the possibility of identifying not only the crystalline modification but also the amorphous phase, and of localising the position of the other elements (^{13}C, ^{15}N, ^{25}Mg, ^{27}Al, ^{89}Y, ^{189}La), as was stated above in the context of the sintering problem. Fig. 16 shows the forms of the ^{29}Si NMR spectral lines for the different modifications of silicon nitride.[116] As can be seen the NMR method offers information on both the α and the β modification, as well as the amorphous phase.

Though the covalent or covalent-ionic character of the bonds in silicon nitride has long been recognised, a clarification of the details of the electronic structure of this compound remains a topic for discussion.[117-121] Fig. 17 shows a general scheme of the transformation of the atomic orbitals of silicon and nitrogen during the transition to the electronic states of silicon nitride.[119] The conduction band is formed mainly from the 3*s* and 3*p* states of the silicon, and the *s* and *p* states of the nitrogen give rise to the valence band. Of course, this is a simplified picture of the electronic structure of silicon nitride, whose details are being determined by quantum-chemical calculations and by an experimental study of the emission and absorption spectra by various methods (XPES and others). The results of a calculation of the density of states in Si_3N_4 by the tight binding approximation and the corresponding spectroscopic data are shown in Fig. 18. The electronic structure of Si_3N_4 is controlled mainly by the local short-range order, and therefore the α and the β modification and the amorphous phase have almost identical pictures of the density of states. According to quantum-chemical calculations[119] the width of the optical gap is 5.3 eV, which is fairly close to the experimental results (see Table 6). The constitution and the electronic structure of the Si-H and N-H bonds and the defect states in amorphous silicon nitride films (α-SiN_x:H) have been

Table 7. Crystal structure and density parameters of Si_3N_4 (see Ref. 4).

Modification	Space group	Lattice parameters/nm			Length of Si-N bond/nm	Number of formula units in cell	X-ray density/g cm^{-3}
		a	*c*	*c*/*a*			
α	$P31c$	0.78183	0.55914	0.715	0.1715-0.1759	4	3.148
β	$P6_3$	0.7595	0.29023	0.382	0.1704-0.1767	2	3.211

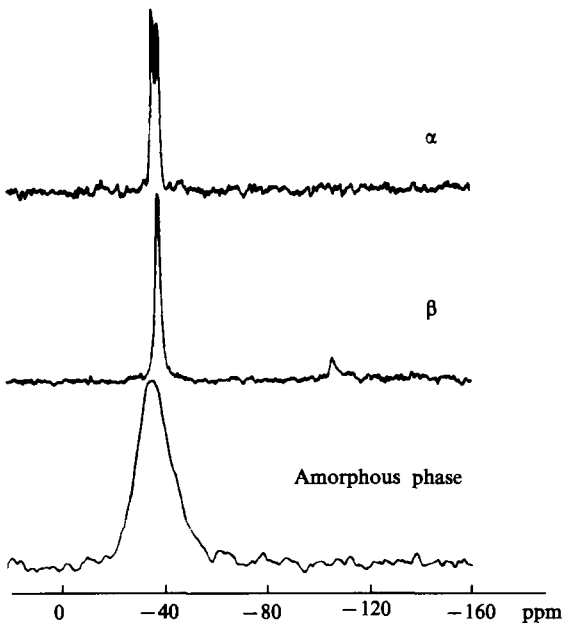


Figure 16. Forms of the NMR spectral lines of ^{29}Si for different modifications of Si_3N_4 (see Ref. 116).

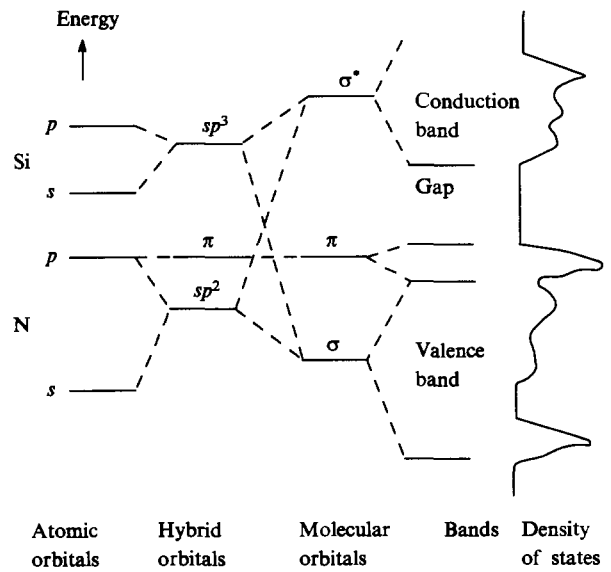


Figure 17. Scheme of the transformation of the atomic orbitals of nitrogen and silicon into the band structure of Si_3N_4 (see Ref. 119).

studied in depth.[119-121] The contribution of the ionic component to the bond energy of Si_3N_4 was estimated to be between 30% and 50%.[114,119]

Calculations of the band structure in β-Si_3N_4 and in the hypothetical compound β-C_3N_4 have been reported.[118] In silicon nitride the crystal structure parameters and the bulk elastic modulus based on these calculations were satisfactorily consistent with experimental data. A substantial amount of charge transfer towards the nitrogen atoms and a higher ionicity contribution were also observed in Si_3N_4 as compared with SiC and C_3N_4.

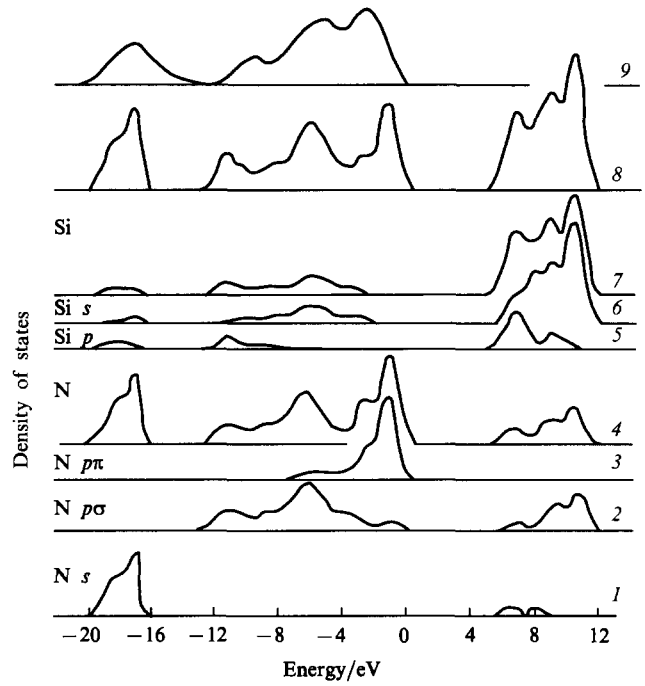


Figure 18. Calculated partial (*1*-*7*) and total (*8*) densities of states for β-Si_3N_4, and results obtained by the photoemission method (*9*) for amorphous films.[119]

2. Phase equilibria and physicochemical properties

The silicon-nitrogen phase diagram has been known for more than 30 years, and very few changes have been made during this period. Fig. 19 shows the diagram calculated for a pressure of 10^5 Pa.[122] Unfortunately, variants of this diagram for pressures above 10^5 Pa have not been produced. For a long time the melting point (T_m) of silicon nitride was given as ~1900 °C in standard handbooks, this being the temperature at which the dissociation pressure of the compound reaches ~10^5 Pa.

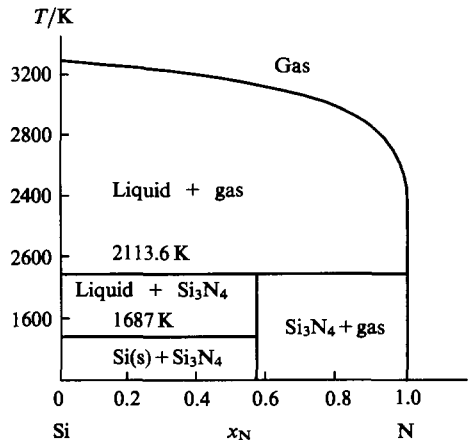


Figure 19. Silicon-nitrogen phase diagram calculated for a pressure of 10^5 Pa (see Ref. 122).

An attempt to determine the melting point was made by me earlier.[4,69,123,124] A value of $T_m \approx 2600$ °C was obtained by using the correlation between the melting point and the elastic modulus. An analysis of the diffusional mobility in silicon carbide and silicon nitride gave a similar value ($T_m \approx 2700$ °C). An analysis of data on the sintering of Si_3N_4 (see Fig. 7) suggested an intermediate value of T_m (2650 °C), which led to fully acceptable results.

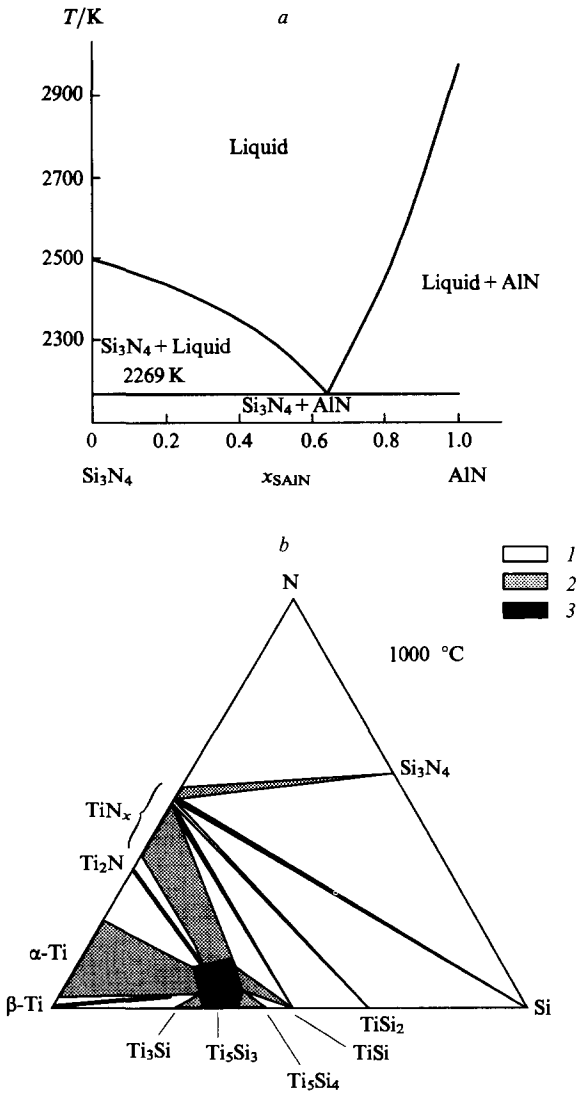


Figure 20. Calculated phase diagrams for Si_3N_4 + AlN (*a*) and Ti–N–Si (*b*).[122,133] Regions in the isothermal section: (*1*) three-phase; (*2*) two-phase; (*3*) region of existence of Ti_5Si_3.

Other workers adopted the following values of T_m in calculations of the phase diagram and of the isostatic hot pressing diagrams: ~2400 °C;[125,126] ~2330 °C;[122,127] 2564 °C.[78] It was pointed out[127] that the value $T_m \approx$ 2330 °C was calculated by comparing the properties of BeO and ZnO (see Weiss's thesis[128]). The entropy of melting of Si_3N_4 was given as 80.5 J K^{-1} mol^{-1}. An experimental determination of the melting point of Si_3N_4 under high nitrogen pressures showed that in the pressure region 120–198 MPa this parameter varies between ~2290 and ~2500 °C, and that the melting is incongruent.[129] Thus our estimates of T_m have been confirmed on the whole, but the need for further and more exact experimental determinations of the melting point has not disappeared.

Information on the phase diagrams of Si_3N_4 can be found in many publications (for example in Refs 4, 122, 125–128, 130–134). Computational methods are now widely applied, and have been used (for example) to construct the diagrams for Si–N–O (see Refs 126 and 130), Si–C–N–O (see Refs 130 and 131), Si–Al–N (see Refs 122 and 125), Si–M–O–N, where M = Al, Mg, Y, Ce, Ti (see Refs 130, 132, 133), and others. The regions of existence of the condensed phases in the Si–N–C–H system were shown above in Fig. 14.[106] In Fig. 20 we show as an example the Si_3N_4–AlN (see Ref. 122) and Ti–N–Si diagrams (see Ref. 133), calculated ignoring the gas phase (whose role, however, is substantial in the first of these systems). Experimental data on the polythermal sections of these and other diagrams for systems including Si_3N_4 are few.

Until recently data on the dissociation of silicon nitride were mostly inferred from results obtained at relatively low temperatures (up to 1500–1700 °C). In the writer's laboratory this temperature was increased to 2000 °C, and the samples included powders prepared by DS, GS, and SHS methods (see Table 4).[58,59,62,135] In Table 8 we show some of the results obtained in this way; Fig. 21 illustrates the temperature

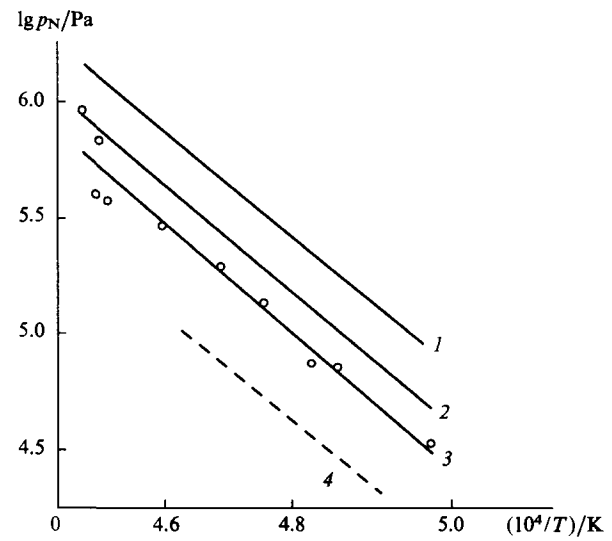


Figure 21. Temperature dependence of the dissociation pressure of silicon nitride. (*1*) GS powder (see Table 8); (*2*) DS powder; (*3*) SHS powder;[58,59] (*4*) from Ref. 136.

Table 8. Thermodynamic properties of silicon nitride.

Method of preparation	Composition (mass%)					$\lg p_N(Pa) = A - B/T$		$-\Delta_f H_{298}$/ kJ mol^{-1}	$\Delta_f G_T$/ kJ mol^{-1}	T/K (p_N = 10^5 Pa)
	O	C	Fe	Al	Ca	A	$10^{-3}B$			
GS	1.6	0.021	0.0043	0.0006	0.0002	16.13	22.30	763(II) 763.4(III)	$-854+0.426T$	2005
DS	1.25	0.15	0.0045	0.03	0.004	15.92	22.37	752(II) 775(III)	$-856+0.418T$	2050
SHS	0.5	0.05	0.08	–	–	15.93	22.76	795(II) 803.6(III)	$-871+0.418T$	2084

dependence of the dissociation pressure of silicon nitride. The effect of the composition of the powders, and in particular of the oxygen content, on the dissociation pressure is evident. Some results published more than 30 years ago [136] and included in most of the standard handbooks [137,138] were obtained in a manometric study of the monovariant equilibrium in the $Si-Si_3N_4-N_2$ system using pure components (99.95% Si, and Si_3N_4 in the form of a nitrided layer with a purity of 99.94%) at nitrogen pressures up to 10^4 Pa. The results of our experiments on the determination of the dissociation pressure by using powders were higher, which we attribute to the effect of oxygen though the detailed mechanism of this effect is not yet clear. This is because before the determination of the dissociation pressure all the powders were degassed to remove adsorbed gases (see Fig. 5 and Table 3), i.e. a substantial part of the oxygen was eliminated. However, the proportion of remaining (lattice) oxygen and its distribution in the surface layers and in the bulk of the particles, and therefore the mechanism of the effect of oxygen on the dissociation pressure, need to be more accurately determined.

It should be noted that no singularities associated with the $\alpha \rightarrow \beta$ transition can be seen in the $\lg p_N = f(T)$ plots, probably because of the close similarity between the thermodynamic properties of these modifications. The results of the determination of the dissociation pressure (see Fig. 21) also suggest that more attention should be paid to the oxygen content in the determination of the melting points and the ignition temperatures in the $Si-N_2$ system (see the already mentioned reports, [21,129] and Figs 1 and 2), because it can affect the dissociation pressure by a substantial factor and erroneously identify the character of the melting.

Values of the enthalpy and of the Gibbs free energy of formation of silicon nitride are shown in Table 8. The values of $\Delta_f H_{298}$ were calculated by the writer by the second and the third law of thermodynamics from data on the dissociation of Si_3N_4. As we know, the agreement between $\Delta_f H_{298}$ values calculated in this way and their closeness to independently obtained calorimetric data confirm the validity of the evaporation or dissociation effects. Only one paper [139] on the calorimetric determination of the heat of formation of Si_3N_4 ($\Delta_f H_{298}$ = 787.8 kJ mol^{-1}) has been published so far. Thus our results appear to be reasonably good, though the need for further studies is evident.

Values of the specific heat and entropy, and also of the thermodynamic functions of silicon nitride over a wide range of temperatures have been reported, [140,141] but no allowance was made for the purity of the samples.

The self-diffusion parameters of silicon nitride have been studied in several laboratories. [142-145] These results are shown in Table 9. The higher diffusional mobility in the β phase as compared with the α phase is noteworthy. The practical problems met in the study of diffusional processes in silicon nitride were analysed by Kunz et al. [144] Comparing the results obtained by different workers [145] reveals a difference of 2-4 orders of magnitude in the absolute values of D. A TEM study of dislocation loops [146] gave an estimate of the diffusion coefficient of the vacancies of $\sim 10^{-18}$ $m^2 s^{-1}$ (T = 1700 °C), which is more than 5 orders of magnitude greater than the value of the same coefficient obtained [142] by extrapolation to this temperature. Therefore the need for further detailed studies of the self-diffusion over a wide range of temperatures and using monocrystalline samples is obvious.

Problems of oxidation and corrosion resistance in silicon nitride materials have recently achieved prominence, and call for a special discussion. Related problems are dealt with in several monographs, handbooks, and reviews, [147-152] and we shall only briefly mention these sources. It should be noted that materials based on Si_3N_4 have undergone substantial corrosion when under stress, and that both tensile and compressive stresses can influence the oxidation processes. [152,153] It is also evident that the dissociation and the oxidation of silicon nitride at high temperatures are two factors which seriously limit the application of materials of this type above 1500-1600 °C. [154] Therefore further studies of the high-temperature thermodynamics of Si_3N_4 in conjunction with corrosion tests under the same conditions, including the development of satisfactory coatings, are urgently needed.

Data on the contact angles and on the energy parameters of wetting of silicon nitride materials by liquid metals and alloys have been reported. [4,147]

3. Physicochemical aspects of the high-temperature strength

Some information on the mechanical properties and structure of silicon nitride has already been given above in the discussion of the consolidation of these materials (see Figs 8 and 9). More detailed information on the physico-mechanical properties can be found in various monographs, handbooks, and reviews, [4,6-12,155-158] in addition to the many original papers in scientific journals, and therefore a complete analysis of this problem goes beyond the scope of the present review. Some of the characteristics obtained recently for single crystals of the α modification are listed in Table 10. [44-46] As can be seen, some properties of the single crystals have been redefined and made more specific, [45,46] though it should be noted that the results of Ref. 45 apply to thin fibres.

Table 9. Parameters of the self-diffusion in silicon nitride.

T/°C	Component	D_i/$m^2 s^{-1}$ (see [a])	Method	Notes	Ref.
1200-1410	Nitrogen	$1.2 \times 10^{-16} \exp(-233.2/RT)$ $6.8 \times 10^{2} \exp(-777.5/RT)$	Isotope exchange	α-Si_3N_4 β-Si_3N_4	142
1230-1450	Nitrogen	$2 \times 10^{-15} \exp(-132.7/RT)$ $4 \times 10^{-4} \exp(-212.8/RT)$	Nuclear microanalysis	Bulk diffusion in the β phase Grain boundary diffusion in the β phase	143
1400-1600	Silicon	$(0.45-2) \times 10^{-19}$	Spectrometric analysis	α-Si_3N_4	144
900-1300	"	$6 \times 10^{-10} \exp(-183/RT)$	Processing of data obtained by hot isostatic pressing	Effective grain boundary diffusion in (α+β)-Si_3N_4	145

[a] The activation energy is given in kJ mol^{-1}.

Table 10. Some physicochemical characteristics of α-Si_3N_4.

Parameter	Value[a]	Ref.
Young's modulus, GPa	550–750	45
	(380)	44
Tensile strength, GPa	30–50	45
	(3–11)	44
Temperature of the transition from the brittle to the ductile state, °C	1760–1820 (> 1800)	46
Slip system at 1820 °C	$\{1\bar{1}01\}\langle 11\bar{2}0\rangle$ ($\{1\bar{1}01\}[0001]$)	46
K_{Ic}/MPa $m^{1/2}$	1.5–2.0	46
H_V $[P = (2-5)H]$/GPa	34 ± 5 $\{1\bar{1}00\}$	
	(32–36)	
	26 ± 5 (0001)	
	(26–28)	46

[a]The values shown in parentheses are known for single crystals and polycrystals,[4] and also for whisker crystals.[44,46]

The temperature dependence of the hardness for two crystallographic planes is shown in Fig. 22. For the (0001) plane these results are similar to those reported earlier.[100] The high values for the $(1\bar{1}00)$ and $(11\bar{2}0)$ plane denote a substantial anisotropy of the hardness. Furthermore the high-temperature hardness values for monocrystalline Si_3N_4 are much greater than those for polycrystalline and for amorphous samples, even ignoring the values for silicon nitride containing oxide impurities.[77,100,158,159] At 1400–1500 °C the hardness of silicon nitride exceeds that in all the data previously reported for other substances, as was first pointed out by Niihara and Hirai.[100]

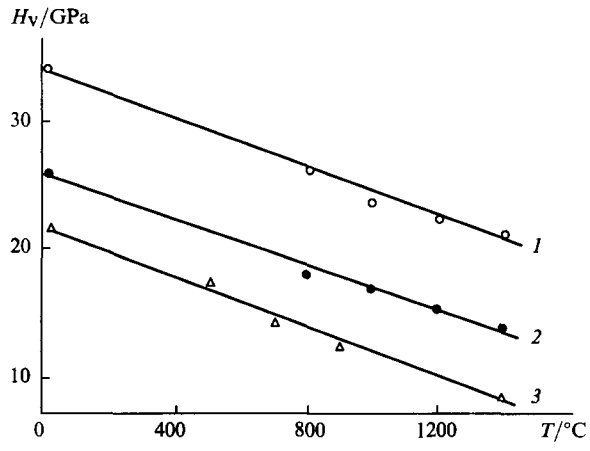


Figure 22. Temperature dependence of the hardness for the $\{1\bar{1}00\}$ (*1*) and (0001) (*2*) of a single crystal,[46] and for a sample of Si_3N_4 containing 2–4.6 mass% of O (*3*).[159] Data for relationships (*1*) and (*2*) were kindly supplied by I E Reimanis.[46]

In this section we shall confine ourselves to an analysis of only a limited number of the physicochemical aspects of the high-temperature strength, in view of the wide range of possible applications of Si_3N_4 in high-temperature technology. In this context problems of impurity effects are of major importance.

It has long been recognised that the presence of oxide additives, introduced in order to activate sintering and hot pressing processes, is accompanied by the formation of liquid interlayers during heating, which in its turn leads to a substantial lowering of the strength indices at temperatures above 1100–1200 °C. The formation of silicate or oxide nitride phases at the grain boundaries and at triple joints has been established by electron microscopy (see Fig. 9).[10] Analyses of the effects of various additives (MgO, Al_2O_3, Y_2O_3, SiO_2, SiC, and REE oxides) on the high-temperature and other properties have been reported by several workers (see, for example, Refs 4, 76, 85, 160–165). We can distinguish at least two approaches to improving the high-temperature behaviour. Firstly the use of silicon nitride powders without oxide additives,[51,77,160,163,166] and secondly the use of a special doping designed to avoid the formation at grain boundaries of vitreous low-melting phases and to encourage the formation of high-temperature crystalline compounds (see, for example, Refs 56, 85, 165).

In a high-temperature study of the strength, rate of propagation of subcritical cracks, elastic modulus, and internal friction it was shown that silicon nitride without added oxides can retain its mechanical properties up to 1450 °C.[51,77,166] It was also pointed out that calcium and halogen impurities play an important role in the high-temperature degradation of the strength, and that the presence of these impurities affects the crystallisation and the behaviour of the silicate phases.

As was pointed out above, oxygen impurities are invariably found in silicon nitride powders. It was shown[85] that samples of Si_3N_4 containing 3.4 mass% of oxygen (in which the oxide nitride Si_2N_2O was detected by XPA in addition to the α phase) retained their strength at the level of ~600 MPa at 1600 °C. However, the microstructure of these samples did not contain the characteristic columnar β crystals (see Figs 8 and 9), and the overall level of strength and crack resistance in this case (as also found by other workers)[51,77,166] was low. According to one report[165] substantial additions of yttrium oxide (up to 15–18 mass%), like additions of other REE oxides,[85] improve both the level and the retention of the strength: at 1400–1500 °C we have σ = 800–850 MPa, the fracture surface being characterised by transgranular features and the K_{Ic} value reaching 13 MPa $m^{1/2}$. These high indices are associated with the formation of a complex Y–Si oxynitride having a high melting point (1850 °C) and with the formation of columnar crystals 7–10 μm long and having a diameter of 0.2–0.7 μm. It is also interesting to note that according to microprobe measurements the distribution of yttrium in the structure was uniform.

The findings mentioned above offer only an empirical outline of new developments in heat-resisting silicon nitride materials. Other data include the effect of the surroundings on the mechanical properties,[148,149,152] the problem of compatibility of the components in composite materials,[12,167] and problems of high-temperature superplasticity.[162,168,169] All these conclusions underline the importance of the concept of controlling the grain boundaries in silicon nitride, as was mentioned above. Unfortunately the nature of the boundaries in these materials has been studied only on a very limited scale.

V. Conclusion

Because of their many desirable physicochemical and physico-mechanical characteristics materials based on Si_3N_4 are finding increasingly wide applications in ordinary industry and in industrial chemical equipment, electronics, turbine construction, and other parts of modern technology.[6–9,170] One of the most promising scientific areas for the application of these materials is in high-temperature techniques. It is thought that the striking progress in the measurement of the melting point could lead to the creation of a new generation of silicon nitride refractory materials, working at temperatures of ~2000 °C. The results shown in Fig. 22 also suggest major possibilities for the use of Si_3N_4 as a material for cutting tools, allowing an increase in the temperature of the cutting site and in the corresponding machining parameters. Of course, these forecasts assume the solution of many nontrivial research and construction technology problems, some of which are mentioned above. Another recent

review[154] also deals with problems in the fundamental study of the creation of a new generation of refractory ceramic materials for use at temperatures up to ~2000 °C.

Silicon nitride is far from having been fully studied as an objective of physicochemical research, and has continued to attract the attention of researchers. Because of the very large number of publications and of the shortage of space, our treatment of some aspects of the silicon nitride problems has been unavoidably superficial. The results of studies carried out mainly during the past 5–10 years have been selectively considered. Again we must stress the large number of publications and the important results obtained in the synthesis of the material and in the study of its high-temperature properties. Recent data on the properties of films of silicon nitride and oxynitride have been reviewed by Habraken and Kuiper.[171] It should also be noted that the unique properties of silicon nitride have allowed the prediction[118] of the new compound carbon nitride, which is now being studied intensively in thin film form.[172]

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Thermodynamics of organoselenium and organotellurium compounds

V I Tel'noi, M S Sheiman

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Abstract. Experimental values of the enthalpies of formation (ΔH_f°) and of the specific heat (C_p°) of the organic compounds of selenium and tellurium are discussed, including their complexes with dialkylzinc and dialkylcadmium. Different forms of the methods of combustion enthalpy and of reaction calorimetry, used to determine the ΔH_f° values, are examined. The enthalpies of breaking of the chemical bonds formed by selenium and by tellurium are calculated from the ΔH_f° values. Data on the temperature dependence of the specific heat are used to find the absolute entropy of these compounds, their temperature, enthalpy, and entropy of melting, their entropy of formation, and other thermodynamic parameters. Special features of the changes in enthalpy, entropy, and Gibbs free energy of the breaking of the chemical bonds are pointed out. The bibliography includes 62 references.

I. Introduction

The organic compounds of selenium and tellurium are used in the preparation of semiconductor and optoelectronic materials. A thermodynamic analysis of the thermal dissociation, hydrogenation, and oxidation processes in these materials should provide a better understanding of their properties. Data on the thermodynamic characteristics of the reactants (in particular, on their enthalpies of formation and vaporisation, and on their entropy) are needed for the calculation of the parameters of the corresponding reactions. These data are important also in relation to the theory of the chemical bond and the theory of heterogeneous catalysis.

Until recently published data on the thermochemistry of this class of compounds were scarce.[1,2] Thus, a detailed review[1] gave the enthalpies of formation of only two organic compounds of selenium and one of tellurium. A substantial volume of information on these topics is now available, and should allow us to establish general trends in the changes in the thermodynamic characteristics of several compounds of this class. The need to correlate the published data is made even more urgent by the fact that the thermodynamic parameters of some of these compounds are given in the relatively inaccessible symposia and abstracts of specialised conferences.

In the present review we shall discuss the enthalpies of formation (ΔH_f°) and other thermodynamic characteristics of organic compounds of selenium and tellurium published up to the middle of 1994, and we shall tabulate those shown to be the most reliable. In the selection of the ΔH_f° values consideration was given to the method of determination, the purity of the starting preparations, the statistical significance of the results obtained in the analysis of the products given by the reactions under test, and the level of precision of the calorimetric experiment (allowance for all the necessary corrections and measurement and calculation errors).

An analysis of the published information showed that the true precision of the determinations of ΔH_f° for these compounds is not usually better than 3–4 kJ mol^{-1}. The achievement of higher precisions is limited partly by the specific properties of the given calorimetric experiment and partly by the need to use several auxiliary thermochemical quantities in the calculations. Their values are tabulated in the standard handbooks,[3–5] but often their precision is low and they are not mutually consistent. Therefore the experimental values of ΔH_f° are rounded off in the present review.

The vaporisation enthalpies, needed in the calculation of the ΔH_f° value of these substances in the gaseous monomeric state, are quoted (in most cases) in the papers which give the experimental values of their enthalpies of formation in the condensed state. In other cases they are quoted from Refs 6–9.

Experimental values of the enthalpies of formation, the specific heats, and other thermodynamic functions were used in calculations of the average enthalpies, entropies, and Gibbs functions of the breaking of the chemical bonds formed by selenium and tellurium in the various compounds. The error in the thermodynamic quantities corresponds to a 95% confidence level.

II. Auxiliary parameters

To ensure mutual compatibility of the thermochemical parameters discussed in this review the parameters were calculated from a single set of key values, listed in Table 1.

The most important quantities in these calculations were the ΔH_f° parameters for crystalline SeO_2 and TeO_2.

V I Tel'noi, M S Sheiman Thermochemistry Laboratory, Chemical Research Institute of the Lobachevskii Nizhegorod State University, 603 600 Nizhny Novgorod, prospekt Gagarina 23/25.
Fax (7-831) 235 64 80

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Table 1. Enthalpies of formation used in the calculation of the thermodynamic parameters of formation of organic compounds of selenium and tellurium.

Substance[a]	ΔH_f° kJ mol^{-1}	Ref.	Substance	ΔH_f° kJ mol^{-1}	Ref.
O (g)	249.2 ± 0.1	4, 5	$CH_2=CH$ (g)	261.5 ± 8.4	4, 5
S (g)	272.8 ± 1.3	4	C_2H_5 (g)	107.5 ± 4.2	4
Se (g)	227.7 ± 4.2	4	C_3H_7 (g)	87.9 ± 8.4	12
Te (g)	191.7 ± 1.0	4	i-C_3H_7 (g)	73.6 ± 4.2	12
CO_2 (g)	−393.51 ± 0.13	4, 5	C_4H_9 (g)	71.1 ± 8.4	12
H_2O (l)	−285.81 ± 0.04	4	C_5H_{11} (g)	38 (estimate)	12
SeO_2 (cr)	−225.5 ± 2.1	10	i-C_5H_{11} (g)	32 (estimate)	12
TeO_2 (cr)	−328.9 ± 1.7	11	C_6H_5 (g)	325 ± 8	12
CH_3 (g)	146.3 ± 0.5	5	$C_6H_5CH_2$ (g)	188 ± 4	12

[a] Here and elsewhere the physical states of the substances for which thermodynamic parameters are denoted by cr (crystal), l (liquid), and g (gas).

The ΔH_f° value for SeO_2(cr) taken from Barnes and Mortimer[10] had been determined from measurements of the enthalpy of combustion of hexagonal selenium by the rotating bomb method (a high-precision measurement). Their result was indistinguishable from those of other workers,[13,14] who used a stationary calorimetric bomb for the combustion of selenium.

On the other hand the ΔH_f° values for TeO_2 obtained in different laboratories differed by ~80 kJ mol^{-1} (Table 2). Therefore the present writers redetermined[11] the enthalpy of formation of TeO_2 by burning very pure crystalline (hexagonal) tellurium in a calorimetric bomb. The value thus obtained for TeO_2(cr) (Table 1) was significantly higher than some reported values,[15,19,20] and differed very markedly from others.[16–18]

Table 2. Enthalpies of formation of crystalline tellurium dioxide (298.15 K).

$-\Delta H_f^\circ$/kJ mol^{-1}	Method of determination	Ref.
321.7 ± 5.0	Combustion calorimetry	15
379.1 ± 1.3	"	16
351.9 ± 12.0	Mass spectrometry	17
301.2 ± 2.1	Measurement of the emf of a reaction involving TeO_2 (cr)	18
321.1 ± 1.3	"	19
320.4 ± 3.0	Reaction calorimetry	20
328.9 ± 1.7	Combustion calorimetry	11

Some of the previous measurements[15,16] had been made by burning tellurium in oxygen in a stationary calorimetric bomb. However, the need to use relatively large samples of tellurium in these experiments led to incomplete oxidation and to the formation of combustion products having a complex composition. The difficulty of determining the appropriate energy corrections is mainly responsible for the inconsistency of the previous results[15,16] and for the difference between those results and ours.[11]

The high value of ΔH_f° for TeO_2(cr) obtained mass-spectroscopically (see Table 2) is probably due to the difficulty of allowing for the excess energy of the products formed from the starting material under the influence of electron collisions.[21]

Cordfunke et al.[20] determined the enthalpy of formation of TeO_2 by two independent methods: by studying the enthalpy of dissolution of solid Te, TeO_2, UO_3, and U_3O_8 in an aqueous solution of H_2SO_4 + $K_2Cr_2O_7$ + $MnSO_4$ and the enthalpy of dissolution of Te, TeO_2, Na_2SO_3, and Na_2SO_4 in an aqueous solution of NaClO + NaOH. By combining the measured effects, enthalpies of dissolution of tellurium dioxide equal respectively to −318.74 ± 7.35 and −320.71 ± 3.22 kJ mol^{-1} were obtained (an averaged value is given in Table 2). Obviously, the reliability of these results[20] depends on the reliability of the auxiliary data. Thus, the use of the parameter ΔH_f° (Na_2SO_3) = −1096.78 ± 0.81 kJ mol^{-1} instead of that used by the writers[20] (−1101.83 ± 0.72 kJ mol^{-1}) makes the value of ΔH_f° for Te_2O(cr) −330.8 ± 3.3 kJ mol^{-1} (see Refs 22 and 23), which differs by more than 10 kJ mol^{-1} from the value given in Table 2 but agrees with our value within experimental error.

III. Enthalpies of formation of organoselenium compounds

The combustion of Se compounds in a calorimetric bomb leads to the formation of solid selenium dioxide, which is easily soluble in the water present in the bomb. The energy corrections associated with the dissolution are applied during the processing of the experimental data.

Because of the rapid dissolution of the SeO_2 in water the combustion of selenium compounds can be carried out successfully in calorimeters with both stationary and rotating bombs. This conclusion is confirmed, in particular, by the good agreement between the enthalpies of combustion (ΔH_f°) of crystalline selenium obtained in a rotating[10] and in a stationary bomb respectively.[13,14]

Because of the relatively small enthalpy of dissolution of selenium dioxide in an excess of water (3.85 ± 0.08 kJ mol^{-1}) possible differences in the concentration of the aqueous solutions in different parts of the stationary calorimeter can be ignored.

The method of combustion in a stationary bomb has been widely used for selenium compounds.[24–29]

In a series of experiments in our laboratory[26–29] the compounds (held in thin-walled glass bulbs) were placed in the bomb in a quartz crucible together with a wafer of the benzoic acid standard. The mass of substance burned was determined from the amount of carbon dioxide formed during the experiment. It was established calorimetrically (from the depression of freezing point) that the total content of organic impurities in samples of dialkyl compounds purified by fractional distillation was not more than 0.05–0.10 mol%, and the content of metals was found (by spectroscopic analysis) to be 1×10^{-3} mol%.

Our value[28] of ΔH_f° for liquid diethyl selenide (−59.8 ± 3.3 kJ mol^{-1}, Table 3) differs markedly from the value reported by Merten and Schlüter[24] (−90.8 ± 3.8 kJ mol^{-1}). The latter was obtained by a low-level calorimetric technique, and it cannot be considered reliable. Thus, though the method of synthesis of the diethyl selenide was stated,[24] the purity of the resulting samples was not characterised, the completeness of the combustion was not established, and only ~20% of the total energy evolved in the experiment was ascribed to the compound under study.

Tsvetkov and Kozyrkin[30] obtained ΔH_f° for liquid $(C_2H_5)_2Se$ by studying the reaction of diethyl selenide with an excess of bromine. It was assumed that $SeBr_4$ was the only product containing selenium formed under these conditions. However, as has been reported,[31] the reaction of $(C_2H_5)_2Se$ with liquid bromine can lead to the formation of $(C_2H_5)_2SeBr_2$: even a trace of this compound among the reaction products could seriously distort the results.[30] Our ΔH_f° value[28] for $(C_2H_5)_2Se$ is given

Table 3. Standard enthalpies of formation (in kJ mol^{-1}) of organoselenium compounds at 298.15 K.

Compound	ΔH_f° (l or cr)	ΔH_f° (g)	Method of determination[a]	Ref.
$(CH_3)_2Se$ (l)	-12 ± 8	18 ± 8	SB	26–28
$(CH_2=CH)_2Se$ (l)	166 ± 8	208 ± 8	SB	26–28
$(C_2H_5)_2Se$ (l)	-60 ± 3	-21 ± 4	SB	28
$(i\text{-}C_3H_7)_2Se$ (l)	-151 ± 3	-108 ± 4	RB	33
$(C_5H_{11})_2Se$ (l)	-225 ± 4	-173 ± 5	RB	33
$(C_6H_5)_2Se$ (l)	226 ± 6	290 ± 6	RB	10
$(C_6H_5CH_2)_2Se$ (cr)	2 ± 20	–	SB	24
$C_8H_7N_2Se$ (cr)	358 ± 8	452 ± 8	SB	25
$(CH_3)_2Se_2$ (l)	9 ± 8	54 ± 8	SB	28
$(C_2H_5)_2Se_2$ (l)	-63 ± 12	-16 ± 12	SB	29
$(C_4H_9)_2Se_2$ (l)	-144 ± 21	-88 ± 21	SB	29
$(C_6H_5)_2Se_2$ (cr)	121 ± 8	237 ± 11	RB	32
$(C_6H_5CH_2)_2Se_2$ (cr)	171 ± 3	301 ± 3	SB	25
C_6H_5SeBr (cr)	34 ± 5	112 ± 6	R	34
$C_6H_5SeBr_3$ (cr)	8 ± 5	79 ± 6	R	34

[a] Here and elsewhere the following symbols are used: SB for combustion in a stationary bomb; RB for combustion in a rotating bomb; R for reaction method.

as the recommended value in Table 3. The combustion of organoselenium compounds in a rotating bomb was first used by Mortimer and coworkers [10,32] to determine the enthalpy of combustion of diphenyl selenide and diphenyl diselenide. The diphenyl selenide (in a polyester bulb) was burned in a thin-walled quartz crucible. By determining the mass of carbon dioxide in the resulting products it was shown that the extent of combustion in the compound under study was not less than 99.94%. 50 cm^3 of distilled water was previously placed in the bomb to dissolve the selenium dioxide produced by the combustion. In order to allow for various side effects (for example, the dissolution of carbon dioxide in the aqueous solution of SeO_2) the authors [10,32] carried out a set of 'comparison experiments'. In these experiments they burned benzoic acid, choosing its mass and the concentration of the aqueous solution of SeO_2 added to the bomb so as to ensure that the final states of the reacting systems in the comparison experiments and in the experiments on the combustion of selenium compounds were as nearly as possible identical.

The rotating bomb method was used also in a study [33] of a series of organic compounds of sulfur, selenium, and tellurium (see Tables 3 and 4).

Table 4. Standard enthalpies of formation (in kJ mol^{-1}) of organotellurium compounds at 298.15 K.

Compound	$-\Delta H_f^\circ$ (l or cr)	ΔH_f° (g)	Method of determination	Ref.
$(CH_3)_2Te$ (l)	-9 ± 5	-44 ± 5	SB	27, 28, 42
$(CH_2=CH)_2Te$ (l)	-216 ± 8	-261 ± 9	SB	27, 28, 42
$(C_2H_5)_2Te$ (l)	46 ± 5	4 ± 5	SB	28
$(C_3H_7)_2Te$ (l)	89 ± 3	44 ± 3	SB	28
$(i\text{-}C_3H_7)_2Te$ (l)	87 ± 3	46 ± 3	SB	28
$(C_4H_9)_2Te$ (l)	107 ± 4	56 ± 4	SB	33
$(C_5H_{11})_2Te$ (l)	196 ± 6	137 ± 6	SB	43
$(i\text{-}C_5H_{11})_2Te$ (l)	200 ± 7	148 ± 7	SB	43
$(C_6H_5)_2Te$ (l)	-240 ± 5	-307 ± 10	SB	44, 45
$(C_3H_7)_2Te_2$ (l)	24 ± 4	-29 ± 4	RB	33
$(C_4H_9)_2Te_2$ (l)	70 ± 5	13 ± 5	RB	33
$(C_6H_5)_2Te_2$ (cr)	-250 ± 5	–	SB	44
$CH_3(C_2H_5)_2TeBr$ (cr)	156 ± 8	–	R	30

A calorimetric determination of the enthalpy of interaction of $(C_6H_5)_2Se_2$ with one and with three moles of bromine, dissolved respectively in carbon tetrachloride and in trichlorobenzene, has been reported. [34] In the first case C_6H_5SeBr was formed quantitatively, in the second $C_6H_5SeBr_3$. The enthalpies of formation of crystalline and of gaseous C_6H_5SeBr and $C_6H_5SeBr_3$ were calculated from the results thus obtained and from the ΔH_f° value for crystalline $(C_6H_5)_2Se_2$ previously obtained. [32] Recommended values of the enthalpies of formation of these organoselenium compounds are shown in Table 3.

There are several reports [35–40] of the enthalpy of reaction (ΔH_r°) of the selenides SeR_2 (R = CH_3, C_2H_5) with the compounds MR_2 (M = Zn, Cd). In the liquid phase this interaction led to the formation of the corresponding equimolecular complexes of the donor-acceptor type. In some cases the ΔH_r° values were obtained directly (by studying a mixture of the compounds in a 1:1 ratio) [35,36] in other cases they were obtained by studying the liquid–vapour equilibrium of the corresponding equimolecular mixtures. [37–40]

The enthalpies of vapour formation of the $R_2Se \cdot MR_2$ complexes and of the starting substances were determined [38–40] at 298.15 K in an isothermal differential micro-calorimeter. It had previously been established that the compounds under study were fully dissociated in the gas phase. This allowed the ΔH_r° values to be calculated as the difference between the vaporisation enthalpies of the equimolecular solution and the corresponding individual substances.

The vaporisation enthalpies (ΔH_v°) of the complexes, the reaction enthalpies of the starting components in the liquid phase calculated from them, and the enthalpies of formation of the liquid complexes (in kJ mol^{-1}), obtained experimentally, [38–40] are listed below:

Complexes	ΔH_v°	$-\Delta H_f^\circ$	ΔH_f°
$Zn(CH_3)_2 \cdot Se(CH_3)_2$	66.3 ± 1.9	6.2 ± 2.0	6 ± 8
$Zn(C_2H_5)_2 \cdot Se(C_2H_5)_2$	79.9 ± 0.8	4.2 ± 1.1	-48 ± 4
$Cd(CH_3)_2 \cdot Se(CH_3)_2$	74.6 ± 1.4	6.0 ± 1.4	49 ± 9

In the calculation of the ΔH_f° values allowance was made for the enthalpies of formation of the selenides (see Table 3) and for published data [1] on the enthalpies of formation of liquid $Zn(CH_3)_2$ (23.8 ± 2.1), $Zn(C_2H_5)_2$ (16.3 ± 2.1), and $Cd(CH_3)_2$ (66.9 ± 4.2) kJ mol^{-1}. ΔH_r° values close to those in the above tabulation have also been obtained in a calorimetric study [35,36] of the mixing of the initial components.

IV. Enthalpies of formation of organotellurium compounds

In spite of the large number of organotellurium compounds whose synthesis has been reported [41] and of their great practical interest a systematic study of the thermochemistry of these materials was only recently started: in 1988, when the present writers' laboratory reported a determination [42] of the enthalpies of combustion of dimethyl and divinyl tellurides (see Table 4). The combustion enthalpies of these substances were determined in a calorimeter fitted with a stationary calorimetric bomb. The weight of sample consumed was determined from the quantity of carbon dioxide formed by its combustion to within ~0.1%.

According to the X-ray phase analysis results the solid combustion product was a mixture of tetragonal tellurium dioxide and a small amount (not more than 5%) of the orthorhombic modification. The amount of tellurium in the washings of the bomb after the combustion of the starting compounds was determined by atomic absorption spectroscopy, thus allowing the energy corrections associated with the dissolution of the tellurium products in the water produced by the reaction to be calculated.

A similar method was used[27,28,43-45] to find the enthalpies of formation of several alkyl and phenyl tellurides (see Table 4).

Several tellurium compounds were studied by the rotating bomb method.[33] The sample in a Terylene bulb was placed on an iridium grid below which a platinum crucible containing a wafer of benzoic acid was located. The experimental compounds were located in the maximum temperature region of the burning wafer, and therefore were oxidised almost completely.

An aqueous solution of HNO_3 has been used[33] as the bomb liquid. According to the authors this procedure led to the formation of amorphous hydrated TeO_2, whose enthalpy of formation had been determined in separate experiments. However, the report[33] omits many essential experimental details needed to substantiate the correctness of the proposed method. In particular, combustion equations for the experimental substances are not given, and therefore the chemical mechanism of the processes taking place in the calorimetric bomb cannot be established. The formation of stable hydrates of TeO_2 among the combustion products is arguable, because of the very low solubility of this dioxide in water (1 g TeO_2 dissolves in 15×10^4 g of H_2O).[46] Furthermore the use of a platinum crucible may cause alloying of the platinum with the combustion products containing tellurium.[46] Nevertheless some of the results from Ref. 33 are included in Tables 3 and 4, and have been used to calculate the enthalpies of the breaking of the corresponding bonds.

The only reported use of reaction calorimetry[30] is in an investigation of the enthalpy of interaction of diethyl telluride with an excess of liquid bromine. It was assumed[30] that the products of this interaction are solid $TeBr_4$ and ethyl bromide dissolved in bromine. However, as was pointed out,[31] the products of this reaction can include diethyl dibromotelluride, which requires an allowance for the appropriate energy corrections.

Pavlovskii and coworkers[39,40] determined the enthalpies of vaporisation of the complexes of dimethyl telluride with the methyl compounds of zinc and cadmium. By combining their results with the ΔH_v° values previously obtained for the starting components they calculated the enthalpies of their interaction in the liquid phase, as was done for the selenide complexes discussed above.

The enthalpies of vaporisation of the tellurium complexes, the reaction enthalpies of the starting components in the liquid phase, and the enthalpies of formation of the liquid complexes (in kJ mol^{-1}, the latter two calculated from the former) are listed below:

Complex	ΔH_v°	$-\Delta H_r^\circ$	ΔH_f°
$Zn(CH_3)_2 \cdot Te(CH_3)_2$	70.4 ± 1.1	4.8 ± 1.3	10 ± 6
$Cd(CH_3)_2 \cdot Te(CH_3)_2$	80.4 ± 1.2	6.4 ± 1.3	52 ± 7

The enthalpy of formation of dimethyl telluride (shown in Table 4) and the enthalpies of formation of the dimethyl compounds of zinc and cadmium recommended in Ref. 1 were used to calculate the ΔH_f° values.

We may conclude from these results that the ΔH_f° values for $(CH_3)_2Te$ and those of the same parameter for dimethyl selenide are indistinguishable within the uncertainties of the determination. the enthalpy of the reaction

$$(NH_4)_2PdCl_4(cr) + 2\,Te(C_2H_5)_2(l) \longrightarrow$$

$$\longrightarrow PdCl_2 \cdot 2\,Te(C_2H_5)_2(cr) + 2\,NH_4Cl(cr),$$

was determined calorimetrically[47] as -175.7 ± 4.8 kJ mol^{-1}.

ΔH_f° for $PdCl_2 \cdot 2Te(C_2H_5)_2(cr)$ was calculated from the enthalpies of formation of liquid $(C_2H_5)_2Te$ (see Table 4) and of crystalline $(NH_4)_2PdCl_4$ (-841.0 ± 1.7) and NH_4Cl (-314.4 ± 0.1 kJ mol^{-1}).[47] The result was -480 ± 10 kJ mol^{-1}, which is close to the previously reported value $\Delta H_f^\circ = -456 \pm 10$ kJ mol^{-1} for $PdCl_2 \cdot 2Se(C_2H_5)_2(cr)$, recalculated by the present writers[48] by using a new value of the enthalpy of formation of $(C_2H_5)_2Se$ (see Table 3).

By using the calculated[47] enthalpies of sublimation of the tellurium (192 kJ mol^{-1}) and the selenium complex (160 kJ mol^{-1}) the following ΔH_f° values were obtained: -288 for $PdCl_2 \cdot 2Te(C_2H_5)_2(g)$ and -296 kJ mol^{-1} for $PdCl_2 \cdot 2Se(C_2H_5)_2(g)$.

In this calculation[47] the enthalpy of mixing of liquid diethyl telluride with liquid bromine (-188 ± 4 kJ mol^{-1}) was erroneously taken from Ref. 30 instead of its enthalpy of formation (see Table 4), and this led to an erroneous determination of the ΔH_f° value for crystalline $PdCl_2 \cdot 2Te(C_2H_5)_2$ (-763.8 ± 14.6 kJ mol^{-1}).

V. Specific heats, entropies, and Gibbs free energies of formation of organoselenium and organotellurium compounds

The temperature dependence of the specific heat (C_p°) for a series of alkyl and vinyl compounds of selenium and of tellurium has been determined[49-56] experimentally at 5–310 K. The measurements were made in a vacuum adiabatic calorimeter whose design and methods of calibration, measurement, and calculation offered results with an uncertainty of ~0.2% at 30–310 K, 0.5% at 12–30 K, and 1.5% at even lower temperatures. The experimental materials were specially purified, and according to chromatographic and mass spectrometric analyses their purity was 99.9 mol%. According to the depression of freezing point, measured during the study of the specific heat for each of the samples, the total content of impurities not forming solid solutions with the main substance was less than 0.1 mol%.

In these studies of the specific heat it was found that when rapidly cooled divinyldipropyl-, and dibutyl telluride are easily supercooled with formation of glasses, whereas the dimethyl and the diethyl compound show polymorphism. The thermodynamic characteristics of these transitions were determined in the course of these studies. The melting point (T_m) and the enthalpy (ΔH_m°) and entropy (ΔS_m°) of melting of the compounds were also determined (Table 5).

A special feature of liquid alkyl compounds of selenium and tellurium is an anomalous change in their specific heat. Immediately after melting the specific heat falls a little with increase in temperature, but after going through a minimum it shows the normal behaviour and begins to rise again. It has been suggested that these liquids are partially associated at temperatures close to T_m. Therefore the observed heat capacity includes both the true heat capacity of the liquid and the heat capacity contributed by the dissociation of the associated species. The decrease in the degree of association with increase of temperature suppresses this contribution to the specific heat, leading to the appearance of a minimum on its temperature dependence.

The entropy $[S^\circ(T)]$, the enthalpy of heating $[H^\circ(T) - H^\circ(0)]$, and the Gibbs function $[G^\circ(T) - H^\circ(0)]$ of these compounds in the condensed state were calculated from experimental data on the temperature dependence of the specific heat. The values thus obtained for 298.15 K are shown in Table 5.

From the absolute entropy values for a group of selenium and tellurium compounds their entropies of formation (ΔS_f°) from the elements in the condensed and the gaseous state were calculated. Published data[6-9] on the vapour pressure and on the enthalpies of vaporisation were used in these calculations. The entropies of the elements (needed in these calculations) were taken from standard tabulations.[4,5]

The Gibbs free energy of formation for these compounds (ΔG_f°) were calculated from the enthalpies of formation (see Tables 3 and 4). The results are shown in Table 6.

Table 5. Thermodynamic functions (298.15 K) and melting parameters of selenium and tellurium compounds

Compound	C_p°	S°	$[H^\circ(T)-H^\circ(0)]$	$-[G^\circ(T)-H^\circ(0)]$	T_m°/K	ΔH_m°	ΔS_m°
$(CH_3)_2Se$	121.1	210.8	31.78	31.08	185.14	8.499	49.90
$(CH_2=CH)_2Se$	165.7	262.0	39.94	38.17	178.08	9.374	52.64
$(C_2H_5)_2Se$	174.0	284.9	44.17	40.77	175.30	12.60	71.85
$(CH_3)_2Se_2$	155.0	261.4	38.78	36.16	190.89	8.545	44.76
$(CH_3)_2Te$	125.1	220.5	33.10	32.64	201.87	7.766	38.47
$(C_2H_3)_2Te$	166.1	268.1	41.26	38.67	182.65	9.593	52.52
$(C_2H_5)_2Te$ [a]	183.4	291.0	42.48	44.27	161.50	7.621	47.20
					153.33	7.525	40.87
$(C_3H_7)_2Te$	233.7	362.2	56.38	51.60	191.80	14.28	74.43
$(C_4H_9)_2Te$	286.4	426.0	65.73	62.08	177.05	14.57	82.30
$(C_5H_{11})_2Te$	345.9	501.0	80.88	69.42	215.41	23.11	107.8
$(C_6H_5)_2Te$	305.7	332.4	57.04	42.05	268.53	15.35	57.16

Notes. The parameters C_p°, S°, ΔS_m° are in J mol^{-1} K^{-1}; the functions $[H^\circ(T)-H^\circ(0)]$ and $-[G^\circ(T)-H^\circ(0)]$, and ΔH_m°, are in kJ mol^{-1}. [a] Crystallises in two modifications.

Table 6. Absolute entropies (S°, J mol^{-1} K^{-1}), entropies ($-\Delta S_f^\circ$, J mol^{-1} K^{-1}) and Gibbs free energies (ΔG_f°, kJ mol^{-1}) for the formation of selenium and tellurium compounds at 298.15 K.

Compound	S° (g)	$-\Delta S_f^\circ$ (l)	$-\Delta S_f^\circ$ (g)	ΔG_f° (l)	ΔG_f° (g)
$(CH_3)_2Se$	302.7	234.8	145.5	58	61
$(CH_2=CH)_2Se$	357.6	195.0	99.4	224	237
$(C_2H_5)_2Se$	386.1	431.8	330.6	69	77
$(CH_3)_2Se_2$	–	226.4	–	76	–
$(CH_3)_2Te$	317.7	231.5	130.9	78	83
$(CH_2=CH)_2Te$	361.7	194.7	101.3	274	291
$(C_2H_5)_2Te$	392.4	432.9	331.5	83	95
$(C_3H_7)_2Te$	496.6	633.7	526.3	100	113
$(C_4H_9)_2Te$	534.9	841.8	732.9	144	162
$(C_5H_{11})_2Te$	617.8	1038.7	921.9	114	138

The specific heat and the entropy of the dimethyl compounds of selenium and tellurium in the ideal gas state were calculated also by statistical thermodynamics from spectroscopic data and from information on the structure of the molecules.[57] The calculations were carried out in the rigid rotator–harmonic oscillator approximation for the 273–1500 K temperature range.

The reliability of the calculated results [57] can be established by comparing them with experimental data. For example, the calculated entropies of $(CH_3)_2Se$ and $(CH_3)_2Te$ at 298.15 K are 300 and 309 J mol^{-1} K^{-1} (see Ref. 57), whereas calorimetric measurements for these compounds gave 302.7 and 317.7 J mol^{-1} K^{-1} (see Table 6).

It can be seen that for $(CH_3)_2Se$ the agreement between calculated and experimental results is good, but for $(CH_3)_2Te$ the calculated entropy differs from the calorimetric value by almost 3%, suggesting that the method of calculation used by Mosin et al. [57] should be reconsidered.

Studies of the specific heat in the 6–10 K range have been reported also for some complexes formed by selenium and tellurium compounds with zinc and cadmium alkyls.[58–60] From these values of the specific heat the absolute entropies were calculated, and by using the entropies of the starting components [61] (see Table 6) and their interaction enthalpies the entropies and Gibbs free energies of the reaction (ΔS_r° and ΔG_f° respectively) were also calculated:[38–40]

$$R_2M\ (l) + R_2M'\ (l) \longrightarrow R_2M \cdot R_2M'\ (l),$$

where R = CH_3, C_2H_5; M = Se, Te; M′ = Zn, Cd.

The results of these calculations are shown in Table 7.

Table 7. Specific heats (J mol^{-1} K^{-1}) and entropies of the complexes, entropies (J mol^{-1} K^{-1}) and Gibbs free energies (kJ mol^{-1}) of the synthesis reactions of the liquid complexes at 298.15 K.

Complex	C_p°	S°	$-\Delta S_r^\circ$	$-\Delta G_r^\circ$
$(CH_3)_2Se \cdot Zn(CH_3)_2$	287.2	401.1	11.3	2.8 ± 2.0
$(CH_3)_2Se \cdot Cd(CH_3)_2$	277.7	413.6	−0.8	6.2 ± 1.4
$(CH_3)_2Te \cdot Zn(CH_3)_2$	284.0	420.7	1.4	4.3 ± 1.3
$(CH_3)_2Te \cdot Cd(CH_3)_2$	275.2	413.1	9.5	3.5 ± 1.3
$(C_2H_5)_2Te \cdot Zn(C_2H_5)_2$	399.0	556.9	10.6	–

The uncertainties in the determination of the $\Delta G_r^\circ(l)$ values shown in Table 7 are determined mainly by the errors in the enthalpies of interaction of the corresponding components.[38–40] As can be seen from Table 7 the $\Delta G_r^\circ(l)$ values for all the complexes have small and not very different negative values.

VI. Average enthalpies, entropies, and Gibbs free energies of the breaking of chemical bonds in the organic compounds of selenium and tellurium

It is interesting to consider the dependence of the strength of chemical bonds on the nature of the atoms and radicals from which the bonds are formed. The determination of the enthalpy of breaking of individual bonds in various compounds is usually a difficult experimental problem, and therefore the average enthalpies of bond breaking ($\bar{D}$) are often calculated.

The $\bar{D}$ values shown in Table 8 for the M–R bonds in the compounds MR_2 (M = Se or Te, R is a radical) are the enthalpy of the reaction $MR_2(g) \rightarrow M(g) + 2R(g)$ divided by the number of bonds. This quantity is calculated by using the formula

$$\bar{D}(M-R) = \tfrac{1}{2}[\Delta H_f^\circ(M, g) + 2\Delta H_f^\circ(R, g) - \Delta H_f^\circ(MR_2, g)],$$

and employing data for the enthalpies of formation of the gaseous reactants in the appropriate reaction.

The $\bar{D}(M-M)$ values in the compounds (MR_2) were calculated by means of the equation

$$\bar{D}(M-M) = 2\Delta H_f^\circ(M, g) + 2\Delta H_f^\circ(R, g) - \Delta H_f^\circ[(MR)_2, g] - 2\bar{D}(M-R).$$

It is assumed that the enthalpies of breaking of the M–R bonds are identical in the corresponding MR_2 and $(MR)_2$ compounds.

Table 8. Average enthalpies of bond breaking (298.15 K).

Compound	Bond	$\bar{D}$/kJ mol^{-1}	Compound	Bond	$\bar{D}$/kJ mol^{-1}
$(CH_3)_2O$	$O-CH_3$	360 ± 4	$(C_4H_9)_2Se_2$	$Se-Se$	211 ± 22
$(C_2H_5)_2O$	$O-C_2H_5$	356 ± 4	$(C_6H_5)_2Se_2$	$Se-Se$	280 ± 13
$(C_6H_5)_2O$	$O-C_6H_5$	427 ± 8	C_6H_5SeBr	$Se-Br$	258 ± 12
$(CH_3)_2S$	$S-CH_3$	297 ± 4	$C_6H_5SeBr_3$	$Se-Br$	172 ± 4
$(C_2H_5)_2S$	$S-C_2H_5$	285 ± 4	$(CH_3)_2Te$	$Te-CH_3$	220 ± 3
$(C_6H_5)_2S$	$S-C_6H_5$	347 ± 8	$(CH_2=CH)_2Te$	$Te-C_2H_3$	227 ± 9
$(CH_3)_2Se$	$Se-CH_3$	251 ± 4	$(C_2H_5)_2Te$	$Te-C_2H_5$	206 ± 5
$(CH_2=CH)_2Se$	$Se-C_2H_3$	271 ± 8	$(C_3H_7)_2Te$	$Te-C_3H_7$	206 ± 8
$(C_2H_5)_2Se$	$Se-C_2H_5$	232 ± 5	$(i\text{-}C_3H_7)_2Te$	$Te-i\text{-}C_3H_7$	192 ± 4
$(i\text{-}C_3H_7)_2Se$	$Se-i\text{-}C_3H_7$	241 ± 5	$(C_4H_9)_2Te$	$Te-C_4H_9$	195 ± 8
$(C_5H_{11})_2Se$	$Se-C_5H_{11}$	238	$(C_5H_{11})_2Te$	$Te-C_5H_{11}$	202
$(C_6H_5)_2Se$	$Se-C_6H_5$	294 ± 8	$(i\text{-}C_5H_{11})_2Te$	$Te-i\text{-}C_5H_{11}$	202
$(CH_3)_2Se_2$	$Se-Se$	192 ± 12	$(C_6H_5)_2Te$	$Te-C_6H_5$	267 ± 9
$(C_2H_5)_2Se_2$	$Se-Se$	222 ± 13	$(C_3H_7)_2Te_2$	$Te-Te$	119 ± 5
			$(C_4H_9)_2Te_2$	$Te-Te$	149 ± 6

Table 9. Average values of the entropy (J mol^{-1} K^{-1}) and the Gibbs free energy (kJ mol^{-1}) for the breaking of bonds at 298.15 K.

Compound[a]	Bond	$\Delta\bar{S}$	$\Delta\bar{G}$
$(CH_3)_2O$	$O-CH_3$	141	318
$(C_2H_5)_2O$	$O-C_2H_5$	161	308
$(CH_3)_2S$	$S-CH_3$	135	257
$(C_2H_5)_2S$	$S-C_2H_5$	152	240
$(CH_3)_2Se$	$Se-CH_3$	131	208
$(CH_2=CH)_2Se$	$Se-C_2H_3$	143	229
$(C_2H_5)_2Se$	$Se-C_2H_5$	147	188
$(CH_3)_2Te$	$Te-CH_3$	126	182
$(CH_2=CH)_2Te$	$Te-C_2H_3$	143	184
$(C_2H_5)_2Te$	$Te-C_2H_5$	147	162

[a] Because of the lack of the appropriate auxiliary data the quantities $\Delta\bar{S}$ and $\Delta\bar{G}$ cannot be calculated for all the compounds listed in Tables 3 and 4.

For comparison we show in Table 8 the $\bar{D}$ values for various bonds which include oxygen or sulfur. These calculations relied on data given in Tables 1, 3, and 4 and in published tabulations.[3-5,12,62]

In Table 9 we list the average entropies ($\Delta\bar{S}$) of bond breaking, obtained by the expression

$$\Delta\bar{S}(M-R) = \tfrac{1}{2}[S^\circ(M,\ g) + 2\,S^\circ(R,\ g) - S^\circ(MR_2,\ g)],$$

where S° are the standard entropies of the reactants in the dissociation of the compound MR_2 (see Table 6) into the fragments M and 2R (see Refs 3-5).

The $\Delta\bar{S}(M-R)$ and $\bar{D}(M-R)$ values were used to calculate the average values of the Gibbs free energy ($\Delta\bar{G}$) for the breaking of the M-R bonds, which we used as a measure of their thermodynamic stability (Table 9). The calculations for a temperature of 298.15 K were carried out using the equation

$$\Delta\bar{G}(M-R) = \bar{D}(M-R) - 298.15\,\Delta\bar{S}(M-R).$$

* * *

An analysis of the calculated and the experimental data reported above or previously published has established the following features of the thermodynamic characteristics of the bonds formed by selenium and by tellurium.

1. In the compounds R_2M (where M = O, S, Se, Te) of the same radical R the average enthalpy, entropy, and Gibbs free energy of the breaking of the M-R bond decrease as the atomic number of the element M increases.

2. For a given element M the average enthalpies of bond breaking vary in the following sequence:

$$M-C_6H_5 > M-C_2H_3 > M-CH_3 > M-C_2H_5$$

$$\approx M-C_3H_7 \approx M-C_4H_9 \approx M-C_5H_{11}.$$

3. The enthalpy of breaking of the $Te-C_3H_7$ bond in $Te(n\text{-}C_3H_7)_2$ is higher by 14 kJ mol^{-1} than the same parameter in $Te(i\text{-}C_3H_7)_2$, as is also found in the propyl compounds of mercury, boron, and tin.[1]

4. The parameters $\bar{D}(M-M)$ in the compounds $(RM)_2$ (except diphenyl diselenide) are not markedly dependent on the nature of the R radical; they are much smaller than the $\bar{D}(M-R)$ values in the R_2M compounds with the same radicals (see Table 8) and $\bar{D}(M-M)$ in the M_2 (g) molecules,[11] for which $D(Se-Se)$ = 305 and $D(Te-Te)$ = 259 kJ mol^{-1}.

In spite of the experimental ΔH_f° values available for the crystalline dibenzyl selenide and diselenide (see Table 3) a precise calculation of the enthalpy of breaking of the Se-Se bond in $(C_6H_5CH_2)_2Se_2$ is impossible because of the lack of data on the enthalpy of sublimation of $(C_6H_5CH_2)_2Se$, needed to calculate ΔH_f° for this compound in the gas phase. However, an approximate estimate of $\bar{D}(Se-Se)$ in dibenzyl diselenide can be made by assuming that $\bar{D}(Se-CH_2C_6H_5)$ in dibenzyl selenide is $\sim$63 kJ mol^{-1} lower than $\bar{D}(Se-C_2H_5)$ in diethyl selenide (see Table 8), i.e. as is observed in tetraethyl- and tetrabenzyl-germanium,[1] for which $\bar{D}(Ge-C_2H_5) = 243 \pm 4$ and $\bar{D}(Ge-CH_2C_6H_5) = 180 \pm 4$ kJ mol^{-1}. In this case the calculation of $\bar{D}(Se-Se)$ in dibenzyl diselenide by the equation given above gives a value of 192 kJ mol^{-1}, identical to $\bar{D}(Se-Se)$ for $(CH_3)_2Se_2$ (see Table 8).

The large difference between the $\bar{D}(Se-Se)$ values for the diphenyl and the dialkyl compounds can be ascribed to lack of precision of the available experimental data or to specific properties of the chemical bonds formed by selenium in these compounds.

5. By using the given values of ΔH_f° for gaseous $PdCl_2 \cdot 2\,M(C_2H_5)_2$ and $M(C_2H_5)_2$ (M = Se or Te) and the ΔH_f° ($PdCl_2$, g) value 128.4 $\pm$ 10.5 kJ mol^{-1} (see Ref. 4) the $\bar{D}(Pd-M)$ values for these complexes were calculated by the equation

$$\bar{D}(Pd-M) = \tfrac{1}{2}\{\Delta H_f^\circ(PdCl_2,\ g) + 2\,\Delta H_f^\circ[M(C_2H_5)_2,\ g]$$

$$- \Delta H_f^\circ[PdCl2.2M(C2H5)2, g].$$

This calculation gave the very similar values $\overline{D}$(Pd–Se) = 191 ± 10 and $\overline{D}$(Pd–Te) = 204 ± 10 kJ mol^{-1}.

It is interesting to note that $\overline{D}$(Pd–Se) is close to $\overline{D}$(Se–Se) in dialkyl diselenides, and $\overline{D}$(Pd–Te) coincides within the error of the determination with $\overline{D}$(Te–R) in dialkyl tellurides and is significantly higher than $\overline{D}$(Te–Te) in the alkyl compounds R_2Te_2 (see Table 8).

6. The main contribution to the parameter $\Delta\overline{G}$(M–R) comes from the enthalpy factor $\overline{D}$, whereas only 15%–20% of the $\overline{D}$ value contributes to the entropy component (298.15$\Delta\overline{S}$). It follows that the relative thermodynamic stability of these compounds can be established from the $\overline{D}$(M–R), values, which are experimentally much better characterised than the $\Delta\overline{G}$(M–R) values.

Further developments in the experimental thermochemical studies of selenides and tellurides should offer a more detailed understanding of the special features found in the thermodynamic characteristics of compounds of this type.

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Synthesis of five- and six-membered nitrogen-containing heterocyclic compounds from carboxylic acid iminoesters

V I Kelarev, V N Koshelev

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Abstract. The review surveys and gives a systematic account of literature data concerning the application of carboxylic acid iminoesters in the synthesis of five- and six-membered nitrogen-containing heterocycles with several heteroatoms as well as heterocycles containing in the ring oxygen and sulfur atoms together with nitrogen atoms. The bibliography includes 350 references.

I. Introduction

Carboxylic acid iminoesters (imidates) and their salts, first obtained and described by Pinner[1] as early as the end of the previous century, have been attracting increasing attention by investigators, in view of their high reactivity, as synthons in the preparation of compounds of various classes — esters, amides, orthoesters, amidines, amidrazones, hydrazidines, amidoximes, etc. However, iminoesters and their salts are of special interest as key compounds in the syntheses of a wide variety of five- and six-membered nitrogen-containing heterocycles — imidazoles, benzimidazoles, 1,2,4-triazoles, pyrimidines, triazines, etc., as well as heterocycles containing nitrogen, oxygen, and sulfur atoms (oxazoles, oxazines, oxadiazoles, thiadiazoles, etc.).

The available information about the synthesis, structures, and chemical reactions of iminoesters and their salts is described in monographs[2-4] and reviews.[5,6] However, the data concerning the reactions of iminoesters which lead to the formation of heterocyclic structures, examined in the above communications, are far from complete from our point of view and the systematic treatment employed there requires improvement. We may note, in particular, that a review devoted to the synthesis of compounds of the 1,3,5-triazine series from carboxylic acid iminoesters was published in 1992.[7] In addition, new effective methods have been developed for the synthesis from iminoesters of heterocyclic compounds possessing practically useful properties. Thus, there has been recently a considerable growth of the number of publications on this field. In the present review, we have attempted to give a systematic account and to examine critically the information on the use of iminoesters in the synthesis of heterocycles, which has appeared during the period between 1975 and 1994. Earlier data concerning the preparation of heterocycles from iminoesters may be found in a monograph[4] published in 1975. We shall make use of them only when necessary.

We have arranged the relevant data in terms of the type of the heterocycle formed — initially five- and six-membered nitrogen-containing heterocycles in order of increasing ring size and increasing number of nitrogen atoms in the ring and then five- and six-membered nitrogen heterocycles containing also oxygen and sulfur atoms. Such systematic treatment provides a clear idea about the synthetic possibilities of the method and may be useful in selecting the direction of further research.

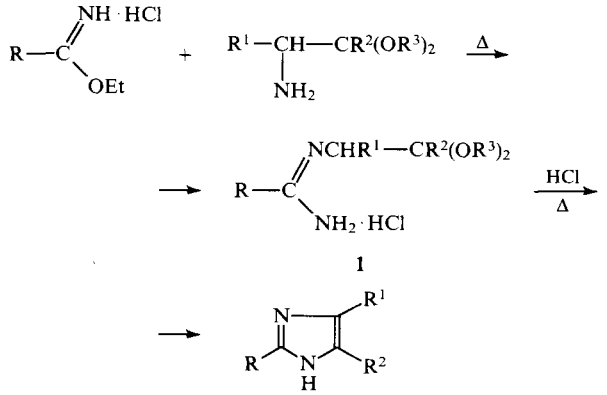
V I Kelarev, V N Koshelev Department of Organic Chemistry and the Chemistry of Petroleum, Gubkin State Academy of Petroleum and Gas, Leninskii prosp. 65, 117917 Moscow, Russian Federation.
Fax (7-095) 135 88 95. Tel. (7-095) 930 93 67 (V I Kelarev)

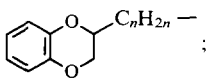
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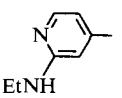
II. Synthesis of five- and six-membered nitrogen-containing heterocycles

1. Synthesis of substituted imidazoles and Δ^2-imidazolines

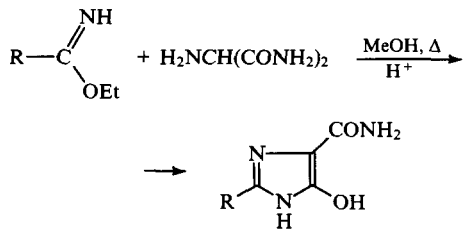
When the hydrochlorides of the iminoesters of various acids are condensed with the acetals of α-aminoketones in ethanol (refluxing for 1 – 6 h), the hydrochlorides of *N*-substituted amidines **1** are formed. On treatment with hydrochloric acid (50 – 100 °C, 0.5 – 6 h), these cyclise to substituted imidazoles (yield 30% – 85%)[8-16]

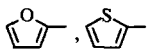


R = Me, Ar, $ArOCH_2$,  ;

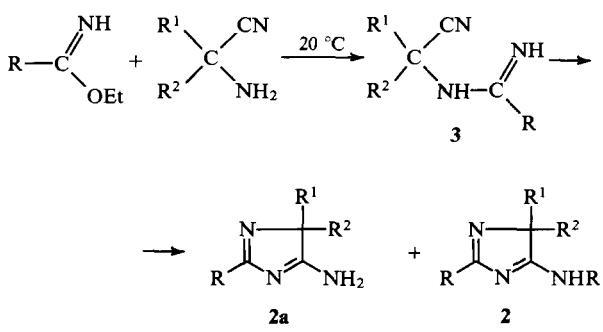
R^1 = H, Me; R^2 = H,  ; R^3 = Me, Et.

According to patent data,[17-19] the interaction of carboxylic acid iminoesters with aminomalonic acid diamide leads to the amides of 2-substituted 5-hydroxy-1*H*-imidazole-4-carboxylic acids, which exhibit an immunostimulating activity.



R = H, Alk, cyclo-(C_3–C_7), 1-Ad, Ar, $PhCH_2$, Ph_2CH, 3-Py, 

It has been reported[20] that the interaction of equimolecular amounts of α-aminonitriles with the iminoesters of pyridine-2-carboxylic and ethoxycarbonylformic acids results in the formation of 5-amino-4*H*-imidazoles **2a** in 44%–86% yield together with insignificant amounts (4%–10%) of *N*-substituted 5-amino-4*H*-imidazoles **2**.

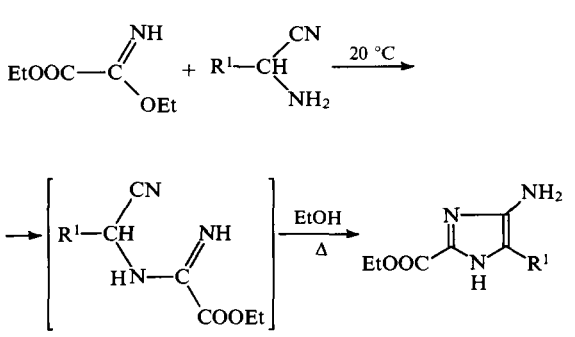


R = 2-Py, EtOOC; $R^1 = R^2$ = Me;

R^1 = Me, R^2 = Et; $R^1 + R^2 = -(CH_2)_4-$, $-(CH_2)_5-$

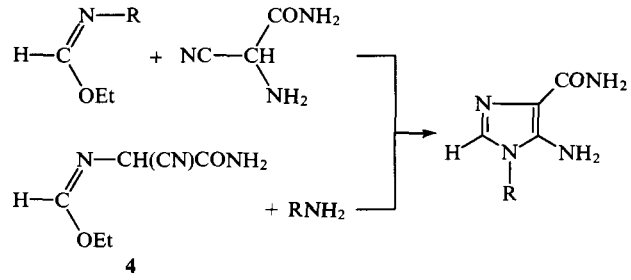
The authors suggest that the *N*-substituted amidine **3** is an intermediate in this reaction and also note that the iminoesters of other acids (R = Me, Ph, Cl_3C, 4-$NO_2C_6H_4$) do not form the imidazoles **2a** at all, but in certain cases afford *N*-substituted 5-amino-4*H*-imidazoles **2** in a low yield (4%–12%).

The condensation of the ethyl iminoester of ethoxycarbonylformic acid with α-substituted α-aminonitriles in ether leads to the amidines **3** (R = EtOOC), which cyclise on refluxing in alcohol to the ethyl esters of 4-amino-5-substituted 1*H*-imidazole-2-carboxylic acids (yield 51%–92%).[21,22]



R^1 = H, Me, EtOOC, H_2NCO, Ar

The condensation of *N*-substituted formic acid iminoesters with α-aminocyanoacetamide or the condensation of the *N*-substituted iminoester **4** with aromatic amines have been used to synthesise the amides of 1-substituted 5-amino-1*H*-imidazole-4-carboxylic acids.[23]

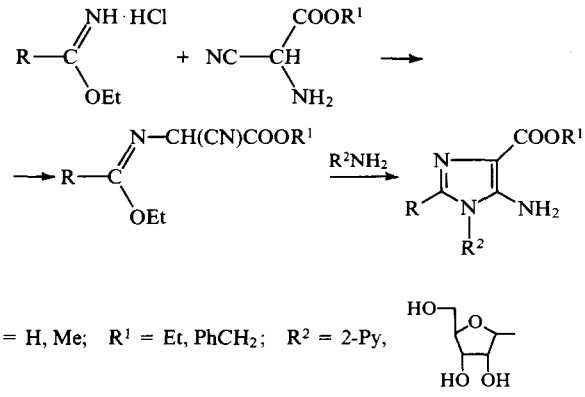


4

R = Ph, 4-MeC_6H_4, 4-$MeOC_6H_4$, 4-ClC_6H_4

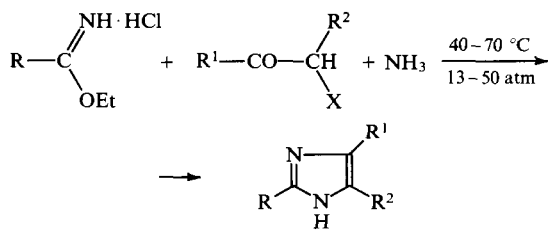
The iminoester **A** was obtained in its turn from the hydrochloride of the iminoester of formic acid with α-aminocyanoacetamide.

English investigators[24,25] used the latter method to obtain the esters of 1-substituted 5-amino-1*H*-imidazole-4 carboxylic acids, which are key compounds in the synthesis of purines.



R = H, Me; R^1 = Et, $PhCH_2$; R^2 = 2-Py,

In 1973, German investigators[26] proposed a convenient method of synthesis of imidazoles, which consists in the interaction of equimolecular amounts of the hydrochloride of an iminoester and of an α-substituted carbonyl compound in liquid ammonia under pressure. The carbonyl compounds employed in this reaction were 1,3-dihydroxyacetone,[26,27,29-31] α-hydroxyketones,[28,31] α-haloketones,[28,32] and α-acetoxyketones.[28] The reactions were carried out by heating the reactants (40–70 °C) under a pressure of 13–50 atm for 3–48 h; the yields of the target 2,4,5-trisubstituted 1*H*-imidazoles were then 10%–90% (Table 1).



(1)

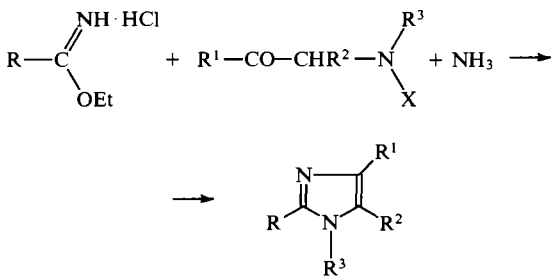
R = H, Me, Pr^i, Ar, $PhCH_2$, α-$C_{10}H_7CH_2$, cyclo-C_6H_{11}, Py, $ClCH_2CH_2$, $TsNHCH_2CH_2$, Me_2NCH_2, $Me_2NCH_2CH_2$, cyclo-$C_5H_{10}NCH_2CH_2$;

R^1 = H, $HOCH_2$, $HOCH_2CH_2$, Alk, Ph;

R^2 = H, Me, Ph, $MeOCH_2$; $R^1 + R^2 = -(CH_2)_4-$;

X = HO, Br, Cl, AcO.

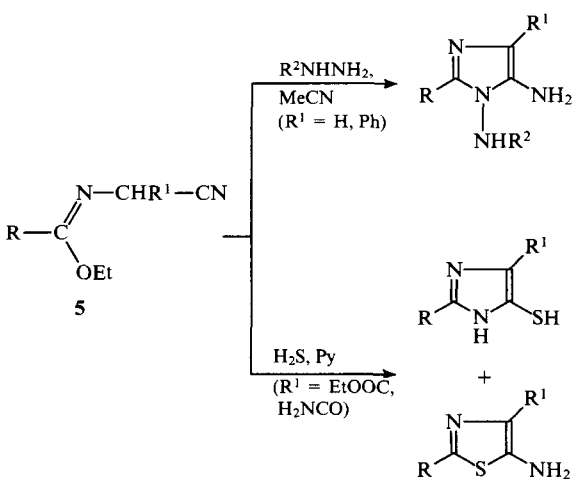
It was shown subsequently that *N*-substituted 1*H*-imidazoles are formed in a satisfactory yield from α-amino- and α-acylamino-ketones under similar conditions (80 °C, 35 atm, 15 h).[33,34]



R = Me, Ar, 4-$ClC_6H_4CH_2$, cyclo-C_6H_{11}, 3-Py;
R^1 = Alk, Ph;
R^2 = H, Alk, Ph, $PhCH_2$, $MeSCH_2CH_2$;
R^3 = H, Me, Ph, cyclo-C_6H_{11}; X = H, Ac.

The *N*-cyanomethylimidates **5** are convenient intermediates in the synthesis of 1*H*-imidazoles with functional group substituents. For example, treatment of compound **5** (R^1 = H, Ph) with hydrazine or phenylhydrazine afforded 1,5-diamino-1*H*-imidazoles — key compounds in the synthesis of azaindoline heterocycles.[35] The interaction of compounds **5** (R^1 = EtOOC, H_2NCO) with hydrogen sulfide in pyridine results in the formation of 5-mercapto-1*H*-imidazoles (yield 20%–35%) together with 5-aminothiazoles (yield 10%–20%, see Scheme 1).[36]

Scheme 1



R = H, Me, Ph, $PhCH_2$;
R^1 = H, Ph, EtOOC, H_2NCO; R^2 = H, Ph.

Table 1. Synthesis of 2,4,5-trisubstituted 1*H*-imidazoles by the condensation of iminoester hydrochlorides with α-substituted carbonyl compounds reaction (1) in liquid ammonia.[26–30]

R	R^1	R^2	Reaction conditions			Yield (%)
			P/atm	*T*/°C	*t*/h	
H	$HOCH_2$	H	20	70	5	35
H	H	H	25	50	5	20
H	Me	Me	25	50–60	10	43
H	Ph	H	25	50–60	10	16
Me	$HOCH_2$	H	45–50	60–70	6	68
Pr^i	$HOCH_2$	H	30	68	3	48
Ph	$HOCH_2$	H	20	70	5	73
Ph	Ph	Ph	25	50–60	15	25
Ph	Me	H	25	50–60	5–15	50
Ph	Ph	H	25	50–60	5–15	10
Ph	Ph	H	25	50	5	50
Ph	Ph	H	30	50–60	5–15	10
4-MeC_6H_4	$HOCH_2$	H	18	60	15	69
4-$MeOC_6H_4$	$HOCH_2$	H	29	70	4	76
$PhCH_2$	$HOCH_2$	H	15	50	20	85
4-$ClC_6H_4CH_2$	$HOCH_2$	H	20	70	15	42
cyclo-C_6H_{11}	$HOCH_2$	H	20	70	15	63
$PhCH_2$	$HOCH_2$	H	18	60	20	59
3-Py	$HOCH_2$	H	28	68	3	63
4-Py	$HOCH_2$	H	28	68	3	39
Ph	$HOCH_2CH_2$	H	13	40	48	61
Ph	$-(CH_2)_2-$		25	50–60	15	62
4-MeC_6H_4	Me	H	25	50–60	10	90

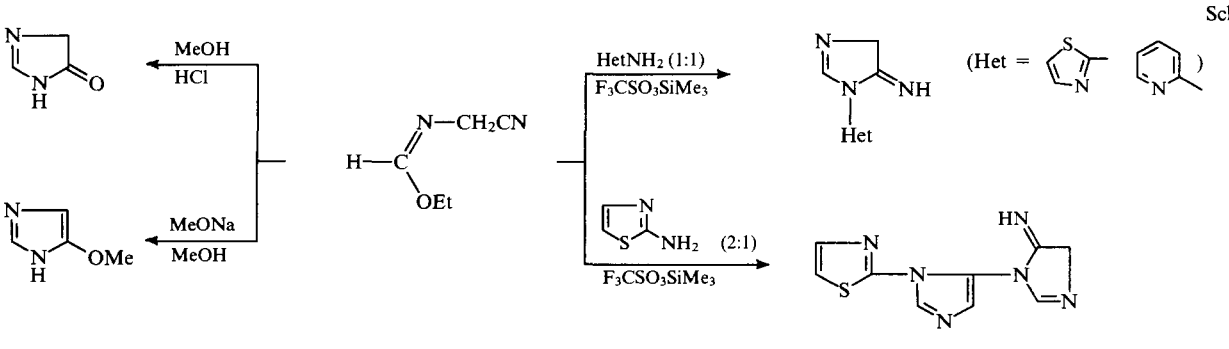
The reaction of the *N*-cyanomethyliminoester of formic acid with a methanol solution of HCl (20 °C, 0.5 h) leads to Δ^2-imidazolin-4(5)-one (yield 90%),[37,38] whilst refluxing with sodium methoxide in methanol gives rise to 4(5)-methoxyimidazole (yield 60%, see Scheme 2).[38]

The interaction of the same *N*-cyanomethyliminoester with heterocyclic amines (in molar proportions of 1 : 1) in the presence of trimethylsilyl triflate in acetonitrile (20 °C, 2 h) led to the synthesis of 1-heteroaryl-5-imino-Δ^2-imidazolines in 82%–91% yield.[38,39] On the other hand, the reaction of 2-aminothiazole with two equivalents of the *N*-cyanomethylimidate under similar conditions leads to the formation of the 1,5-disubstituted imidazole **6**.[38,39]

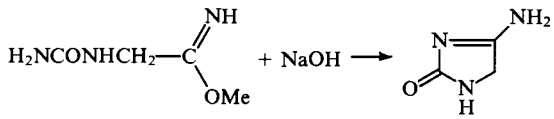
The condensation of the iminoester of ethoxycarbonylformic acid with *N*-phenylurea in tetrahydrofuran (THF) in the presence of HCl results in the formation of 3-phenylimidazolidine-2,4,5-trione (yield 56%).[22]

According to patent data,[40] 4-amino-Δ^3-imidazolin-2-one is formed in 95% yield on refluxing the iminoester of uredioacetic acid with alkali in aqueous alcohol.

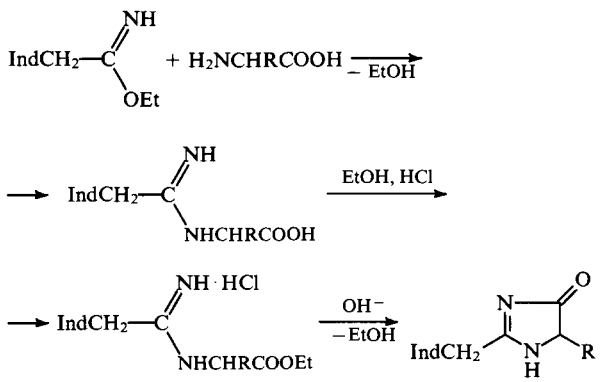
Scheme 2



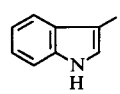
6



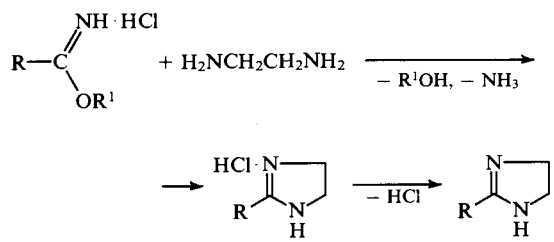
Fel'dman et al.[41] synthesised 2-(3-indolylmethyl)-Δ^2-imidazolin-4-ones, which are unstable under the usual conditions, from the ethyl iminoester of 3-indolylacetic acid and α-aminoacids in accordance with the following scheme:



R = H, Pr^i, Bu^i, Bu^s, $IndCH_2$;

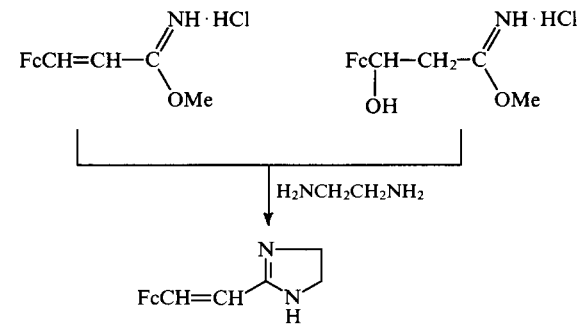
Ind = 

Some of the most interesting derivatives of the imidazole series are 2-substituted Δ^2-imidazolines, in view of their high and varied biological activity and valuable applied properties.[42,43] Compounds of this type are formed on condensation of iminoester salts with aliphatic 1,2-diamines.[4,5,42] It is noteworthy that investigators have devoted considerable attention in recent years to the synthesis of Δ^2-imidazolines from the hydrochlorides of ring-substituted iminoesters of benzoic,[44-49] phenylacetic,[44,47-49] 3,4-dihydro- and 1,2,3,4-tetrahydro-naphthalene-2-carboxylic acids,[50] adamantane-1-carboxylic acid,[51,52] ferrocenecarboxylic acid,[53] heterocyclic acids derived from furan,[54-57] benzofuran,[58] indole,[55,59-64] benzimidazole,[55] pyridine,[55] 4,5,6,7-tetrahydrobenzothiophene,[55] imidazo[1,2-a]-pyrazine,[65] isoxazoline,[66] etc., as well as aliphatic acids with functional-group substituents containing nitro-groups,[67-69] silylalkyl groups,[70-72] *N*-acylamino-groups,[73] alkoxy- and aryloxy-groups,[74-77] alkylthio- and arylthio-groups,[49,78] and organophosphorus fragments,[79,80] sterically hindered phenols,[81] etc.



R = Alk, cyclo-C_nH_{2n-1}, 1-Ad, $AlkOCH_2CH_2$, $ArOCH_2$, $MeC(NO_2)_2CH_2CH_2$, $Me_2C(NO_2)CH_2CH_2$, $Me_3SiCH_2CH_2$, $PhCH_2$, $XC_6H_4CH_2$, Ar, $ArCH_2SCH_2CH_2$, $(EtO)_2P(O)CH_2$, $(AlkO)_2P(O)CH_2CH_2$, Het; R^1 = Me, Et, $MeOCH_2CH_2$.

There are also isolated literature data concerning the synthesis of 2-substituted Δ^2-imidazolines from the iminoesters of α,β-unsaturated acids and their hydrochlorides. For example, (*E*)- and (*Z*)-2-(β-ferrocenylvinyl)-Δ^2-imidazolines **7** have been synthesised in 82%–88% yield by the reaction of the hydrochlorides of the methyl iminoesters of (*E*)- and (*Z*)-β-ferrocenylacrylic acids with ethylenediamine (0 °C, 0.5 h; 50–60 °C, 2 h).[82]



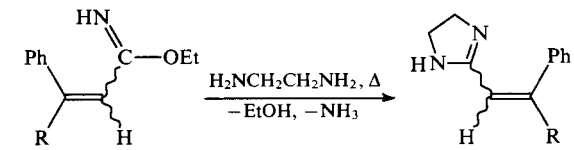
(*E*)- and (*Z*)-**7**

Fc = $(\eta^5\text{-}C_5H_5)Fe(\eta^5\text{-}C_5H_4)$–

The same workers showed[83] that a 3:1 mixture of the (*E*)- and (*Z*)-isomers **7** is formed under similar conditions from the hydrochloride of the methyl iminoester of 3-hydroxy-3-ferrocenylpropionic acid.

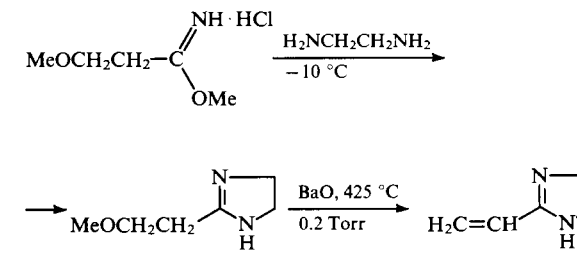
The *p*-tosylate of 2-[β-(5-nitro-2-furyl)vinyl]-Δ^2-imidazoline, which inhibits the growth of pathogenic bacteria, has been obtained in 83% yield by the reaction of the iminoester of β-(5-nitro-2-furyl)acrylic acid with the di-*p*-tosylate of ethylenediamine in ethanol (50–55 °C, 18 h).[84,85]

Ishikawa[86] synthesised (*E*)- and (*Z*)-(β-R-styryl)-Δ^2-imidazolines in 54%–88% yield by refluxing the ethyl iminoesters of (*E*)- and (*Z*)-β-R-cinnamic acids with ethylenediamine (molar ratio 1:2) in ethanol. These compounds exhibit a hypoglycemic activity.

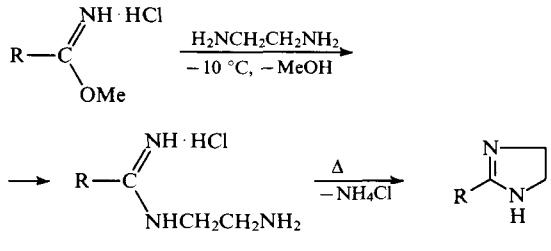


R = Ph, Py

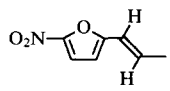
We may note that 2-vinyl-Δ^2-imidazoline, which is used as the monomer in the synthesis of water-soluble polymers, may be synthesised in a high yield from 2-(β-methoxyethyl)-Δ^2-imidazoline.[74-77,87]



Despite the extensive application of the condensation of iminoester salts with ethylenediamine for the synthesis of Δ^2-imidazolines, there is hitherto hardly any information about the mechanism of this reaction. The condensation apparently proceeds with the intermediate formation of the hydrochlorides of *N*-(2-aminoethyl)amidines **8**, which subsequently cyclise to Δ^2-imidazolines.[88] In certain cases, when the reaction was carried out at −10 °C, it was possible to isolate and identify intermediates of this type, which on refluxing in ethanol (2–3 h) were converted quantitatively into 2-substituted Δ^2-imidazolines.[89]

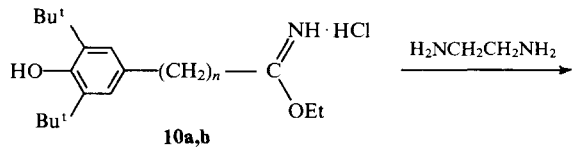


8

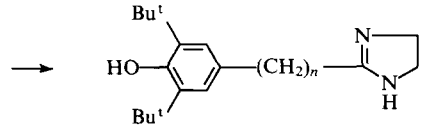
R = PhCH(OH), 4-$O_2NC_6H_4$, Ind, 3-Py, 

Since the first stage of the reaction proceeds with evolution of heat, the hydrochlorides of the iminoesters are mixed with ethylenediamine in an anhydrous solvent (methanol, ethanol, dioxane, methylene chloride, etc.) whilst cooling the system (0–10 °C). In order to complete the cyclisation, the reaction mixture is heated (40–78 °C) for several hours. The hydrochlorides of Δ^2-imidazolines formed under these conditions are converted into the free bases by treatment with a solution of sodium alkoxide in methanol or ethanol and also with a saturated solution of alkali whilst cooling. This results in the formation of the target 2-substituted Δ^2-imidazolines in fairly high yields (73%–95%) and without impurities.

There are only isolated literature data on the correlation between the structure of the acid components of the iminoester molecule, the reaction time, and the yields of the corresponding Δ^2-imidazolines. For example, the synthesis of the Δ^2-imidazoline **9a** from the hydrochloride of the iminoester of 3,5-di-*tert*-butyl-4-hydroxybenzoic acid **10a** requires prolonged heating (8–10 h), whereas the formation of the Δ^2-imidazoline **9b** from the hydrochloride of the iminoester of 3-(3,5-di-*tert*-butyl-4-hydroxyphenyl)propionic acid **10b** is completed in 1.5–2 h.[44,45,81]



10a,b



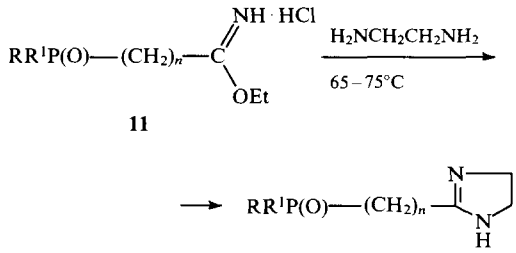
9a,b

n = 0 (**a**), 2 (**b**).

The lower reactivity of the iminoester hydrochloride **10a** with respect to ethylenediamine can be accounted for by the influence of the electron-donating hydroxyaryl group, which diminishes the positive charge on the carbon atom of the iminoester group and lowers its electrophilicity. In the case of the iminoester hydrochloride **10b**, the influence of this group is much smaller, since the groups are separated by two methylene units.[44,45]

A similar behaviour was found in a study of the condensation of ethylenediamine with the hydrochlorides of the iminoesters of indole-3-carboxylic and 3-indolylacetic acids containing the electron-donating indolyl group.[61]

It has been noted,[79] that the hydrochlorides of the iminoesters of β-phosphorylated propionic acids **11** (n=2) react with ethylenediamine twice as slowly as the corresponding acetic acid derivatives **11** (n=1).



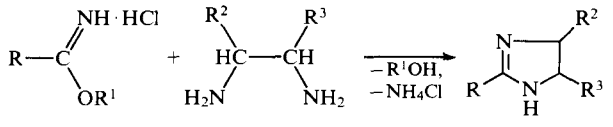
11

R = Ph, AlkO; R^1 = AlkO; n = 1, 2.

The authors explained this by the fact that the approach of the electron-accepting phosphoryl group to the reaction centre increases its electrophilicity, which facilitates the reaction with ethylenediamine.

One should also note that iminoester hydrochlorides are much more reactive in the reaction with ethylenediamine than the iminoesters themselves. In the latter case, the formation of Δ^2-imidazolines in a satisfactory yield requires prolonged (10–22 h) refluxing of the reactants in ethanol or in another suitable solvent,[52,59,73] while the iminoesters of phosphorylated acids do not react with ethylenediamine at all.[79] This finding can be explained by the increase in the electrophilicity of the carbon atom of the C=N group in the iminoester hydrochlorides as a consequence of the greater shift of the π-electron pair of the double bond towards the nitrogen atom of the iminoester group.[4]

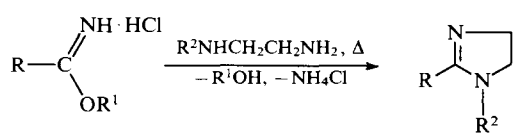
Apart from ethylenediamine, other aliphatic 1,2-diamines have been condensed with iminoesters and their hydrochlorides, for example, 1,2-diaminopropane,[90,91] 2,3-diaminopropan-1-ol,[49] and erythro-1,2-diamino-4,4,4-trifluoro-1-phenylbutane.[46] The 2,4-disubstituted or 2,4,5-trisubstituted Δ^2-imidazolines formed as a result of these reactions exhibit hypotensive,[92] hypertensive,[49] analgesic, and anti-inflammatory[46] activities.



R = Et, Ar, $PhCH_2OCH_2$,
$PhCHR^4CH_2$ (R^4 = Ph, cyclo-C_6H_{11}, 4-Py);
R^1 = Me, Et; R^2 = Me, $HOCH_2$, Ph; R^3 = H, F_3CCH_2.

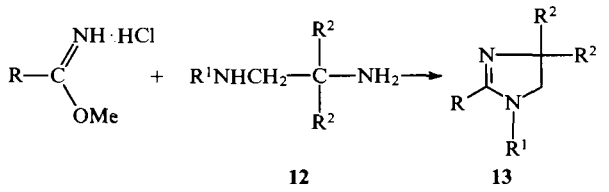
The condensation of iminoester hydrochlorides with *N*-monosubstituted ethylenediamines, leading to 1,2-disubstituted Δ^2-imidazolines which are difficult to obtain by other methods, is of definite interest.[42]

There are literature data on the condensation of iminoester hydrochlorides with *N*-alkyl-,[48,81] *N*-(2-cyanoethyl)-,[55,61,62,89,93] *N*-(1-adamantylmethyl)-,[52] *N*-(trimethylsilylmethyl)-,[71,94] *N*-aryl-,[95–97] *N*-benzyl-,[54,55,61,62,81,89,98] *N*-(2-aryl-2-hydroxyethyl)-,[99] *N*-furfuryl-,[54,55,64,89,100] *N*-tetrahydrofurfuryl-,[64,100] *N*-(2-thienylmethyl)-,[54,89] *N*-(4-phenyl-2-thiazolyl)-, *N*-(2-benzothiazolyl)-,[89,101] and *N*-(1-benzotriazolylmethyl)-ethylenediamines.[89]



R = Alk, $HOCH_2$, Ph, $PhCH_2$, $XC_6H_4CH_2$,
cyclo-C_nH_{2n-1}, Het, 1-Ad;
R^1 = Me, Et; R^2 = Alk, Ar, $PhCH_2$, Het.

The interaction of iminoester hydrochlorides with the 1,2-diamines **12** — ethylenediamine, *N*-(trimethylsilylmethyl)-ethylenediamine, and 2-amino-2-methyl-1-(trimethylsilylmethyl)aminopropane — has been studied in detail.[71,94]

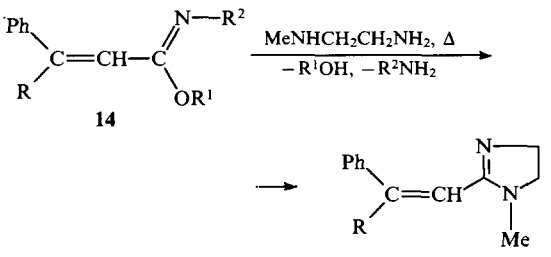


12 **13**

R = Me, Ph, $PhCH_2$, $Me_3SiCH_2CH_2$;
R^1 = H, Me_3SiCH_2; R^2 = H, Me.

It was established that the yield of the Δ^2-imidazolines **13** depend to a greater extent on the structure of the initial 1,2-diamine and to a much lesser extent on the structure of the iminoester hydrochlorides. This fact can evidently be accounted for by the steric hindrance generated by the presence of bulky substituents next to the reaction centres in the 1,2-diamine. The yields of the Δ^2-imidazolines **13** decrease from ethylenediamine (yield 68%–90%) to the *N*-substituted ethylenediamine **12** ($R^1 = Me_2SiCH_2$, R^2 = H; yield 53%–58%) and to the *N*-substituted 1,2-diaminopropane **12** (R^1-Me_3SiCH_2, R^2 = Me) (yield 23%–34%).

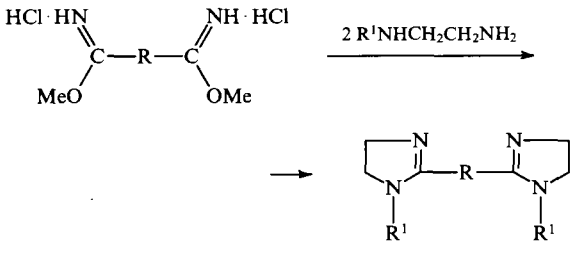
Heating of the *N*-substituted iminoesters **14** with *N*-methylethylenediamine (120–130 °C, 1.5 h) leads to 1-methyl-2-(β-R-styryl)-Δ^2-imidazolines, which exhibit a hypoglycemic activity.[102]



14

R = Me, Ph, Py; R^1 = Alk; R^2 = Pr^i, Bu^t.

There are also literature data on the condensation of the dihydrochlorides of the bisiminoesters of dicarboxylic acids with ethylenediamine[103,104] and *N*-(1-adamantylmethyl)ethylenediamine,[52] which leads to the bisimidazolines **15** in 80%–97% yield.

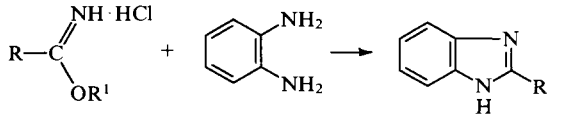


15

R = $-CH_2CH_2CMe(NO_2)CH_2CH_2-$,
$-CH_2CH_2C(NO_2)_2CH_2CH_2-$,
$-CH_2CH_2OCH_2C{\equiv}CCH_2OCH_2CH_2-$;
R^1 = H, 1-$AdCH_2$.

2. Synthesis of substituted benzimidazoles

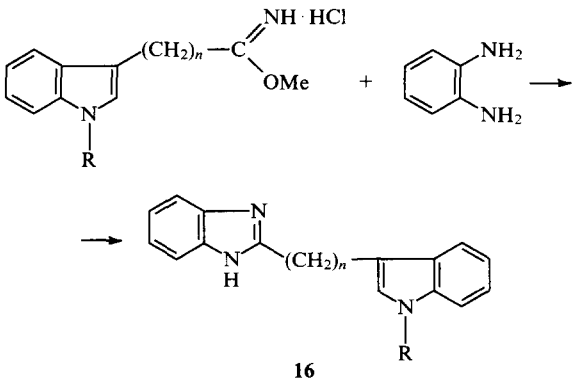
The condensation of the hydrochlorides of the iminoesters of aliphatic, aromatic, and heterocyclic acids with *o*-phenylenediamine leads to 2-substituted benzimidazoles.[4,42,44,51,52,55,57,61,62,69,71,72,80,82,89,103,105–114] Reactions of this type are usually carried out by refluxing (for 1.5–5 h) equimolecular amounts of the reactants in methanol or ethanol; the benzimidazoles are then formed in 36%–92% yields.



R = Me, $EtOOCCH_2$, $Me_2C(NO_2)CH_2CH_2$, $MeC(NO_2)_2CH_2CH_2$, $(O_2N)_3CCH_2CH_2$, $Ac(CH_2)_3$, $Me_3SiCH_2CH_2$, $ArNHCH_2CH_2$, 4-HO-3,5-$Bu^t_2C_6H_2(CH_2)_n$ (n = 0, 2), Ar, $PhCH_2$, Fc, 1-Ad, Het;
R^1 = Me, Et, $MeOCH_2CH_2$.

It has been noted[115,116] that the interaction of iminoesters with *o*-phenylenediamine is rapid only when the reaction is carried out in an acid medium. For example, when the iminoester of *N*-phenylalanine was heated with *o*-phenylenediamine in dioxane or isopentyl alcohol (140 °C, 3 h), the yield of 2-(2-phenylaminoethyl)benzimidazole reached only 55%, whereas the reaction with the dihydrochloride of this iminoester proceeds exothermically and the yield of benzimidazole is 70%–80%.[116]

The 2-substituted benzimidazoles **16**, containing indole fragments, are formed in 85%–92% yield on refluxing equimolecular amounts of the hydrochlorides of the iminoesters of acids of the indole series and *o*-phenylenediamine in ethanol for 4–6 h.[55,61,62,89]

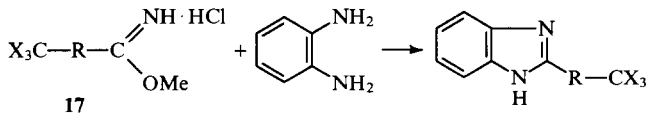


16

R = H, Me; n = 0, 1.

The benzimidazoles **16** have also been synthesised by condensing the iminoesters of the above acids with *o*-phenylenediamine. These reactions were carried out under more severe conditions — at 140–150 °C in dimethylformamide (DMF) for 15–20 h, but the yield of the target products did not then exceed 44%–52%.[89] In view of this, iminoester hydrochlorides are employed as a rule as the initial compounds in the synthesis of benzimidazoles by the above procedure. In those cases where the iminoester hydrochlorides are difficult to obtain or are unstable (for example, the hydrochlorides of the iminoesters of trichloroacetic acid[117]), the hydrochloride of *o*-phenylenediamine is condensed with the iminoesters. For example, 2-trichloromethylbenzimidazole is formed in 85%–95% yield on interaction of the iminoester of trichloroacetic acid with the monohydrochloride of *o*-phenylenediamine in ethanol[118] or in acetic acid.[119]

The condensation of equimolecular amounts of the hydrochlorides of the iminoesters of polyhalogenated carboxylic acids **17** and *o*-phenylenediamine in methanol (refluxing for 1–2 h) afforded 2-polyhaloalkylbenzimidazoles in 45%–86% yields.[114]

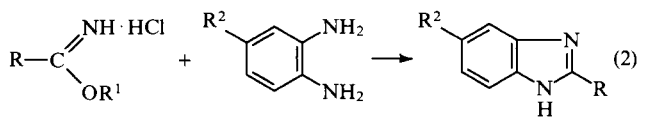


17

X = Br, R = $-(CH_2)_2-$;
X = Cl, R = $-CH_2CHCl-$, $-(CH_2)_2-$.

At the same time, the authors[114] noted that they were unable to synthesise the corresponding benzimidazoles from the hydrochlorides of the iminoesters of 2,4,4,4-tetrabromobutyric acid **17** (X = Br, R = $-CH_2CHBr-$), 4,4,4-tribromobut-2-enoic acid **17** (X = Br, R = $-CH=CH-$), and 4,4,4-trichlorobut-2-enoic acid **17** (X = Cl, R = $-CH=CH-$). According to the authors, the presence of the double bond in the α-position relative to the carbon atom of the iminoester group lowers its electrophilicity, which prevents the occurrence of the target reaction.

The condensation of the hydrochlorides of the iminoesters of various acids with 4-substituted 1,2-diaminobenzenes containing both electron-donating and electron-accepting groups has been widely used in recent years for the synthesis of 2,5(6)-disubstituted benzimidazoles.[107,112,113,120-127]



(2)

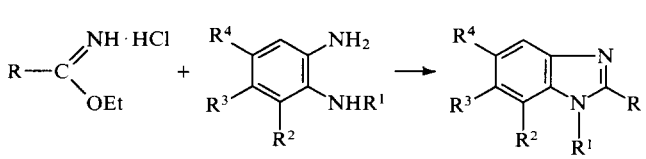
R = $PhCH_2$, $XC_6H_4CH_2$, Ar, Het;
R^1 = Me, Et, $MeOCH_2CH_2$;
R^2 = Alk, AlkO, ArO, O_2N, NC, MeOOC, F_3C, Het.

The above reactions were carried out by refluxing (for 2–8 h) equimolecular amounts of the reactants in methanol, ethanol, dioxane, or acetic acid, the yield of the target benzimidazoles amounting to 30%–62% depending on the structures of the initial iminoester hydrochlorides and on the nature of the substituents R^2 in the *o*-phenylenediamine (Table 2, see over).

It has been noted[121-123,125] that, when the methoxyethyl iminoesters of aromatic acids are condensed with 4-substituted 1,2-diaminobenzene, the yield of the target benzimidazoles increases appreciably compared with the methyl and ethyl iminoesters.

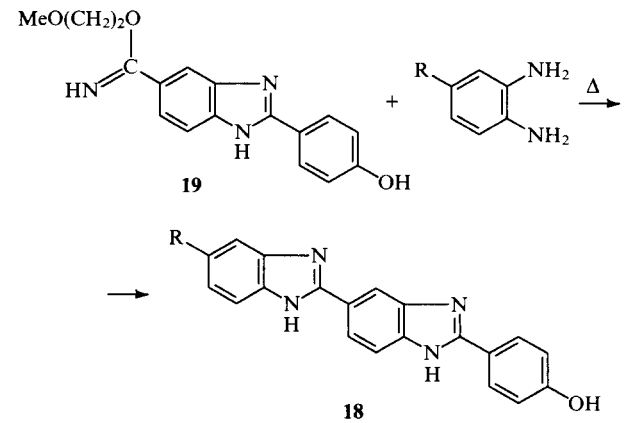
Some of the 2,5(6)-disubstituted benzimidazoles synthesised from the iminoester hydrochlorides possess antihelminthic and fungicidal properties,[107] exhibit antihypertensive, spasmolytic, and vasodilating activities,[120] as well as high cytotoxic,[123] antiproteolytic,[125] analgesic, and anti-inflammatory activities.[127]

The condensation of iminoester hydrochlorides with *N*-monosubstituted *o*-phenylenediamines leads to 1,2-disubstituted benzimidazoles. For example, when the hydrochlorides of aliphatic acid iminoesters are refluxed with *N*-alkyl-*o*-phenylenediamines in ethanol, polysubstituted benzimidazoles are formed in 58%–79% yields. They can be used as selective herbicides.[128-132]

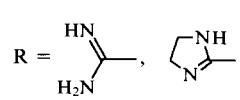


R = H, Alk, $HOCH_2$;
R^1 = Alk; R^2, R^3 = H, Hal, NO_2, NH_2, MeNH, MeO, Me_2N;
R^4 = Alk, cyclo-(C_3–C_6), F_3C, F_2CHSO_2.

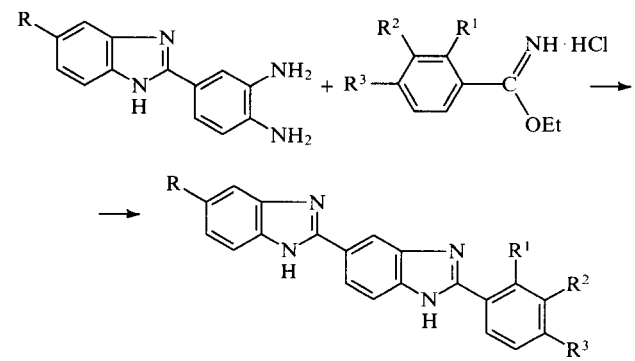
Derivatives of 2,5-bisbenzimidazolyl **18** are of definite interest from the standpoint of the search for new substances with antiproteolytic[125] and chemotherapeutic[126] activities. For example, when the methoxyethyl iminoester **19** is condensed with 4-R-*o*-phenylenediamines in methanol (refluxing for 3 h), 5-(5-R-2-benzimidazolyl)-2-(4-hydroxyphenyl)benzimidazoles **18** are formed in 25%–28% yields.[125]

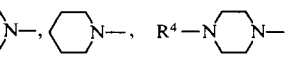


19 18

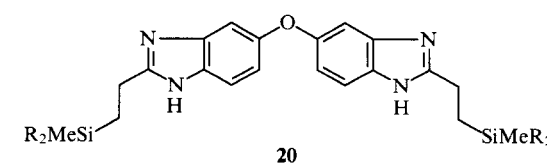


The corresponding bisbenzimidazolyls have also been synthesised in 55%–83% yields by the interaction of 2-(3,4-diaminophenyl)-5-R-benzimidazoles with the hydrochlorides of aromatic acid iminoesters in ethanol (refluxing for 3–5 h).[126]



R = Et_2N,  ;
R^1 = H, HO; R^2 = H, Cl, Me, NO_2, MeO;
R^3 = H, AlkO, Me, Cl, Ph, PhO, NH_2;
R^1 + R^2 = OCH_2O; R^4 = Alk, $PhCH_2$, $HOCH_2CH_2$, Ph, Et_2NCO.

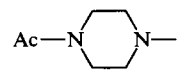
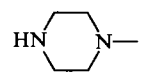
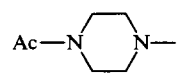
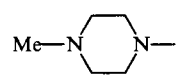
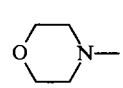
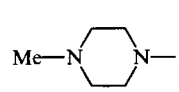
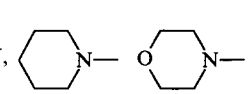
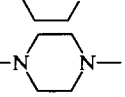
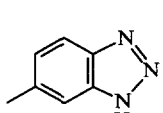
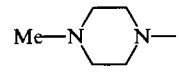
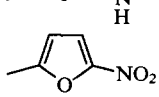
The condensation of the hydrochlorides of the iminoesters of β-trialkylsilylpropionic acids with di(3,4-diaminophenyl) ether (molar ratio 2:1) afforded a 70%–72% yield of the organosilicon dibenzimidazolyl ether **20**.[72]



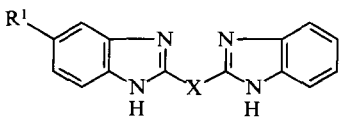
20

R = Me, Et.

Table 2. Synthesis of benzimidazoles from iminoester hydrochlorides and 4-substituted 1,2-diaminobenzenes [reaction (2)].

R	R^1	R^2	Yield (%)	Ref.
Ph	$MeOCH_2CH_2$		48	122
4-HOC_6H_4	$MeOCH_2CH_2$	$Me_2N(CH_2)_3NHCO$	65	121
	$MeOCH_2CH_2$		69	122
	$MeOCH_2CH_2$		74	122
	Me		68	124
	Me	Me	54	124
	Me	Cl	58	124
	Me	NC	75	125
4-$O_2NC_6H_4$	$MeOCH_2CH_2$	$HOOC(CH_2)_5NHCO$	78	119
	$MeOCH_2CH_2$	Me_2N	92	122
4-$AcNHC_6H_4$	$MeOCH_2CH_2$	$Me_2N(CH_2)_3NHCO$	70	119
4-HO-3,5-$Bu^t_2C_6H_2$	$MeOCH_2CH_2$		75	121
	$MeOCH_2CH_2$	$HOCH_2CH_2NH$	82	121
	$MeOCH_2CH_2$		72	121
4-HO-3-IC_6H_3	Me	Me	30	124
4-H_2N-3-$O_2NC_6H_3$	Et	Et_2N,   (R³ = Alk, Ph, $PhCH_2$, $HOCH_2CH_2$)	54–78	126
$PhCH_2$	Et	NO_2	77	107
2,4-$(O_2N)_2C_6H_3CH_2$	Et	Me	68	113
	Et	MeO	75	113
	$MeOCH_2CH_2$		70	122
	Et	Cl	46	112
	Et	MeOOC	25	112
$R^3NHCH(OH)CH_2OC_6H_3R^4$ (R^3 = Alk, cyclo-C_nH_{2n-1}; R^4 = H, F, Cl, Br, Alk, AlkO)	Et	Alk, AlkO, F, Cl, Br	54–72	120

The interaction of the bisiminoesters of dicarboxylic acids or their hydrochlorides with *o*-phenylenediamine or 4-substituted 1,2-diaminobenzenes (molar ratio 1 : 2) results in the formation of the derivatives **21**, in which the benzimidazole fragments are separated by a chain of carbon atoms or by an aromatic or a heterocyclic group.[52,103,104,125,133]

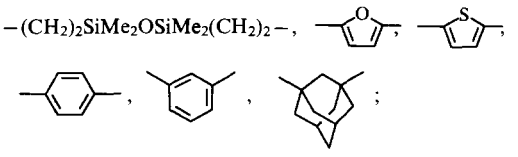


21

X = $-(CH_2)_n-$, where n = 1–3, 5, 6, 8;

$-(CH_2)_2CMe(NO_2)(CH_2)_2-$, $-(CH_2)_2C(NO_2)_2(CH_2)_2-$,

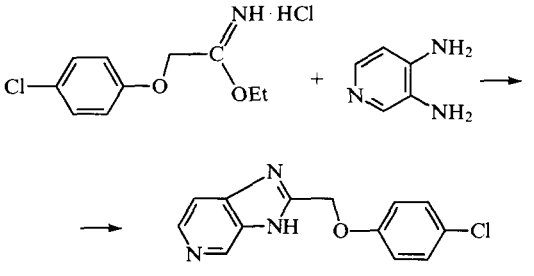
$-(CH_2)_2SiMe_2OSiMe_2(CH_2)_2-$,



R^1 = H, $-C(NH)NH_2$, $-C(NBu)NH_2$,

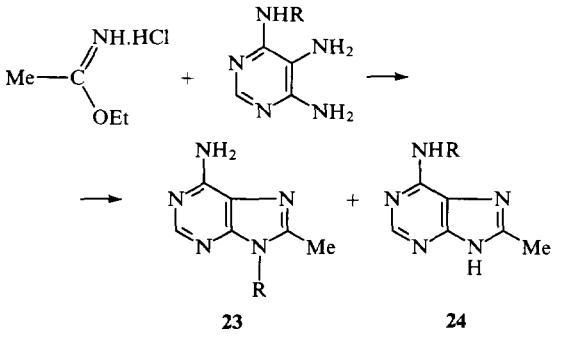


The condensation of iminoester hydrochlorides with heterocyclic *o*-diamines leads to condensed imidazole systems. For example, the interaction of the hydrochloride of the (4-chlorophenoxy)acetic acid iminoester with 3,4-diaminopyridine in ethanol (refluxing for 20 h) gives rise to the imidazo[4,5-*c*]pyrimidine derivative **22** (yield 20%), which exhibits an antihypotoxic activity.[134]



22

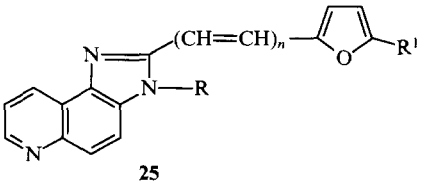
The ring closure in the reaction of 4-*N*-substituted 4,5,6-triaminopyrimidines with the hydrochloride of the acetic acid iminoester proceeds much more readily with participation of the secondary 5-amino-group and not the primary 6-amino-group.[135] This results in a 70%–85% yield of 6-amino-9-R-8-methylpurines **23** together with 6-*N*-substituted 6-amino-8-methylpurines **24** (yield 6%–17%).



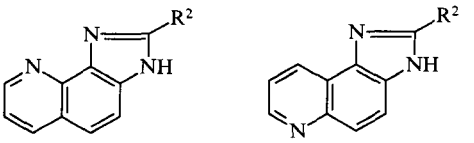
23 **24**

R = Ph, $PhCH_2$.

The condensation of *N*-substituted 5,6-diaminoquinolines with the hydrochlorides of the iminoesters of acids derived from furan afforded 40%–75% yields of 2-(5-R^1-2-furyl)- and 2-[β-(5-R^1-2-furyl)vinyl]-3-substituted 3*H*-imidazo[4,5-*f*]quinolines **25**.[136]



25



26 **27**

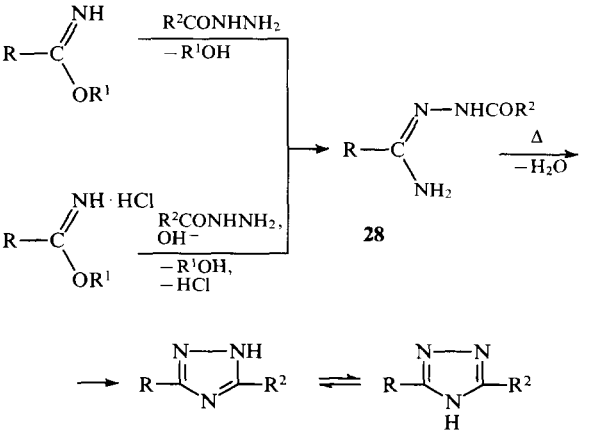
R = H, Me; R^1 = H, Br, NO_2; n = 0, 1; R^2 = Me, Ph, $PhCH_2$.

Refluxing of equimolecular amounts of 7,8-diaminoquinoline and the hydrochlorides of carboxylic acid iminoesters in ethanol gives rise to 60%–67% yields of 2-R-3*H*-imidazo[4,5-*h*]quinolines **26**.[137] 2-R-3*H*-imidazo[4,5-*f*]quinoline **27** have been synthesised from 5,6-diaminoquinoline under similar conditions.

3. Synthesis of substituted 1,2,4-triazoles and derivatives of 1,2,4-triazole with functional group substituents

The interactions of carboxylic acid iminoesters of *N*-acylhydrazines (acid hydrazides) are known to give rise to carboxylic acid *N*-acylamidrazones **28**, which can serve as convenient intermediates in the synthesis of 3,5-disubstituted 1*H*-1,2,4-triazoles.[4,5,138–142]

The *N*-acylamidrazones **28** are formed in high yields (70%–94%) when equimolecular amounts of an iminoester and an acid hydrazide are refluxed in methanol or ethanol[89,142–146] (in the case of *N*-formylhydrazine, the reaction is carried out at 0 °C)[140] or when iminoester hydrochlorides interact with acid hydrazides in the presence of bases—triethylamine,[147,148] aqueous NaOH solution,[139] or sodium ethoxide in absolute ethanol.[149]



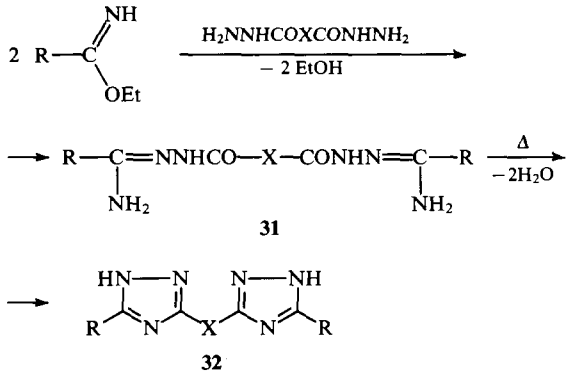
29 **30**

R = Alk, $Me_3SiCH_2CH_2$, $PhCH_2$, $PhCH_2OCONHCH_2$, EtOOC, Ar, Het;

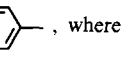
R^1 = Me, Et; R^2 = H, Alk, Ar, Het.

The *N*-acylamidrazones **28** readily undergo cyclodehydration to 3,5-disubstituted 1*H*-1,2,4-triazoles **29**, which can exist in the form of the tautomeric 4*H*-1,2,4-triazoles **30**.[150,151] The cyclodehydration of the *N*-acylamidrazones **28** takes place on heating to a temperature higher by 5–10 °C than the melting point for several minutes[20,89,143–146] and in certain cases on heating in vacuo[142] and in high-boiling solvents (toluene, DMSO).[147,149]

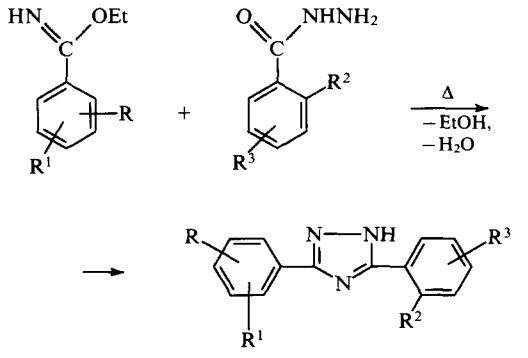
When iminoesters interact with dicarboxylic acid dihydrazides (molar ratio 2:1), the bis-*N*-acylamidrazones **31** are formed. On heating to 200–220 °C in vacuo, the latter give rise to 3,5-disubstituted bis-1*H*-1,2,4-triazoles **32** (yields 31%–74%).[142,149]



R = Me, $Me_3SiCH_2CH_2$, Ph, $PhCH_2$, 4-MeC_6H_4;

X = $-(CH_2)_n-$,  , where n = 0, 1, 4.

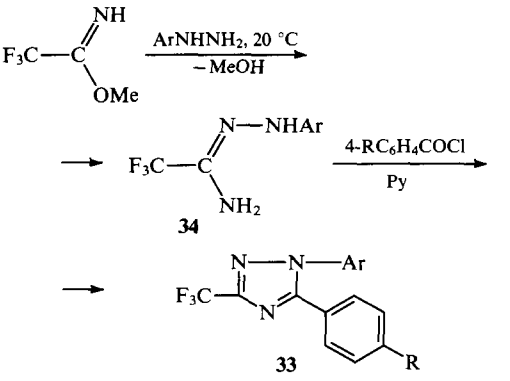
There are literature data concerning the synthesis of 3,5-disubstituted 1*H*-1,2,4-triazoles **29** from acid iminoesters and hydrazides without the isolation of the intermediate *N*-acylamidrazones **28**. For example, when substituted benzoic acid iminoesters were heated with aromatic acid hydrazines (110–125 °C, 10–24 h), 3,5-diaryl-1*H*-1,2,4-triazoles were synthesised in satisfactory yields. They exhibit high sedative and contraceptive activities.[152–155]



R = H, F, Cl, Alk, AlkO, Me_2N, Ph, F_3C;
R^1 = H, F, Cl, Alk; R + R^1 = OCH_2CH_2;
R^2 = Alk; R^3 = H, F, Cl, Alk, AlkO.

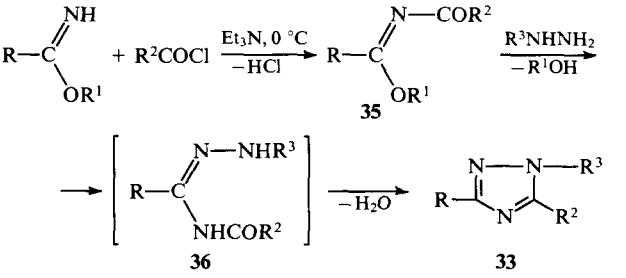
Certain 1*H*-1,2,4-triazoles are also formed in 30%–80% yields when iminoesters are refluxed in ethanol or methanol with reactive hydrazides — *N*-formylhydrazine,[139,156] the hydrazides of carboxylic hydroxyacids,[157,158] and the hydrazides of cyano-,[159,160] methoxy-,[159] and dimethoxy-acetic acids.[159]

As a result of the search for promising substances with anti-inflammatory activity, Hungarian investigators[161,162] proposed a method of synthesis of 1,3,5-trisubstituted 1*H*-1,2,4-triazoles **33** (yield 16%–28%), which involves treatment of the *N*-substituted amidrazones **34** with acid chlorides in dioxane in the presence of pyridine.



R = H, Cl, F.

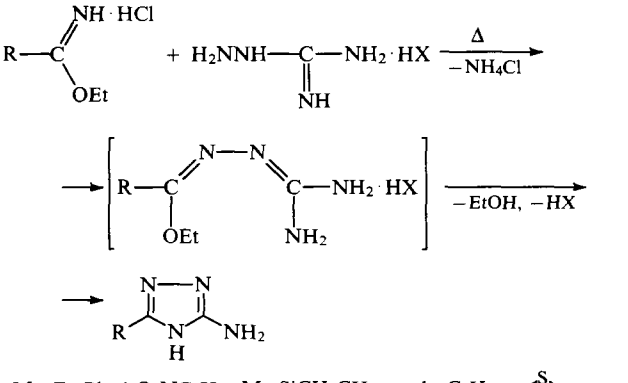
The interaction of the reactive *N*-acyliminoesters **35** with hydrazine or *N*-substituted hydrazines at 20 °C is apparently a more promising method of synthesis of 1,3,5-trisubstituted 1*H*-1,2,4-triazoles **33**.[163,164] The initial *N*-acyliminoesters **35** are formed in satisfactory yields (54%–95%) when iminoesters are acylated by acid chlorides in the presence of triethylamine at 0 °C.[163,165]



R = Me, Ar, Het; R^1 = Me, Et;
R^2 = Me, Ph, 4-ClC_6H_4, 2-$F_3CC_6H_4$;
R^3 = H, Me, Ph, C_nH_{2n-1}.

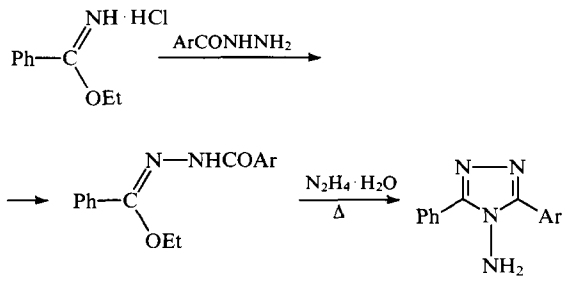
It has been suggested[163] that the intermediate **36** is formed initially as a result of the attack by the NH_2 group of the substituted hydrazine on the carbon atom of the iminoester. The intermediate cyclises at a temperature as low as 20 °C to the 1,2,4-triazole **33** with elimination of a water molecule. When the reaction is carried out under the conditions indicated, the yield of the target 1*H*-1,2,4-triazoles is 55%–87%.

Carboxylic acid iminoesters are also used as the reactants in the synthesis of 1*H*-1,2,4-triazole derivatives with functional group substituents. For example, when the iminoester hydrochlorides were refluxed with aminoguanidine hydrochloride or nitrate in pyridine or tripropylamine, 3-amino-5-substituted 4*H*-1,2,4-triazoles were synthesised in 35%–86% yields.[166,167]



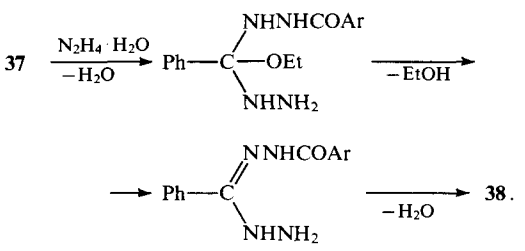
R = Me, Et, Ph, 4-$O_2NC_6H_4$, $Me_3SiCH_2CH_2$, cyclo-C_6H_{11},  .

French investigators isolated the benzoic acid *N*-acylhydrazones **37** in 65%–90% yields after the interaction of the benzoic acid iminoester hydrochloride with aromatic acid hydrazides in ethanol at 0 °C.[168] On refluxing with hydrazine hydrate in 1-propanol, the *N*-acylhydrazones were converted into 4-amino-4*H*-1,2,4-triazoles **38** in 52%–83% yields.



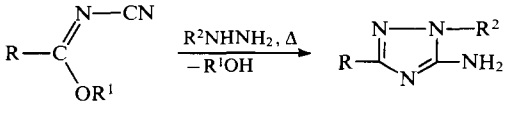
37 **38**

The authors proposed the following mechanism of the formation of 4-amino-1,2,4-triazoles **38** from the *N*-acylhydrazones **37** and hydrazine hydrate:

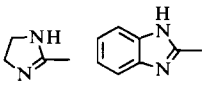


The reactive carboxylic acid *N*-cyanoiminoesters **39** are convenient compounds for the synthesis of amino-1*H*-1,2,4-triazoles. The *N*-cyanoiminoesters are formed when iminoester hydrochlorides react with chlorocyanogen[169] in the presence of triethylamine (yield 70%–80%) or with cyanamide in water in the presence of phosphate buffer (yield 34%–74%).[170]

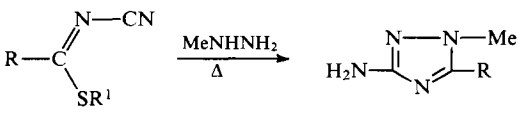
For example, the condensation of the *N*-cyanoiminoester **39** with *N*-substituted hydrazines in ethanol (refluxing for 1–2 h) afforded 73%–82% yields of 1,3-disubstituted 5-amino-1*H*-1,2,4-triazoles.[171–173]



39

R = H, Me, $EtOOCCH_2$; R^2 = Me,  .

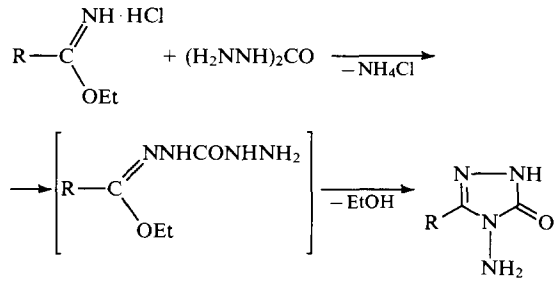
On the other hand, 3-amino-1-methyl-5-substituted 1*H*-1,2,4-triazoles are formed regioselectively in 82%–84% yield on refluxing the *N*-cyanoiminothioesters **40** with methylhydrazine in chloroform.[171]



40

R = Me, Pr^i; R^1 = Me, Et.

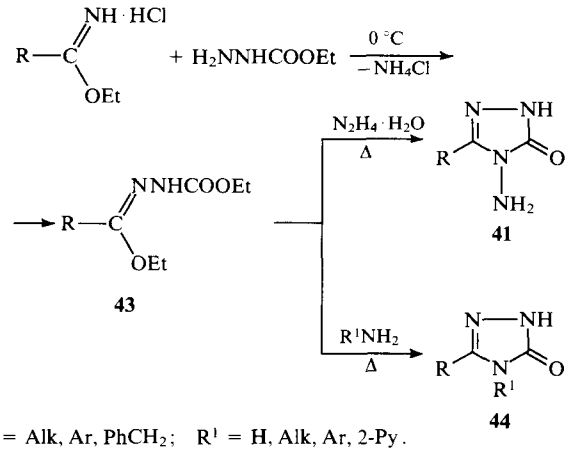
The condensation of equimolecular amounts of iminoester hydrochlorides and carbodihydrazide in ethanol (refluxing for 48 h) leads to 40%–45% yields of 4-amino-3-substituted 1*H*-Δ^2-1,2,4-triazolin-5-ones **41**.[174,175] The intermediate formation of the *N*-substituted hydrazones **42** in this reaction has been postulated.[174]



42 **41**

R = Me, Bu^t.

The interaction of iminoester hydrochlorides with *N*-(ethoxycarbonyl)hydrazine at 0 °C in ethanol affords 60%–85% yields of carboxylic acid ester N^2-(ethoxy-carbonyl)hydrazones **43**, which are convenient intermediates for the synthesis of Δ^2-1*H*-1,2,4-triazolin-5-ones.[174,176,177]

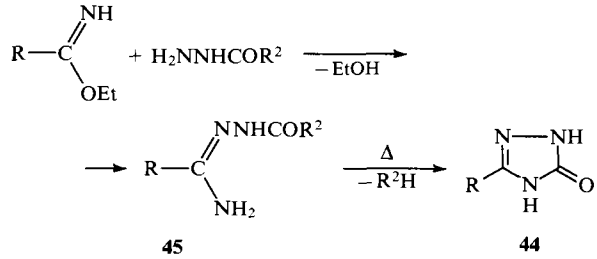


43 **41** **44**

R = Alk, Ar, $PhCH_2$; R^1 = H, Alk, Ar, 2-Py.

On heating with ammonia or primary amines, the hydrazones **43** are converted into 3,4-disubstituted Δ^2-1*H*-1,2,4-triazolin-5-ones **44**,[176,177] while on prolonged refluxing (30 h) with hydrazine hydrate in 1-butanol they cyclise to 4-amino-Δ^2-1,2,4-triazolin-5-ones **41** (yield 62%–95%).[174]

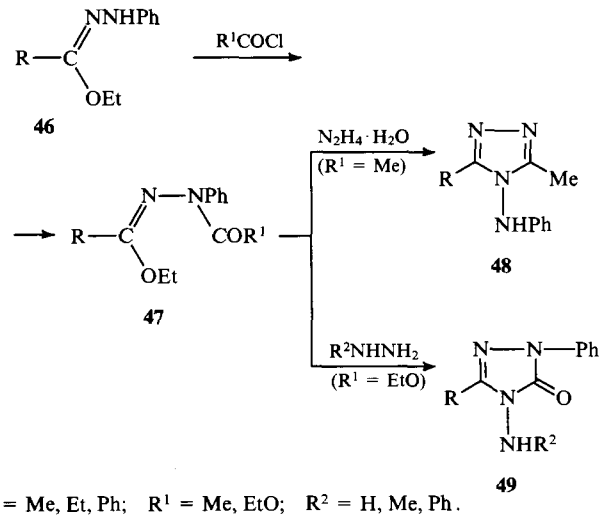
It is noteworthy that reactions of iminoester bases with *N*-(ethoxycarbonyl)hydrazines and semicarbazides give *N*-(R-carbonyl)amidrazones **45**, which cyclise on heating to 3-substituted Δ^2-1*H*-1,2,4-triazolin-5-ones **44** (R^2 = H).[22,176,178,179]



45 **44**

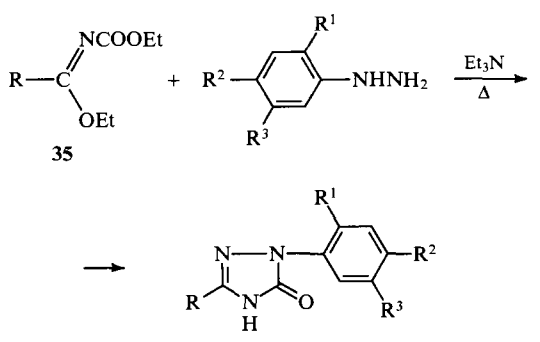
R = Alk, Ar, EtOOC; R^2 = EtO, NH_2, PhNH

The interaction of carboxylic acid *N*-phenylhydrazones **46** with ethyl chloroformate or acetyl chloride in the presence of pyridine or triethylamine gives rise to the formation of the *N*-disubstituted hydrazones **47**, the reactions of which with hydrazine hydrate and monosubstituted hydrazines in methanol lead to 4-phenylamino-4*H*-1,2,4-triazoles **48** or to 1,3-disubstituted 4-amino-Δ^2-1,2,4-triazolin-5-ones **49**.[180,181]



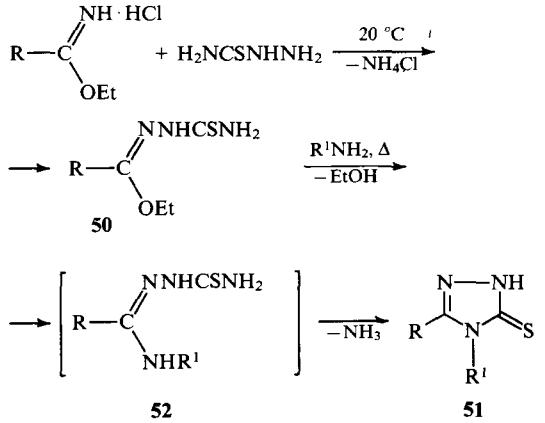
R = Me, Et, Ph; R^1 = Me, EtO; R^2 = H, Me, Ph.

According to patent data,[182-187] 1,3-disubstituted Δ^2-1*H*-1,2,4-triazolin-5-ones, used as intermediates in the synthesis of herbicides, are formed in 50%–95% yields on heating equimolecular amounts of the *N*-(ethoxycarbonyl)iminoesters **35**, *N*-arylhydrazines, and triethylamine (40–90 °C, 3–12 h).



R = H, Alk; R^1 = H, Cl, F, NO_2; R^2 = H, Cl, F, HO, AlkO; R^3 = H, NO_2, COOH, $NCCH_2O$.

The interaction of iminoester hydrochlorides and thiosemicarbazide in DMF at 20 °C affords carboxylic acid ester thiosemicarbazones **50** in 53%–74% yields.[188,189] On heating with primary amines or arylhydrazines in DMF for 2–3 h, the latter are converted into 4,5-disubstituted Δ^2-1*H*-1,2,4-triazoline-5-thiones **51** (yield 20%–95%). The authors suggest that this involves the intermediate formation of the *N*-(thiocarbamoyl)-amidrazones **52**.[188]

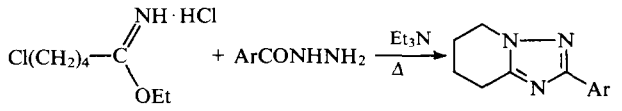


R = Alk, Ar, $PhCH_2$;
R^1 = $PhCH_2$, $HOCH_2CH_2$, Ar, 2-Py, cyclo-C_6H_{11}, ArNH.

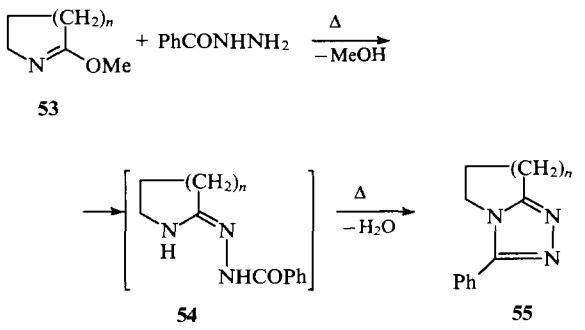
3-Substituted 4-phenyl-Δ^2-1,2,4-triazoline-5-thiones have been obtained in 42%–65% yields by condensing iminoester hydrochlorides with 4-phenylthiosemicarbazide in the presence of bases (pyridine, tripropylamine).[89,167,190,191]

Iminoester hydrochlorides are also convenient key compounds in the synthesis of condensed heterocyclic systems incorporating 1,2,4-triazole fragments.

Refluxing of the 5-chlorovaleric iminoester hydrochloride with aromatic acid hydrazides and triethylamine (molar ratios 1:1:2) in ethanol leads to 2-aryl-5,6,7,8-tetrahydro-1,2,4-triazolo[5,1-*a*]pyridines (yield 26%–35%).[8]

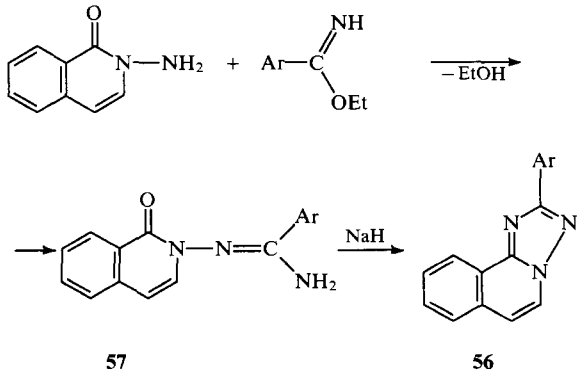


The condensation of the cyclic iminoesters **53** with benzoic acid hydrazide results in the formation of the *N*-acylamidrazones **54**, which, on refluxing in acetic acid (n = 1) or in xylene (n = 2), undergo intramolecular cyclisation to 3-phenyl-6,7-dihydro-5*H*-pyrrolo[2,1-*c*]-1,2,4-triazole **55** (n = 1) or 3-phenyl-5,6,7,8-tetrahydro-1,2,4-triazolo[4,3-*a*]pyridine **55** (n = 2).[8]

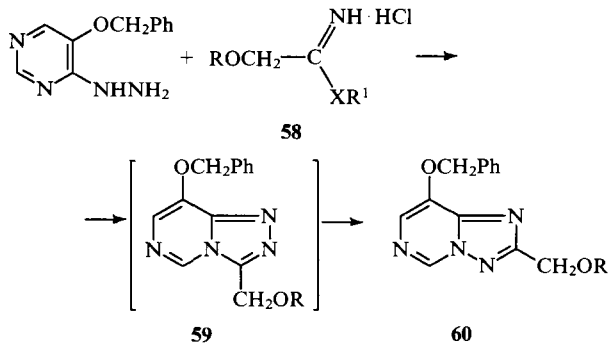


n = 1, 2.

The synthesis of 2-aryl-1,2,4-triazolo[5,1-*a*]isoquinolines **56** by the reaction of 2-amino-2*H*-isoquinolin-1-one with aromatic acid iminoesters and subsequent cyclisation of the intermediate amidrazones **57** on treatment with sodium hydride has been described in patents.[192,193]

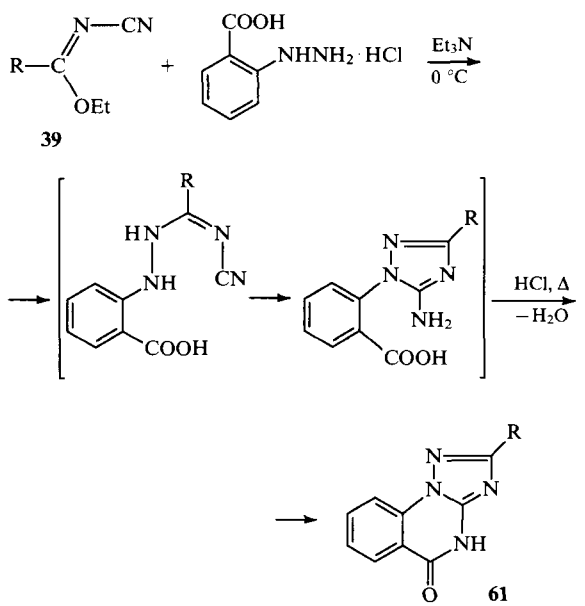


The interaction of 5-benzyloxy-4-hydrazinopyrimidine with the iminoester or iminothioester hydrochlorides **58** in pyridine (80 °C, 3 h) leads initially to 1,2,4-triazolo[4,3-*c*]pyrimidine **59**, which is converted into 2-substituted 8-benzyloxy-1,2,4-triazolo[5,1-*c*]pyrimidine **60** (yield 32%–53%) as a result of the Dimroth rearrangement.[194]



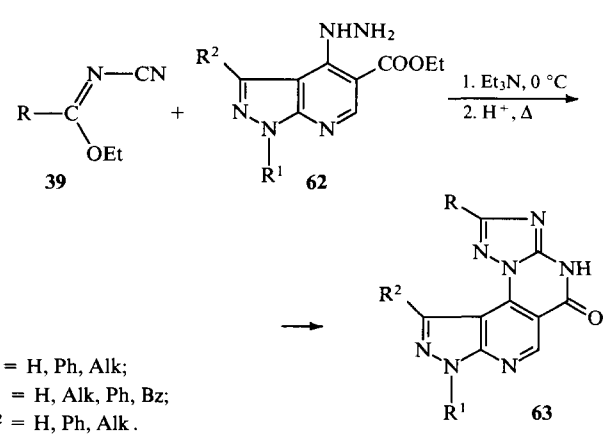
R = $PhCOOCH_2CH_2$; R^1 = Me, Et; X = O, S

2-R-1,2,4-triazolo[5,1-*a*]quinazolin-5(4*H*)-ones **61** have been synthesised in 70%–94% yields by condensing the hydrochloride of 2-hydrazinobenzoic acid with the *N*-cyanoiminoesters **39** and triethylamine (molar ratios 1:1.2:3) in ethanol at 0 °C and subsequent treatment with aqueous HCl (80 °C).[195]



R = H, Me, $NCCH_2$.

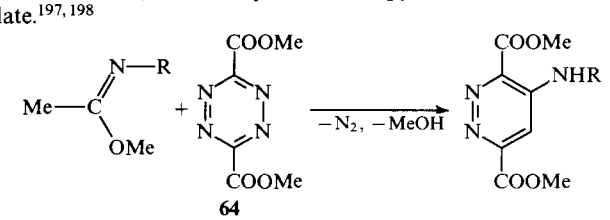
Derivatives of pyrazolo[4',3':5,6]pyrido[3,4-e]-1,2,4-triazolo-[1,5-*a*]pyrimidine **63**, which exhibit an anti-inflammatory activity and a depressant activity on the central nervous system, have been obtained under similar conditions from the *N*-cyano-iminoesters **39** and the 4-hydrazino-derivatives of pyrazolo-[3,4-*e*]pyridine-3-carboxylic acid esters **62**.[196]



R = H, Ph, Alk;
R^1 = H, Alk, Ph, Bz;
R^2 = H, Ph, Alk.

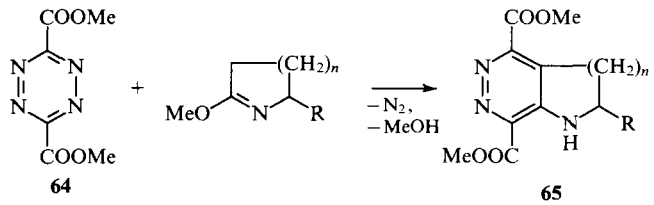
4. Synthesis of pyridazine, pyrazine, and quinoxaline derivatives

Only isolated data on the syntheses of pyridazine, pyrazine, and quinoxaline from iminoesters are so far available in the literature. Thus the interaction of *N*-substituted acetic acid iminoesters with dimethyl 1,2,4,5-tetrazine-3,6-dicarboxylate **64** leads to a low yield (9%–12%) of dimethyl 4-R-aminopyridazine-3,6-dicarboxylate.[197,198]



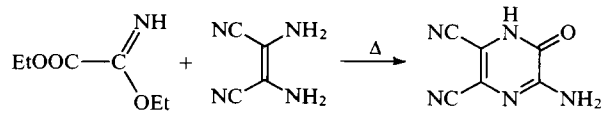
R = Me, Ph

The condensed pyridazines **65** have been synthesised similarly from the *sym*-tetrazine **64** and cyclic iminoesters (yield 8%–47%).[197]

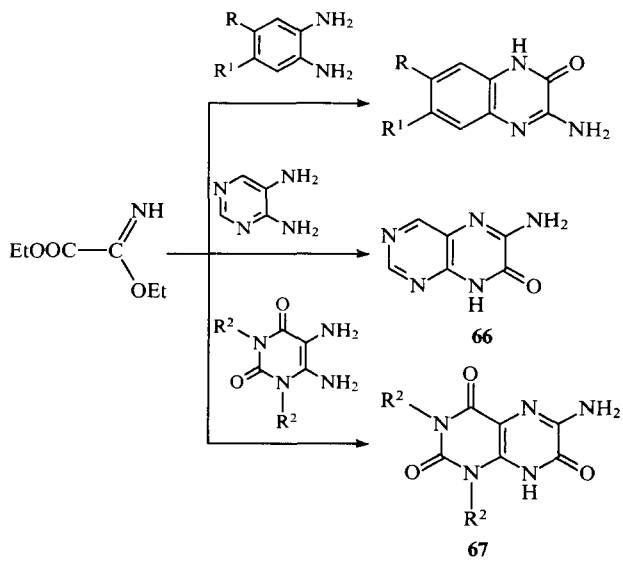


R = H, Me; n = 1–3.

When the ethoxycarbonylformic acid iminoester was refluxed with 1,2-diamino-1,2-dicyanoethene in ethanol, 3-amino-5,6-dicyano-1*H*-pyrazine-2-one was isolated in 72% yield.[21,22]



The interaction of this iminoester with aromatic and heterocyclic 1,2-diamines afforded derivatives of quinoxaline and pteridine.[21,22] For example, on refluxing with substituted *o*-phenylenediamines in ethanol, 6,7-disubstituted 3-amino-1*H*-quinoxalin-2-ones are formed in 58%–99% yield.

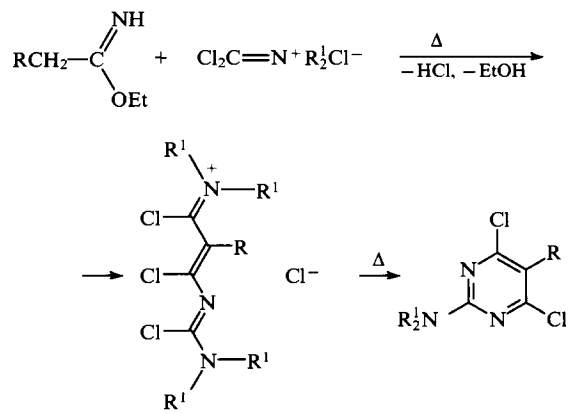


R = H, Me, Cl; R^1 = H, Me, Cl, NO_2; R^2 = H, Me.

6-Amino-8*H*-pteridin-7-one **66** was obtained in 80% yield under similar conditions from 4,5-diaminopyrimidine and trioxopteridines **67** have been synthesised from 5,6-diaminouracils (yield 60%–94%).

5. Synthesis of pyrimidine and quinazoline derivatives

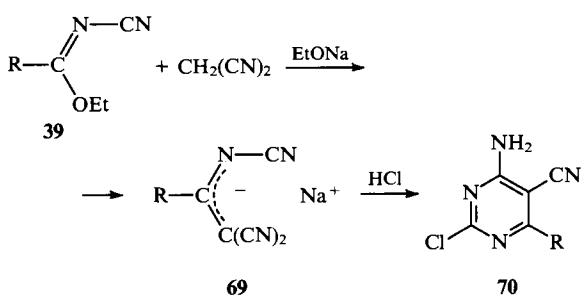
When aliphatic acid iminoesters interact with phosgene iminium salts (molar ratio 1:3) in chloroform (refluxing for 3–4 h), 2,4,6-trichloro-1,3,7-triazaheptatrienium chlorides **68** are formed in 85%–87% yield. On heating in vacuo, these products cyclise to 2-dialkylamino-4,6-dichloro-5-R-pyrimidines (yield 33%–90%).[199]



68

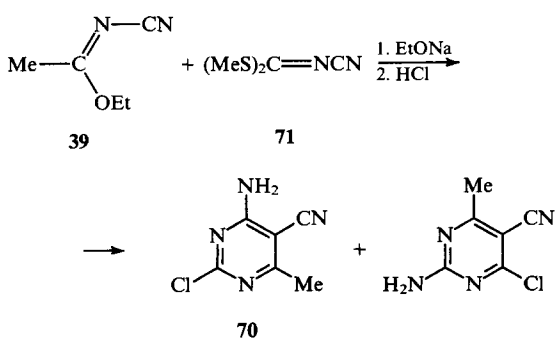
R = H, Me; R^1 = Me, Et.

By treating malonodinitrile with the *N*-cyanoiminoesters **39** in the presence of sodium ethoxide at 20 °C, Kristiansson obtained the reactive sodium salts **69**, which, on treatment with an ethereal solution of HCl, were converted into 4-amino-5-cyano-2-chloro-6-R-pyrimidines **70** in 83%–87% yield.[200]



39 **69** **70**

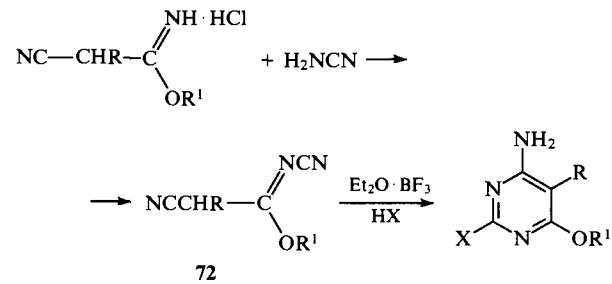
A 2:3 mixture of the 2-chloropyrimidine **70** (R = Me) and 2-amino-6-chloro-5-cyano-4-methylpyrimidine is formed in 88% yield under similar conditions from the acetic acid *N*-cyanoiminoester **39** (R = Me) and the *N*-substituted cyanamide **71**.



39 **71** **70**

On the other hand, it has been reported[201] that, when the *N*-cyanoiminoesters **39** were refluxed with malonodinitrile in methanol in the presence of sodium methoxide (molar ratios 1:1:2), 2-amino-5-cyano-4-methoxy-6-R-pyrimidines (R = H, Me, Ph) were synthesised in 17%–40% yield.

Japanese investigators established[202–205] that the interaction of the hydrochlorides of the iminoesters of carboxylic α-cyanoacids with cyanamide in benzene in the presence of 4 Å molecular sieves (25 °C, 4 h) leads to the formation of the *N*-cyanoiminoesters **72**. On treatment with boron trifluoride etherate and a hydrogen halide in nonpolar solvents (ether, benzene), the latter cyclise to 6-alkoxy-4-amino-2-halo-5-R-pyrimidines in 70%–92% yield.

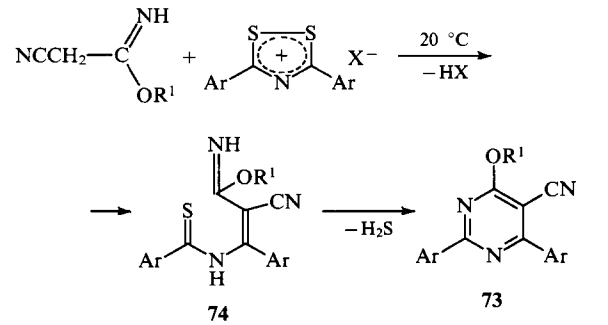


72

R = H, Me, Ph; R^1 = Alk; X = Cl, Br.

It is worth noting that, when the *N*-cyanoiminoester **72** (R = H, R^1 = Me) is treated with gaseous HCl at −15 °C, 2-amino-6-chloro-4-methoxypyrimidine is formed in 70% yield.[206]

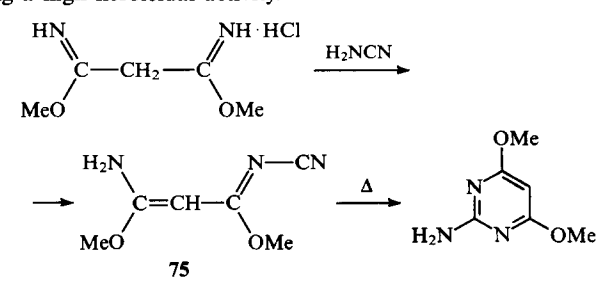
4-Alkoxy-5-cyanopyrimidines **73**, which are intermediates for the synthesis of biologically active compounds, have been obtained in 36%–71% yields by the reaction of cyanoacetic acid iminoesters with 3,5-diaryl-1,2,4-dithiazolium salts in aqueous acetonitrile in the presence of alkali (20 °C, 10 min).[207,208] The authors suggest that the ring in the dithiazolium salt is initially opened with formation of the intermediate **74**, which subsequently cyclises to the pyrimidine **73**.



74 **73**

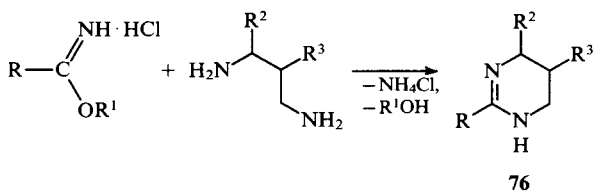
R^1 = Alk; X = ClO_4, I_3, Cl, Br, $FeCl_4$.

The interaction of the monohydrochloride of malonic acid bisiminoester with cyanamide leads to the *N*-cyanoiminoester of 3-amino-3-methoxyprop-2-enoic acid **75**, which, on refluxing in toluene or on heating to the melting point, is converted quantitatively into 2-amino-4,6-dimethoxypyrimidine, exhibiting a high herbicidal activity.[209–211]



75

The cyclocondensation of the hydrochlorides of various carboxylic acid iminoesters with aliphatic 1,3-diamines is a convenient method of synthesis of 2-substituted 1,4,5,6-tetrahydropyrimidines **76**.[47,212,213] These reactions are analogous to the synthesis of 2-substituted Δ^2-imidazolines from 1,2-diamines (see above) and are carried out by refluxing the reactants in ethanol (4–12 h); the yield of the tetrahydropyrimidines **76** is then 50%–86%.

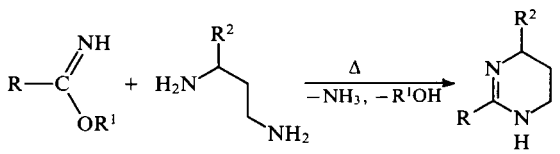


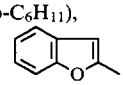
76

R = PhC(OH)Me, ArCH(OH), 2,4,5,6-$Me_4C_6HCH_2$, 2,4,5,6-$Me_4C_6HSCH_2$, , Ar—CH=CH—;

R^1 = Me, Et; R^2 = H, Me; R^3 = H, OH.

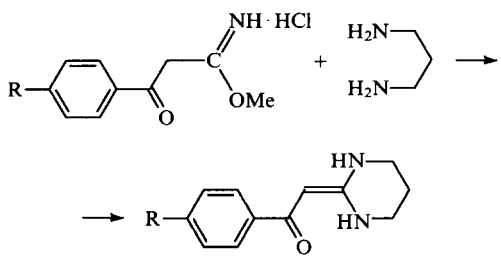
2-Substituted tetrahydropyrimidines have also been obtained in 50%–80% yield by heating iminoesters with 1,3-diamines (80–150 °C, 2–10 h).[58,88,214]



R = $PhCHR^3CH_2$ (R^3 = Ph, 2-Py, cyclo-C_6H_{11}), 4-$R^4C_6H_4CH_2$ (R^4 = Cl, Br, NO_2), 

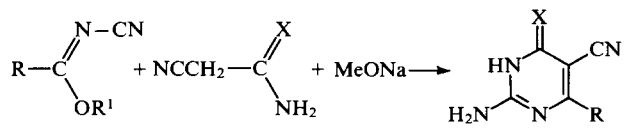
R^1 = Me, Et; R^2 = H, Me.

It has been reported[214] that the condensation of the hydrochlorides of benzoylacetic acid esters with 1,3-diaminopropane in ethanol (refluxing for 10 h) leads to the formation of 2-(benzoylmethylene)perhydropyrimidines in 35%–56% yield.



R = H, Cl, Br, MeO.

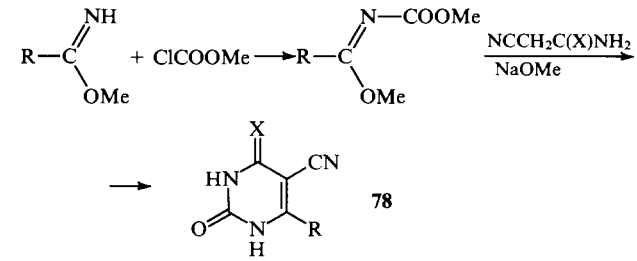
Cyclocondensation of the *N*-cyanoiminoesters **39** with the amide or thioamide of cyanoacetic acid and sodium methoxide [molar ratios 1 : 1 (1.1–2)] in methanol (refluxing for 2–3 h) gives 41%–77% yields of 2-amino-5-cyano-3,4-dihydropyrimidin-4-ones and the corresponding 4-thiones **77**.[176]



39 **77**

R = H, Me, Et, $PhCH_2$, Ar; R^1 = Me, Et; X = O, S.

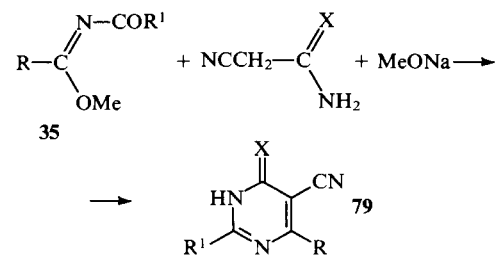
The reaction of iminoesters with methyl chloroformate in hexane in the presence of 2,4,6-trimethylpyrimidine leads to the reactive *N*-(methoxycarbonyl)iminoesters. On heating with equimolecular amounts of cyanoacetic acid derivatives and sodium methoxide in methanol, the latter cyclise to 2,4-dioxo- or 2-oxo-4-thioxo-derivatives of 5-cyano-1,2,3,4-tetrahydropyrimidines **78** (X = O, S) in 38%–98% yield.[215]



78

R = Et, Ph, $PhCH_2$, 4-$MeOC_6H_4$; X = O;
R = Ph, $PhCH_2$; X = S.

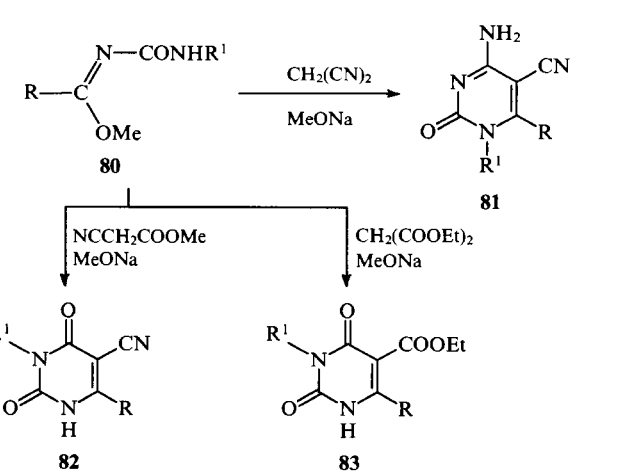
2,6-Disubstituted 5-cyano-4-oxo(or 4-thioxo)-3,4-dihydropyrimidines **79** (X = O, S) have been synthesised in 45%–77% yields under similar conditions from the *N*-acyliminoesters **35**.[215]



35 **79**

R = Me, Et, Ph; R^1 = Me, Bu^t, Ph, 4-ClC_6H_4; X = O, S.

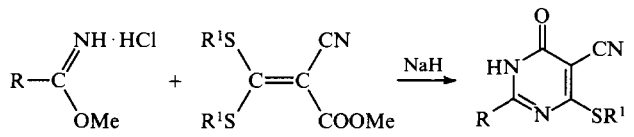
The interaction of iminoesters with isocyanates leads to *N*-substituted aminocarbonyliminoesters **80**, which in the presence of equimolecular amounts of sodium methoxide in methanol condense with malonodinitrile (20 °C, 14 h), cyanoacetic acid ester (refluxing for 15 h), and malonic ester (refluxing for 7 days) to form the corresponding 6-substituted 4-amino-5-cyano-2,3-dihydropyrimidin-2-ones **81** (yield 20%–89%), 3,6-disubstituted 5-cyano-2,4-dioxo-1,2,3,4-tetrahydropyrimidines **82** (yield 56%–70%), and 5-ethoxycarbonyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidines **83** (yield 35%–60%).[216]



80 **81** **82** **83**

R = Et, Ph, 4-MeC_6H_4, 4-ClC_6H_4; R^1 = Et, Ph.

The synthesis of 2-substituted 6-alkylthio-5-cyano-3,4-dihydropyrimidin-4-ones by the reaction of iminoester hydrochlorides with sodium hydride and cyanoacetic acid ester derivatives **84** in DMF (0 °C; 20 °C, 1 h) has been described in a patent.[217]

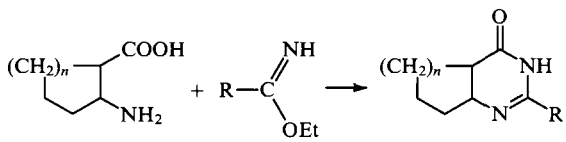


84

R = Alk, cyclo-(C_3-C_6), $PhCH_2$, Ar,  ;

R^1 = Alk, cyclo-(C_4-C_7), Ph, $PhCH_2$.

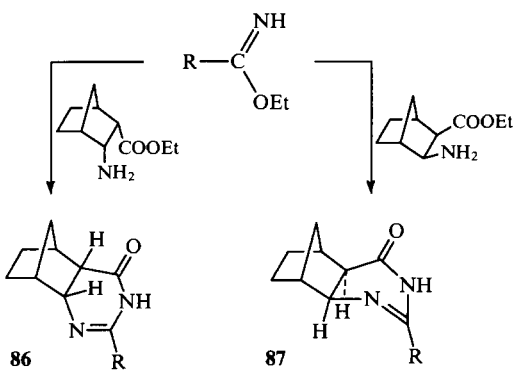
5,6-Dihydro-3*H*-pyrimidin-4-one derivatives **85**, exhibiting anti-inflammatory, antipyretic, and analgesic activities, have been synthesised by condensing *cis*-2-aminocycloalkanecarboxylic acids with iminoesters.[218,219]



85

R = H, Alk, cyclo-C_nH_{2n-1}, Ar, $PhCH_2$, 4-Py.

Hungarian investigators[220,221] studied in detail the condensation of the esters of the stereoisomeric aminonorbornanecarboxylic and aminonorbornenecarboxylic acids with the iminoesters of aromatic and cycloalkanecarboxylic acids. It was established that the interaction of the ester of *endo*-3-aminobicyclo[2.2.1]heptane-2-carboxylic acid with the iminoesters in ethanol (refluxing for 10 h) results in the formation of 2-substituted 4*ar*,5*t*,6,7,8*t*,8*ac*-hexahydro-3*H*-5,8-methano-3-*H*-quinazolin-4-ones **86** in 53%–81% yield.

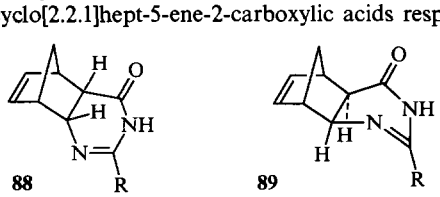


86 **87**

R = Ar, cyclo-C_6H_{11}.

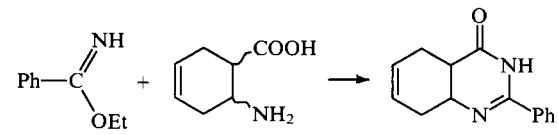
The ester of *exo*-3-aminobicyclo[2.2.1]heptane-2-carboxylic acid reacts with the iminoesters, affording 58%–69% yields of 2-substituted 4*ar*,5*c*,6,7,8*c*,8*ac*-hexahydro-3*H*-5,8-methanquinazolin-4-ones **87**.[220,221]

2-Substituted 4*ar*,5*t*,8*t*,8*ac*-tetrahydro-3*H*-5,8-methanoquinazolin-4-ones **88** (yield 54%–68%) and 4*ar*,5*c*,8*c*,8*ac*-tetrahydro-3*H*-5,8-methanoquinazolin-4-ones **89** (yield 56% to 74%) have been synthesised from the esters of *endo*- and *exo*-3-aminobicyclo[2.2.1]hept-5-ene-2-carboxylic acids respectively.[220,221]

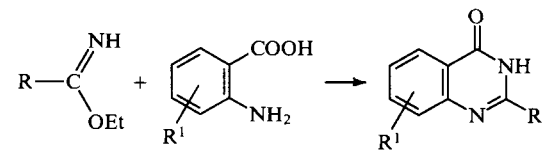


88 **89**

By refluxing equimolecular amounts of the benzoic acid iminoester with *cis*- or *trans*-2-aminocyclohex-4-enecarboxylic acid in chlorobenzene, the same workers obtained 2-phenyl-4*a*,5,8,8*a*, tetrahydro-3*H*-quinazolin-4-one in 62%–65% yield.[222]



The condensation of iminoesters with substituted anthranilic acids in methanol (20 °C, 2 h) resulted in the formation of 6- and 7-substituted 2R-3*H*-quinazolin-4-ones **90** in 21%–51% yields.[223]

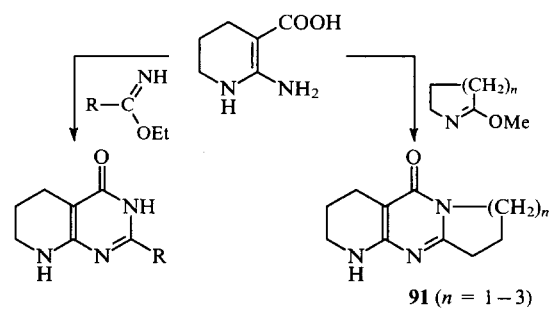


90

R = $PhCH_2$, 4-MeC_6H_4;
R^1 = H, 6-Me, 7-Cl.

The authors note that this reaction is a convenient method of synthesis of the quinazoline alkaloid glucozymine **90** (R = $PhCH_2$, R^1 = H) and related compounds with a high biological activity.

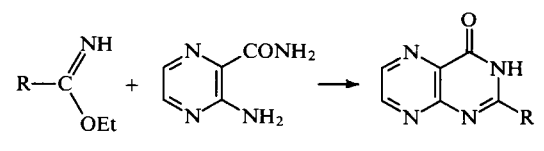
The interaction of iminoesters with heterocyclic *o*-aminoacids or their derivatives leads to the formation of condensed systems incorporating pyrimidine fragments. For example, when the ester of 2-amino-1,4,5,6-tetrahydropyrimidine-3-carboxylic acid was heated with iminoesters in polyphosphoric acid, 2-R-5,6,7,8-tetrahydro-3*H*-pyrido[2,3-*d*]pyrimidin-4-ones were obtained in 47%–48% yields.[224] Under similar conditions, cyclic iminoesters afford the tricyclic systems **91** (yield 58%–68%).



91 (*n* = 1–3)

R = Ph, $PhCH_2$.

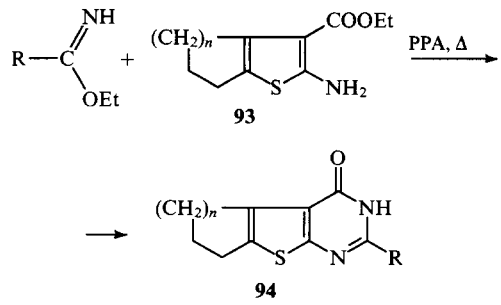
The preparation of 2-substituted 3*H*-pteridin-4-ones **92** by the reaction of iminoesters with the amide of 2-aminopyrazine-3-carboxylic acid has been described in a patent.[225]



92

R = Alk, CHEtCH = CH_2, cyclo-C_3H_5.

Refluxing of iminoesters with the esters of heterocyclic *o*-aminoacids **93** (molar ratio 3:1) in chlorobenzene in the presence of polyphosphoric acid (PPA) leads to derivatives of thieno[2,3-*d*]pyrimidin-4-one **94**.[226]



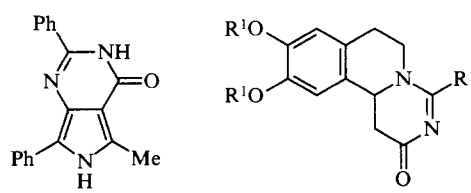
93

94

R = Ph, 3-ClC_6H_4; n = 1, 3.

Italian investigators synthesised derivatives of pyrrolo-[3,4-*d*]pyrimidin-4-one **95** (yield 15%), exhibiting an appreciable anti-inflammatory activity, by heating the benzoic acid iminoester with the ester of 3-amino-5-methyl-2-phenylpyrrole-4-carboxylic acid (140 °C, 18 h).[227]

In the search for new effective substances with analgesic activity, 4-substituted 9,10-dialkoxy-1,6,7,11-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinolin-2-ones **96** have been obtained by condensing iminoesters with the esters of 6,7-dialkoxy-1,2,3,4-tetrahydro-1-isoquinolinylacetic acids.[228]

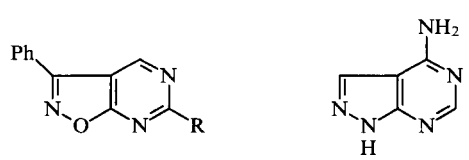


95 **96**

R = Alk, Ar, 4-$ClC_6H_4CH_2$;
R^1 = Me, Et.

The authors note that the pyrimidoisoquinolin-2-ones **96** are formed in 28%–58% yields on refluxing (for 24 h) equimolecular amounts of the reactants in chlorobenzene or are obtained in 40%–70% yields on refluxing (for 16 h) the reactants (molar ratio 10:1) in benzene in the presence of acetic acid.

Japanese investigators synthesised 6-substituted 3-phenylisoxazolo[5,4-*d*]pyrimidines **97** by the reaction of 5-amino-3-phenylisoxazole-4-carbaldehyde with the iminoesters of various acids.[229,230] It is best to carry out the condensation without a solvent at 40–50 °C; under these conditions, the yield of the target isoxazolopyrimidines **97** was 46%–75%.

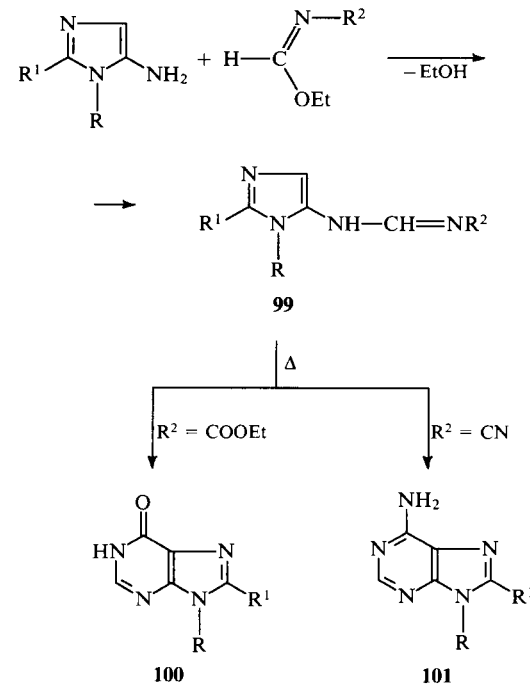


97 **98**

R = Alk, Ph, $PhCH_2$.

Iminoesters are convenient starting materials for the synthesis of purines {imidazo[4,5-*d*]pyrimidines} and their analogues. For example, the synthesis of adenine **98** in 42% yield by the condensation of the formic acid iminoester with 5-(alkoxycarbonylamino)-4-cyanoimidazole in DMF has been described in a patent.[231]

The interaction of 1,2-disubstituted 5-aminoimidazoles with the formic acid *N*-(ethoxycarbonyl)iminoester or *N*-cyanoiminoester leads to the *N,N*-disubstituted amidines **99** (yield 33%–52%), which cyclise to the 8,9-disubstituted hypoxanthines **100** (R^2 = EtOOC) (yield 65%–91%) or to the 9-R-adenines **101** (R^2 = CN) (yield 10%–20%) on heating to 190–260 °C.[232]

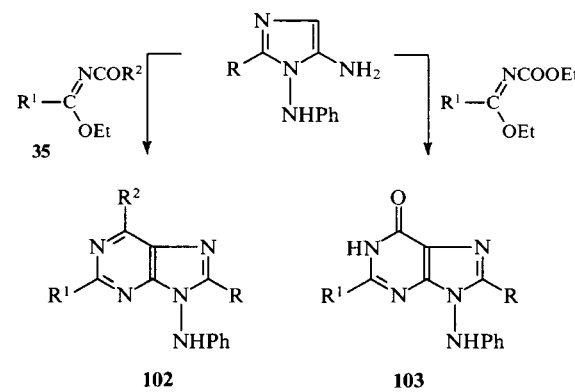


99

100 **101**

R = Me, $HOCH_2CH_2$; R^1 = H, Me; R^2 = EtOOC, NC.

The synthesis of the purine derivatives **102** and the hypoxanthine derivatives **103** by the reaction of 2-substituted 5-amino-1-phenylaminoimidazoles respectively with the *N*-acyliminoesters **35** or with *N*-(ethoxycarbonyl)iminoesters in xylene (refluxing for 1–3 h) has been reported.[233]



35

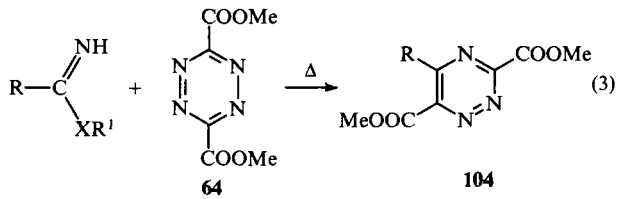
102 **103**

R = Pr^i, Ar, $PhCH_2$, 4-$ClC_6H_4CH_2$;
R^1 = Ph, $PhCH_2$; R^2 = Me, Et.

6. Synthesis of 1,2,4-triazine derivatives

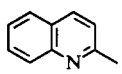
There are hitherto only limited literature data on the synthesis of compounds of the 1,2,4-triazine series using carboxylic acid iminoesters as starting materials.[234]

Boger and Panek obtained the dimethyl esters of 5-aryl-(heteroaryl)-1,2,4-triazine-3,6-dicarboxylic acids **104** (Table 3) as a result of the interaction of dimethyl 1,2,4,5-tetrazine-3,6-dicarboxylate **64** with the iminoesters or iminothioesters of aromatic and heterocyclic acids (molar ratio 2:1) in dioxane at 60–80 °C.[235,236]



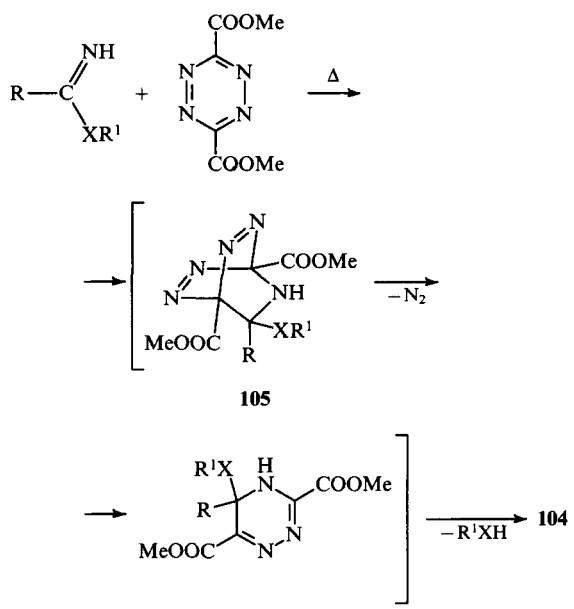
(3)

64 104

R = Ph, 2-Py,  ;

R^1 = Me, Et; X = O, S.

The authors assumed that the initial stage of the reaction is the thermal cycloaddition of the diester **64** to the C=N bond of the iminoester or iminothioester, which in this case are regarded as heterodienophiles. The cyclic adducts **105** formed in this reaction eliminate in succession a nitrogen molecule and an alcohol or mercaptan molecule, being converted into the 1,2,4-triazine derivatives **104.**

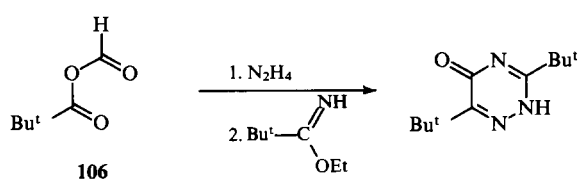


105

The authors note that carboxylic acid amidines and nitriles do not react with the diester **64** under the conditions indicated. Table 3 presents data concerning the influence of the structures of the initial iminoesters and of the reaction time on the yields of the 1,2,4-triazines **104.**

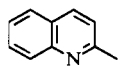
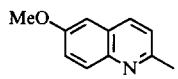
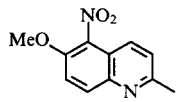
It is noteworthy that the 1,2,4-triazine **104** (R = 6-methoxy-5-nitro-2-quinolinyl) formed in the reaction of the diester **64** with the iminothioester of 6-methoxy-5-nitroquinoline-2-carboxylic acid is a key compound in the total synthesis of the antibiotic streptonigrin.[237]

The successive interaction of equimolecular amounts of the mixed anhydride **106** with anhydrous hydrazine in ethanol (20 °C, 2 h) and then with pivalic acid iminoester (refluxing for 12 h) leads to 3,6-di-*tert*-butyl-1,2,4-triazin-5(2*H*)-one in 40% yield.[238]



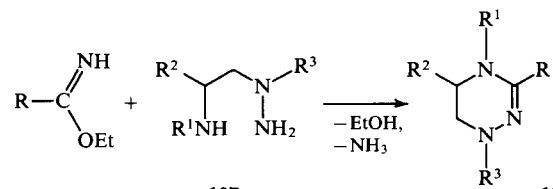
106

Table 3. Synthesis of the dimethyl esters of 5-substituted 1,2,4-triazine-3,6-dicarboxylic acids **104** by the reaction of the dimethyl ester of 1,2,4,5-tetrazine-3,6-dicarboxylic acid **64** with iminoesters or iminothioesters (under a N_2 atmosphere) [reaction (3)].[235,236]

R	R^1X	Reaction conditions		Yield
		T/°C	t/h	(%)
Ph	EtO	60	10	27
	MeS	80	24	64
2-Py	EtO	80	8–12	37
	MeS	80	20	68
	EtO	80	20	33
	MeS	80	4	70
	MeS	80	4	78
	MeS	80	20–24	72–82

The ethyl ester of 3-methyl-5-oxo-2*H*-1,2,4-triazine-6-carboxylic acid has been synthesised in 70% yield by condensing the acetic acid iminoester with the oxomalonic ester hydrazone.[239]

The reactions of *N*-(β-aminoalkyl)hydrazines **107** with iminoester hydrochlorides[240] or iminoesters[241] in ethanol (refluxing for 3–20 h) lead to substituted 1,4,5,6-tetrahydro-1,2,4-triazines **108**, the yield of which varies from 13% to 68% depending on the type of substituents in the initial reactants.

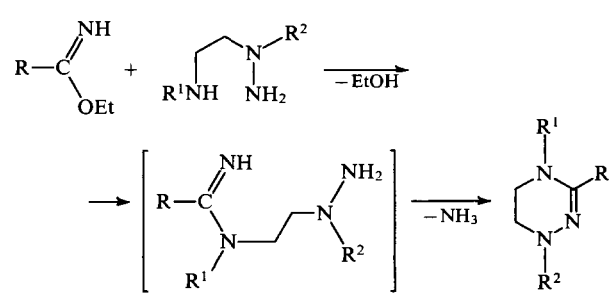


107 108

R = Alk, $Me_3Si(CH_2)_n$ (n = 2, 3), Ph_2CH, Ph_2CHCH_2, $PhCH_2CHPh$, $PhCH_2CH_2$;

R^1 = H, Me; R^2 = H, $HO(CH_2)_2$; R^3 = H, Me.

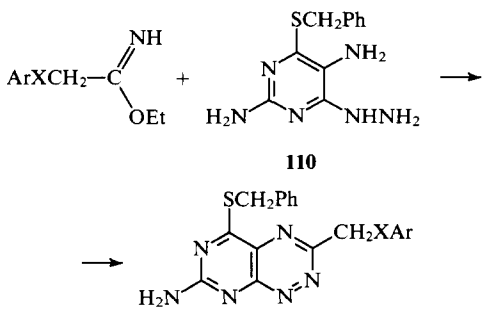
It has been suggested[241] that the electrophilic carbon atom of the iminoester group is attacked by the amine nitrogen atom with formation of the amidine **109**, which cyclises to 1,2,4-triazine with elimination of an ammonia molecule.



109 108

The interaction of equimolecular amounts of aliphatic acid iminoesters and ethylenedihydrazine in ethanol (refluxing for 10 h) led to the synthesis of 3-alkyl-4-amino-1,4,5,6-tetrahydro-1,2,4-triazines in 79%–83% yields.[241]

The condensation of substituted acetic acid iminoesters with 2,5-diamino-6-hydrazinopyrimidine **110** in dioxane at 20 °C results in the formation of derivatives of pyrimido[5,4-*e*]1,2,4-triazine **111** in 37%–64% yields.[242]



110

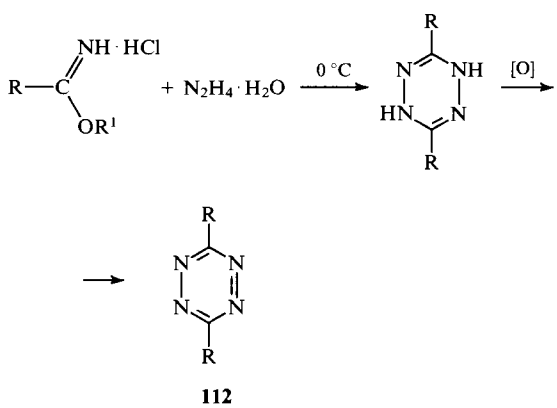
111

Ar = 4-ClC_6H_4, 3,4-$Cl_2C_6H_3$; X = S, NH.

The authors note that the pyrimidotriazines **111** are selective antagonists of folic acid and its analogues.

7. Synthesis of 1,2,4,5-tetrazine derivatives

The interaction of iminoester hydrochlorides with hydrazine hydrate at 0 °C is known[4,5,243–245] to afford 3,6-disubstituted 1,4-dihydro-1,2,4,5-tetrazines, the oxidation of which by atmospheric oxygen, nitrous acid, pentyl nitrite, iron(III) chloride, or hydrogen peroxide leads to symmetrical 3,6-disubstituted 1,2,4,5-tetrazines **112**, the yield of which does not, however, exceed 25%–35%.

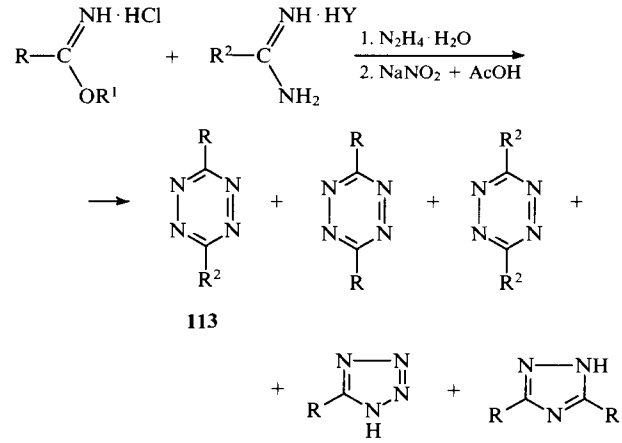


112

R = Alk, Ar, Het.

Investigators have devoted particular attention during the last decades to the development of methods of synthesis of asymmetric 3,6-disubstituted 1,2,4,5-tetrazines **113**, since substances with valuable applied properties have been found among compounds of this type.[198]

In 1975, American investigators[246–248] proposed a method of synthesis of 1,2,4,5-tetrazines **113**, which consists in the condensation of iminoester hydrochlorides with the hydrochlorides or acetates of amidines and hydrazine hydrate in absolute ethanol at −10 to 20 °C (2–3 h) with subsequent oxidation of the intermediate 1,4-dihydro-1,2,4,5-tetrazines (without isolation) by nitrous acid at 5–10 °C. Under these conditions, the target 1,2,4,5-tetrazines **113** are formed in 9%–55% yields together with symmetrical 3,6-disubstituted 1,2,4,5-tetrazines **112**, 5-substituted tetrazoles, and 3,5-disubstituted 1*H*-1,2,4-triazoles.



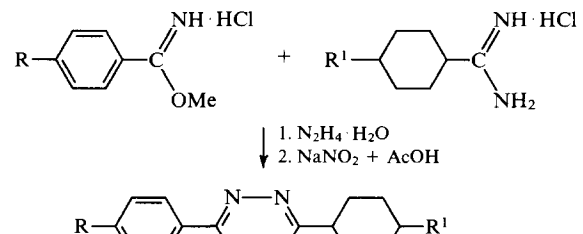
113

R = Bu^t, Ar, 1-Naphth, $PhCH_2$, cyclo-C_6H_{11}, Het; R^1 = Me, Et; R^2 = H, Me, Et, XCH_2 (X = MeO, PhO, MeS, PhS, $PhSO_2$, Cl, HO), $PhCH_2$, 1-Ad, Het; Y = Cl, AcO.

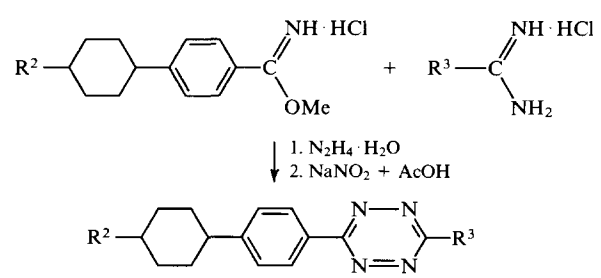
R	R^1	Yield (%)	Ref.
Ph	H	30	246
Ph	Me	11	249
Ph	Et	13	249
4-ClC_6H_4	H	45	246
4-ClC_6H_4	Me	32	246
3-$CF_3C_6H_4$	H	18	246
3-$CF_3C_6H_4$	Me	16	246
4-$MeOC_6H_4$	Me	27	246
4-FC_6H_4	Et	22	246
Bu^t	H	4.5	250
3-$O_2NC_6H_4$	H	25	251

Van der Plas and coworkers[249,250] oxidised the intermediate 1,4-dihydro-1,2,4,5-tetrazines by atmospheric oxygen in solution in methylene chloride or chloroform.

The use of the above method for the synthesis of 3,6-disubstituted 1,2,4,5-tetrazines **114** and **115**, incorporating cyclohexane fragments and alkyl groups with a normal structure, has been described in patents.[251,252]



114



115

R = Alk (C_3–C_5), BuO; R^1, R^2, R^3 = Alk (C_3–C_8).

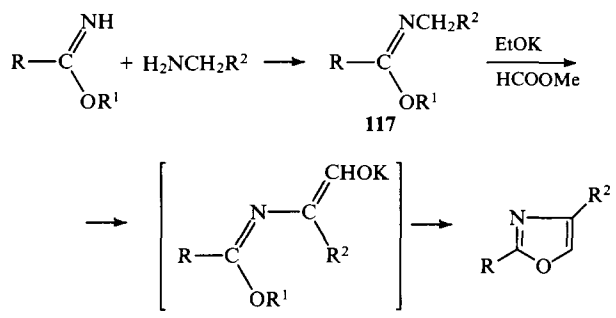
The 1,2,4,5-tetrazines **114** and **115** are used as components of nematic liquid-crystal phases.

III. Synthesis of five- and six-membered heterocycles containing nitrogen and oxygen atoms

1. Synthesis of oxazole and Δ^2-oxazoline derivatives

There are limited data in the literature concerning the synthesis of oxazoles from iminoesters as the initial compounds. This method has found an application only in the synthesis of 2-substituted oxazole-4-carboxylic acids **116** with functional group substitutents.[253,254]

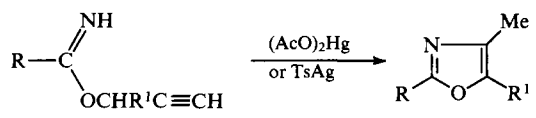
The interaction of iminoesters with aminoacid derivatives — esters, amides, *N*-substituted amides, and nitriles — is known[4,5] to afford the *N*-substituted iminoesters **117**. On treatment with methyl formate and potassium ethoxide (0–20 °C), the latter are converted into the unstable intermediates **118**, which cyclise to derivatives of oxazole-4-carboxylic acids **116**.[4,5,255–257]



117 **118** **116**

R = H, Me, Pr, cyclo-C_6H_{11}, Ar; R^1 = Et, Pr^i;
R^2 = EtOOC, NC, H_2NCO, R^3NHCO; R^3 = Alk.

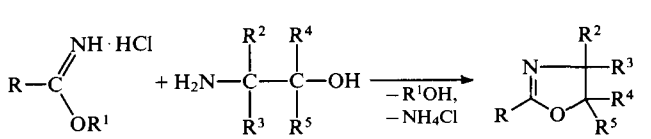
A patent[258] describes the synthesis of trisubstituted oxazoles in 90%–97% yield when propargyl iminoesters are treated with mercury acetate or silver tosylate at 200 °C (1 h).



R = Alk, $Cl(CH_2)_3$, Ph, $PhCH_2$, EtC(OH)Me; R^1 = H, Me.

One of the most important derivatives of the oxazole series are Δ^2-oxazolines, which have been used widely in recent years as intermediates in organic synthesis.[259–262] The cyclocondensation of iminoesters or their hydrochlorides with β-aminoalcohols having different structures is used to obtain ring-substituted Δ^2-oxazolines.[4,5,259,262]

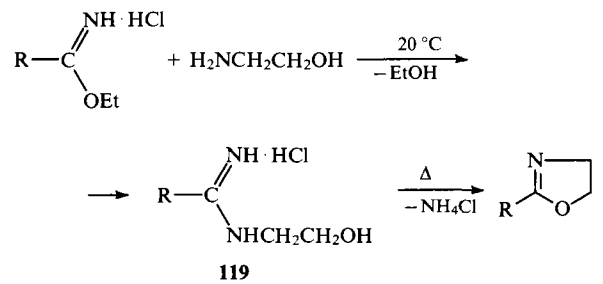
For example, the interaction of equimolecular amounts of iminoester hydrochlorides and β-aminoalcohols in anhydrous solvents (ethanol, methanol, chloroform) affords high yields of substituted Δ^2-oxazolines.[55,62,89,110,263–268]



R = Alk, Ph, PhCH(OH), 4-$MeC_6H_4OCH_2CH(OH)$, 4-HO-3,5-$Bu^t_2C_6H_2(CH_2)_n$ (n = 0, 2), Het;
R^1 = Me, Et; R^2 = H, Me; R^3 = H, Me, EtOOC, $HOCH_2$;
R^4 = H, Me;
R^5 = H, Alk, Ph, (*E*)-$C_{13}H_{27}CH{=}CH$, 4-$MeC_6H_4OCH_2$.

It is noteworthy that the reaction temperature and time as well as the yield of the target Δ^2-oxazolines are determined primarily by the nature of the group in the acid component of the initial iminoester. For example, in the case of iminoester hydrochlorides containing the electron-donating 3-indolyl[55,62,264] or 3,5-di-*tert*-butyl-4-hydroxyphenyl[110] groups, the synthesis of the corresponding Δ^2-oxazolines from ethanolamine in satisfactory yields (46%–62%) requires that the reactants be refluxed in ethanol for 10–12 h. On the other hand, when the hydrochlorides of (3-indolyl)acetic or 3-(3,5-di-*tert*-butyl-4-hydroxyphenyl)propionic acids are used, the cyclisation is completed in 1.5–5 h.

It has been established[266] that the interaction of iminoester hydrochlorides with ethanolamine in methanol at 20 °C (2 h) results in the formation of the hydrochlorides of *N*-substituted amidines **119**, which cyclise on heating to 2-substituted Δ^2-oxazolines in high yields.

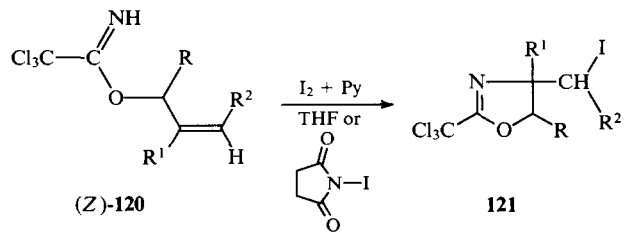


119

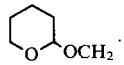
R = Ph, PhCH(OH), 4-$MeC_6H_4OCH_2CH(OH)$.

Substituted Δ^2-oxazolines can also be obtained by condensing iminoester bases with β-aminoalcohols, but in this case the reactions are carried out either with prolonged refluxing in a solvent (chloroform, ethanol)[267] or by heating the reactants without a solvent (160–180 °C) for 16–36 h.[51,264]

Italian investigators have established that the cyclisation of (*Z*)-allyliminoesters of trichloroacetic acid **120** on treatment with iodine and pyridine in THF (20 °C, 12 h)[269] or with *N*-iodosuccinimide in chloroform (20 °C, 12 h)[270,271] leads to the regiospecific formation of 2-trichloromethyl-4-(1-iodoalkyl)-5-R-Δ^2-oxazolines **121** in high yields in the form of a mixture of diastereoisomers. The latter are key compounds in the synthesis of stereoisomeric β-aminoalcohols and certain natural products.[269,270]



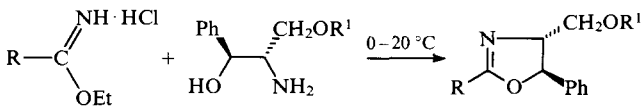
(*Z*)-**120** **121**

R = H, Pr^i, C_5H_{11}, $C_{15}H_{31}$; R^1 = H, Me;
R^2 = H, Et, $C_{15}H_{31}$, $MeOCH_2$, $PhCH_2OCH_2$,  .

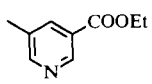
R	R^1	R^2	Yield (%) of **121**
H	Me	H	85
Pr^i	H	H	70
C_5H_{11}	H	H	60
H	H	$C_{15}H_{31}$	90 (*threo*)
$C_{15}H_{31}$	H	H	90 (*cis* : *trans* = 1 : 4)
H	H	Et	88 (*threo*)
H	H	Ph	92
H	H	$MeOCH_2$	87
H	H	CH_2OTHP	81
H	H	$PhCH_2OCH_2$	98

Investigators have devoted much attention in recent years to the synthesis of Δ^2-oxazolines from chiral β-aminoalcohols. The chiral Δ^2-oxazolines formed under these conditions are valuable key intermediates in the asymmetric synthesis of various compounds — 2-hydroxy-, 2-methoxy-, 2-alkyl-, and 2-chloroalkanoic acids, 1,4-dihydropyridines, etc.

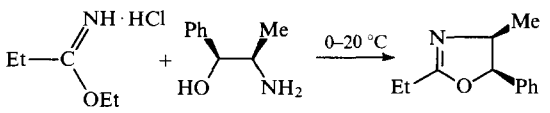
Meyers et al. synthesised (−)-(4*S*,5*S*)-2-substituted 5-phenyl-Δ^2-oxazolines **123** with the *trans*-configuration in 59%–87% yield by the reaction of the hydrochlorides of the iminoesters of various acids with (+)-(1*S*,2*S*)-2-amino-1-phenylpropane-1,3-diol **122** (R^1 = H) or with (+)-(1*S*,2*S*)-2-amino-3-methoxy-1-phenyl-propan-1-ol **122** (R^1 = Me) in methylene chloride (0–20 °C, 6 h).[272–278]



(+)-(1*S*,2*S*)-**122** (−)-(4*S*,5*S*)-**123**

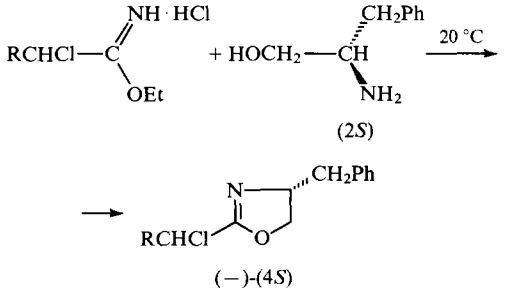
R = Me, Et, Pr, $MeOCH_2$, $ClCH_2$, Ph, $PhCH_2$, 3-Py, 
R^1 = H, Me.

It has been noted[275] that the condensation of the propionic acid iminoester with (+)-(1*S*,2*R*)-2-amino–1-phenylpropan-1-ol in the presence of pyridine in methylene chloride (0 °C; 20 °C, 12 h) affords an 80% yield of (+)-(4*R*,5*S*)-2-ethyl-4-methyl-5-phenyl-Δ^2-oxazoline with the *cis*-configuration.



(+)-(1*S*,2*R*) (+)-(4*R*,5*S*)

Chiral 2-substituted (−)-(4*S*)-4-benzyl-Δ^2-oxazolines have been synthesised in 60%–82% yield by the reaction of equimolecular amounts of 2-chloroalkanoic acid iminoesters with (2*S*)-2-amino-3-phenylpropan-1-ol in methylene chloride at 20 °C.[279,280]



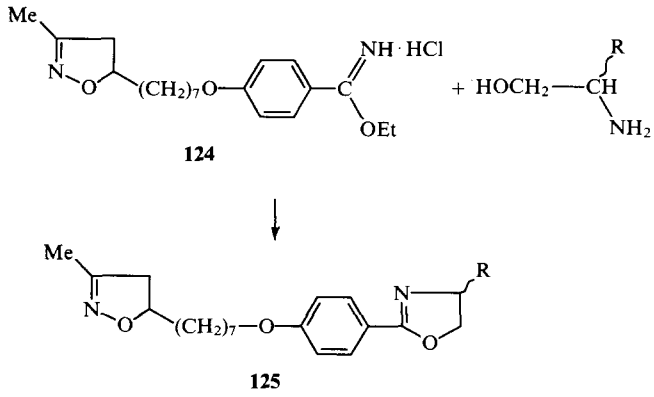
(2*S*)

(−)-(4*S*)

R = Alk.

It has also been noted that, when the phenylacetic acid iminoester is used in this reaction, the corresponding (−)-(4*S*)-2,4-dibenzyl-Δ^2-oxazoline is formed in 71% yield after heating equimolecular amounts of the reactants at 120–130 °C for 12 h without a solvent.[280]

In the search for new effective antiviral preparations — analogues of 3-methyl-5-[7-(4-Δ^2-oxazolin-2-ylphenyloxy)heptyl]isoxazole ('disoxaryl' — an inhibitor of the HPV-14 virus) — individual (4*S*)- and (4*R*)-stereoisomers of the 4-alkyl-Δ^2-oxazolines **125** have been synthesised by condensing the iminoester hydrochlorides **124** with optically active aminoalcohols.[281]

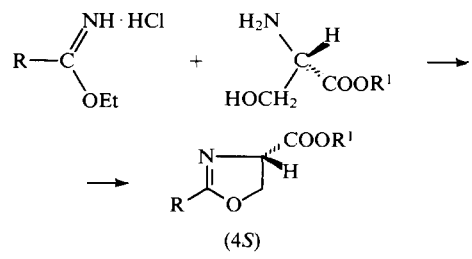


124

125

R = Alk.

The interaction of iminoester hydrochlorides with L-serine esters leads to 75%–76% yields of the chiral esters of 2-substituted (4*S*)-Δ^2-oxazoline-4-carboxylic acids,[282–284] which are used as key compounds in the asymmetric synthesis of 3-substituted alkanoic acids and 3-substituted lactones.[282,283]

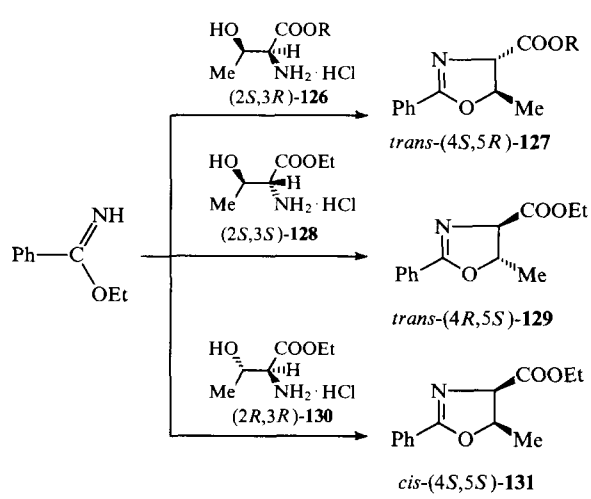


(4*S*)

R = Me, Ph; R^1 = Me, Et.

Racemic esters of 2-phenyl-Δ^2-oxazoline-4-carboxylic acid, which are convenient intermediates in the synthesis of 2-deuterio-D-serine and its derivatives, have been synthesised in 65%–72% yield by condensing the hydrochloride of the benzoic acid iminoester with the hydrochlorides of racemic esters of serine in the presence of triethylamine (molar ratios 1 : 1 : 1) in methylene chloride (20 °C, 8 h).[285,286]

The reaction of the benzoic acid iminoester with the hydrochlorides of L-threonine esters **126** (molar ratio 1 : 1.75) in an ether–water mixture at 20 °C results in the formation of esters of *trans*-(4*S*,5*R*)-5-methyl-2-phenyl-Δ^2-oxazoline-4-carboxylic acid **127** is 70%–72% yield.[287–289]



(2*S*,3*R*)-**126** *trans*-(4*S*,5*R*)-**127**

(2*S*,3*S*)-**128** *trans*-(4*R*,5*S*)-**129**

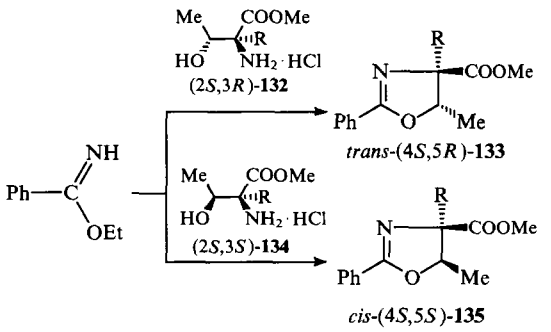
(2*R*,3*R*)-**130** *cis*-(4*S*,5*S*)-**131**

R = Me, Et.

The ester of *trans*-(4*R*,5*S*)-Δ^2-oxazoline-4-carboxylic acid **129** — a key compound in the enantioselective synthesis of the natural azoxyalkene elaiomycin — has been synthesised in 52% yield under similar conditions from the hydrochloride of the D-threonine ester **128**,[290] while the ester of *cis*-(4*S*,5*R*)-Δ^2-oxazoline-4-carboxylic acid **131** — a key compound in the synthesis of L-threonine — has been obtained from the hydrochloride of the ester **130**.[291]

Japanese investigators[292] synthesised the esters of *trans*-(4*S*,5*R*)-Δ^2-oxazoline-4-carboxylic acid **133** (Scheme 3) by the interaction of the benzoic acid iminoester with the hydrochlorides of (2*S*,3*R*)-2-amino-3-hydroxy-2-R-butyric acids **132** (molar ratio 1.2:1) in methanol (refluxing for 14 h). but the yield of the Δ^2-oxazolines did not exceed 12%–18% under these conditions.

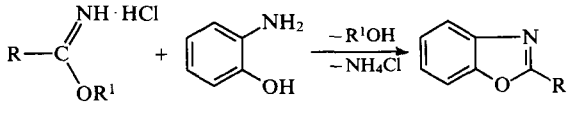
Scheme 3



The esters of *cis*-(4*S*,5*S*)-Δ^2-oxazoline-4-carboxylic acid **135** have been obtained in a low yield (12%–16%) under similar conditions from the hydrochlorides of the esters of (2*S*,3*S*)-2-amino-3-hydroxy-2-R-butyric acid **134** (Scheme 3). The authors note that the Δ^2-oxazolines **133** and **135** are convenient key compounds in the asymmetric synthesis of carboxylic α-alkylamino-β-hydroxyacids.

2. Synthesis of substituted benzoxazoles

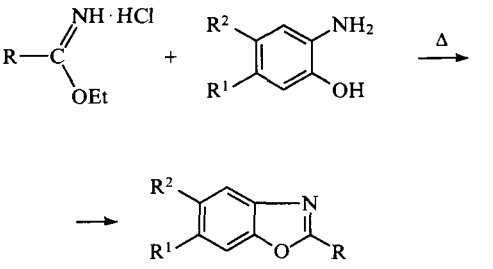
The condensation of carboxylic acid iminoester hydrochlorides with *o*-aminophenyl is known[4,5] to lead to 2-substituted benzoxazoles. It is noteworthy that recently this method has been used most frequently in the synthesis of benzoxazoles from the hydrochlorides of the iminoesters of aliphatic acids with functional-group substituents containing nitro-groups,[67–69] silylalkyl groups,[71,72] halogen atoms,[114,293,294] or an acyl group[106] as well as substituted benzoxazoles,[110] heterocyclic acids,[55,61,62,66,112] and β-substituted acrylic acids.[55,82,295]



R = Alk, $Me_3SiCH_2CH_2$, $Me_2C(NO_2)CH_2CH_2$, $MeC(NO_2)_2CH_2CH_2$, $(O_2N)_3CCH_2CH_2$, $Ac(CH_2)_3$, $Bz(CH_2)_3$, $ClCH_2$, FCH_2, Br_3CCH_2CHBr, $Br_3CCH_2CH_2$, $Cl_3CCH_2CH_2$, $PhCH_2$, Ar, 1-Ad, $4\text{-}O_2NC_6H_4CH{=}CH$, Het.

Reactions of this type are usually carried out by refluxing equimolecular amounts of the reactants in methanol or ethanol for 5–10 h, whereupon the yield of the target 2-substituted benzoxazoles is 63%–97%. The reaction time in each specific case depends primarily on the nature of the group in the acid part of the initial iminoester hydrochloride.[296] We may note that, in the case of iminoester hydrochlorides containing electron-accepting groups, which reduce the thermal stability of the iminoesters, the reactions are carried out at 0–20 °C.[69]

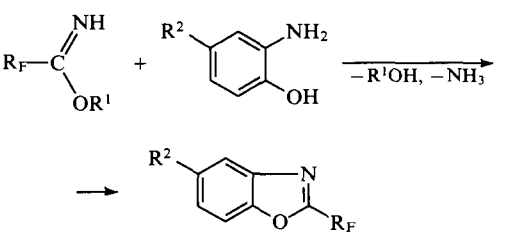
There are isolated literature data on the condensation reactions of iminoester hydrochlorides with ring-substituted *o*-aminophenols, which lead to high yields of 2,5- or 2,6-disubstituted benzoxazoles.[106,297,298]



R = $Ac(CH_2)_3$, $Bz(CH_2)_3$; $R^1 = NO_2$, $R^2 = H$;
R = H, Me, Ph, 3-Py, cyclo-C_6H_{11}; $R^1 = H$, $R^2 = NCCH(Me)$;
R = $ClCH_2$; $R^1 = H$, R^2 = Alk, cyclo-(C_3-C_6).

The synthesis of 1,5-bis(2-benzoxazolyl)-3,3-dinitropentane in 94% yield by the reaction of the hydrochloride of the diiminoester of 4,4-dinitropimelic acid with *o*-aminophenol (molar ratio 1:2) in methanol at 50 °C (1 h) has been reported.[104]

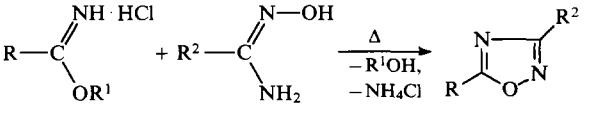
2-Substituted benzoxazoles can also be obtained by condensing iminoester bases with *o*-aminophenol.[296] In the case of iminoesters containing strong electron-accepting groups (for example, the iminoesters of carboxylic perfluoroacids), the condensations take place under mild conditions (20–35 °C, 1–3 h) and the target benzoxazoles are then formed in 75%–86% yields.[296,299]



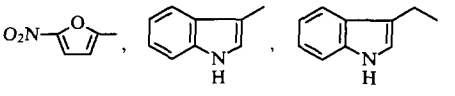
R_F = CF_3, n-C_3F_7, $F_5C_2O(CF_2)_2OCF_2$, n-$C_3F_7O[CF(CF_3)CF_2O]_2CF(CF_3)$;
R^1 = Me, Et; R^2 = H, n-C_3F_7.

3. Synthesis of 3,5-disubstituted 1,2,4-oxadiazoles

Carboxylic acid amidoximes are frequently used as the starting materials for the synthesis of 1,2,4-oxadiazoles.[300] The hydrochlorides of the iminoesters of various carboxylic acids may be used as the second component in the condensation with the amidoximes.[52,56,89,301–305]



R = Alk, Ar, $ClCH_2$, 1-Ad, Het; R^1 = Me, Et;
R^2 = Me, Ph, $ClCH_2$, $4\text{-}O_2NC_6H_4$, $PhCH_2$, 1-Ad,



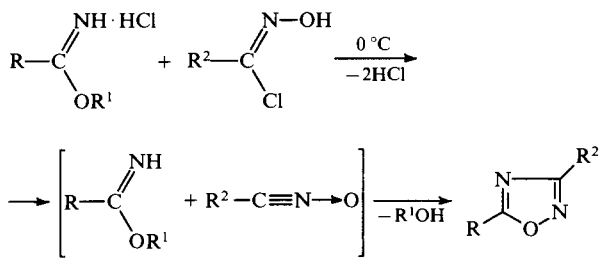
Reactions of this type are usually carried out by refluxing equimolecular amounts of the reactants in ethanol or methanol for 1–12 h, whereupon the yield of the 3,5-disubstituted 1,2,4-oxadiazoles in 38%–92%.

The comparatively low yield (38%–47%) of 3-(3-indolylmethyl)-5,-R-1,2,4-oxadiazoles (R = 3-indolyl, 3-indolylmethyl,

phenyl, *p*-nitrophenyl) has been explained[303] by the thermal instability of the initial amidoxime of (3-indolyl)acetic acid, which decomposes on heating in methanol.

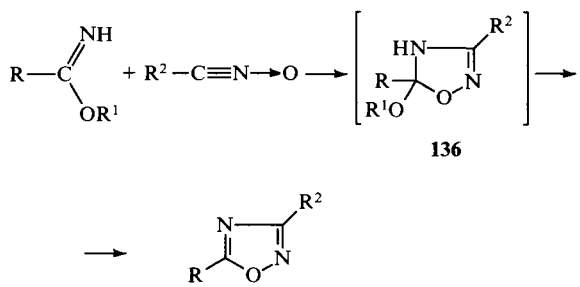
3,5-Disubstituted 1,2,4-oxadiazoles can also be synthesised by the 1,3-dipolar cycloaddition of the *N*-oxides of aromatic and heterocyclic nitriles to the carboxylic acid iminoesters.[107,302,306-312] The 1,3-dipoles (nitrile *N*-oxides) are usually obtained in situ from the chlorides of the corresponding arene- or heteroarene-hydroxamic acids by treatment with bases in the presence of a dipolarophile—the carboxylic acid iminoester. The nitrile *N*-oxides are generated from the hydroxamic acid chlorides by means of either a 5% aqueous solution of sodium carbonate (0–5 °C, 1 h)[302,309] or triethylamine (0–5 °C).[311] In certain cases, the dipolarophile (the iminoester) is also generated from the corresponding iminoester hydrochlorides.[302,308,309]

It has been noted[302,309] that the reactions can be most usefully carried out with a nitrile *N*-oxide : iminoester molar ratio of 1 : (2–2.5) at 0–5 °C for 1 h with subsequent stirring of the reaction mixture at 20 °C for 3 h. When the reactions were performed under the conditions indicated, the yields of 1,2,4-oxadiazoles were 55%–70%.



R = Me, $EtOCH_2CH_2$, 1-Ad, Ar, $PhCH_2$, $PhCH_2CH_2$;
R^1 = Me, Et; R^2 = Ar,  .

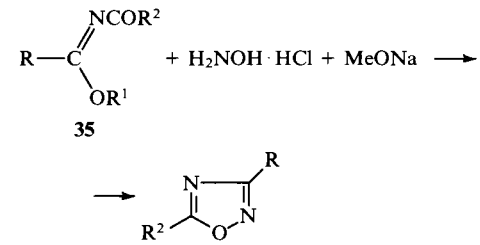
It has been suggested[308,309] that the 1,3-dipolar cycloaddition of nitrile *N*-oxides to the C=N bond of the iminoester involves the formation of Δ^2-1,2,4-oxadiazolines **136** as intermediates, which are subsequently converted into 1,2,4-oxadiazoles as a result of the elimination of an alcohol molecule.



136

An intermediate of this type has been isolated in 34% yield in the reaction of the benzoic acid iminoester with the chloride of 2-methoxycarbonylbenzenehydroxamic acid in the presence of triethylamine.[311] When this intermediate was kept in ether (at 20 °C), it was converted into 3-(2-methoxycarbonylphenyl)-5-phenyl-1,2,4-oxadiazoles in 23% yields.

Certain reactive *N*-substituted iminoesters have also been used as the starting compounds in the synthesis of 1,2,4-oxadiazoles. For example, the interaction of *N*-acyliminoesters with hydroxylamine hydrochloride and sodium methoxide (molar ratios 1 : 1.1 : 1.1) in methanol (20 °C, 12 h; refluxing for 6 h) leads to the formation of 3,5-disubstituted 1,2,4-oxadiazoles in 38%–74% yields.[163]



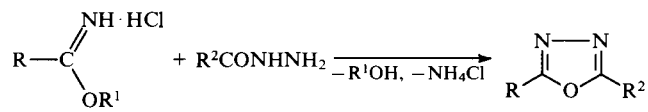
35

R,R^2 = Me, Ar; R^1 = Me, Et.

It is striking that in this case the group R from the acid component of the iminoester occupies the 3-position in the 1,2,4-oxadiazole formed, while the group R^2 from the acyl fragment occupies the 5-position.

4. Synthesis of 2,5-disubstituted 1,3,4-oxadiazoles

It was noted above that on heating with *N*-acylhydrazines (acid hydrazides), carboxylic acid iminoesters give rise either to the *N*-acylamidrazones **28** or to the 3,5-disubstituted 1*H*-1,2,4-triazoles **29**. In 1963, Weidinger and Kranz established[301] that the condensation of the iminoester hydrochlorides with acid hydrazides leads to 2,5-disubstituted 1,3,4-oxadiazoles. Nowadays this method is widely used in the synthesis of 1,3,4-oxadiazoles from iminoester hydrochlorides and the hydrazides of aliphatic, aromatic, and heterocyclic acids.[52,55,56,89,107,168,293,305,313-320]

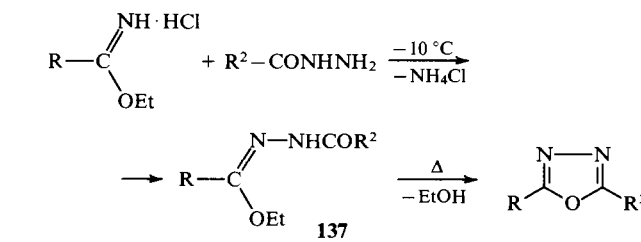


R = Me, $ClCH_2$, $EtOOCCH_2$, $AcCH_2CH_2$, $Me_3SiCH_2CH_2$, cyclo-C_6H_{11}, Ar, PhCH=CH, Het, 1-Ad;
R^1 = Me, Et, Bu; R^2 = H, Me, Ar, cyclo-C_6H_{11}, 1-Ad, Het.

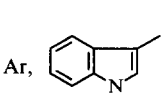
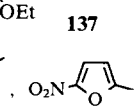
We may note that 1,3,4-oxadiazoles can be obtained by this method in two alternative ways; thus, when the synthesis from two different iminoester hydrochlorides and two hydrazides is planned, the most readily available compounds may be selected.

The condensation of iminoester hydrochlorides with acid hydrazides is carried out as a rule by heating the reactants (78–160 °C) [the iminoester hydrochloride : hydrazide molar ratio is (1–1.35) : 1] in anhydrous solvents—ethanol, DMF, *N*-methylpyrrolidinone, pyridine, or dioxane—for 1–8 h. The yields of the target 1,3,4-oxadiazoles are 55%–94% under these conditions.

The interaction of iminoester hydrochlorides with acid hydrazides involves the formation of the *N*-acylhydrazones of the corresponding esters **137** as intermediates, which in a number of instances have been isolated in 60%–90% yields when the reaction was carried out in ethanol at −10 to 15 °C for 6–24 h.[89,107,168,301,321]



137

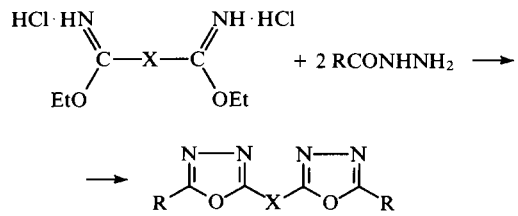
R = Me, Ar,  ,  ;
R^2 = Me, Ar, 4-Py.

On heating to the melting point[89,107,168,301] or on treatment with triethylamine at 20 °C,[321] the esters split off an alcohol molecule and are converted into 1,3,4-oxadiazoles (yield 88%–97%).

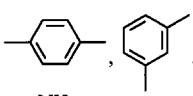
In the search for new substances with anti-inflammatory activity, 2-[ω-(dimethylamino)alkyl]-5-phenyl-1,3,4-oxadiazoles were synthesised by condensing iminoester hydrochlorides with hydrazides.[317] The authors note that, in order to obtain 2-[4-(dimethylamino)butyl]-1,3,4-oxdiazole, it is best to employ the benzoic acid iminoester hydrochloride, while 2-[2-(dimethylamino)ethyl]-1,3,4-oxadiazole is best synthesised from the benzoic acid hydrazide.

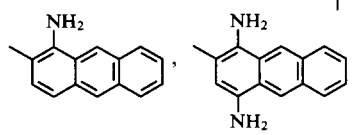
According to patent data,[318–320] the condensation of the hydrochloride of the hydroxyacetic acid iminoester with aromatic acid hydrazides leads to 5-aryl-2-hydroxymethyl-1,3,4-oxadiazoles—important intermediates in the synthesis of compounds with anticonvulsant, analgesic, anti-inflammatory, and diuretic activities.

The condensation of the dihydrochlorides of dicarboxylic acid bisaminoesters with acid hydrazides (molar ratio 1 : 2) results in the formation of bis-1,3,4-oxadiazoles **138**.[301,313]



138

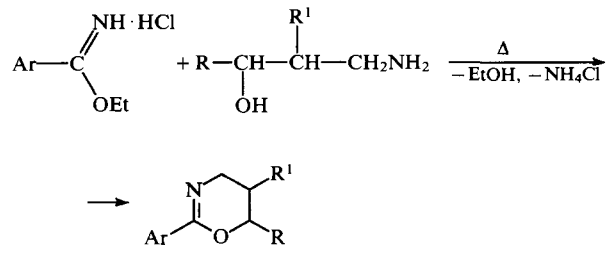
X = $-(CH_2)_n-$ (n = 0, 2, 4),  ;

R = Ar,  .

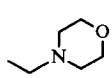
The reactions were carried out by heating the reactants in dioxane, *N*-methylpyrrolidinone, or pyridine and the yield of the bis-1,3,4-oxadiazole **138** was then 40%–80%.

5. Synthesis of 1,3-oxazines and related compounds

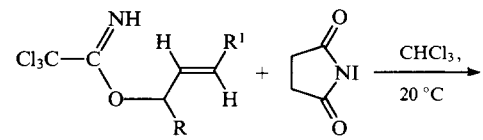
The condensation of aromatic acid iminoester hydrochlorides with substituted 3-aminopropan-1-ols in ethanol (refluxing for 1–2 h) leads to 2,5,6-trisubstituted 5,6-dihydro-4*H*-1,3-oxazines **139**.[322,323]



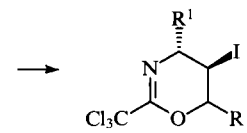
139

R = Ph,  ; R^1 = H, Ph.

It was noted above that the cyclisation of (*Z*)-allyl iminoesters of trichloroacetic acid **120** on treatment with *N*-iodosuccinimide in chloroform (20 °C, 12 h) results in the regioselective formation of 4-(1-iodoalkyl)-2-trichloromethyl-5-substituted Δ^2-oxazolines **121**.[269–271] Under similar conditions, (*E*)-allyl iminoesters of trichloroacetic acid **140** cyclise regioselectively to *trans*-5-iodo-2-trichloromethyl-4,6-disubstituted 5,6-dihydro-4*H*-1,3-oxazines **141**.[271,324]



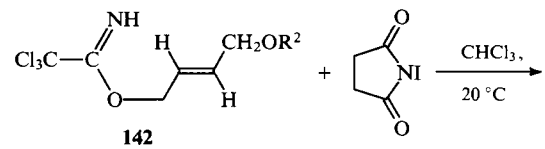
140



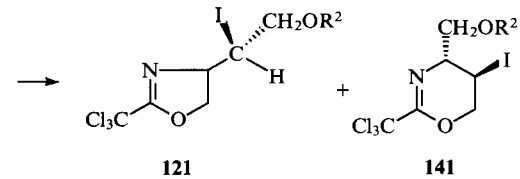
141

R = H, Me; R^1 = Alk, Ph, (*E*)-MeCH=CH, (*E*)-$C_{13}H_{27}$CH=CH.

On the other hand, the (*E*)-allyl iminoesters **142**, containing alkoxy-groups, afford a mixture of Δ^2-oxazolines **121** and 5,6-dihydro-4*H*-1,3-oxazines **141** under the reaction conditions.[318]



142



121 **141**

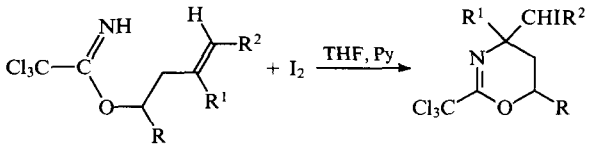
R^2 = Me, $PhCH_2$,  .

Examples of the *trans*-5-iodo-5,6-dihydro-4*H*-1,3-oxazines **141** formed on cyclisation of the (*E*)-allyl iminoesters of trichloroacetic acid **140** and **142** are presented below.

R	R^1	Yield of 1,3-oxazine **141** (%)
H	Ph	80
H	(*E*)-MeCH=CH	90
H	(*E*)-$C_{13}H_{27}$CH=CH	95
Me	Me	85
H	n-$C_{15}H_{31}$	70
H	Et	90
H	Pr	87
H	$MeOCH_2$	30 (61% **121**, R^2 = Me)
H	$PhCH_2OCH_2$	18 (75% **121**, R^2 = $PhCH_2$)
H	CH_2OTHP	38 (55% **121**, R^2 = THP)

(THP = tetrahydropyranyl)

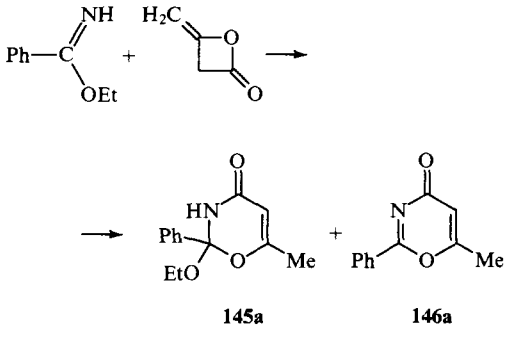
It has been reported[269] that the cyclisation of the homoallyl iminoesters of trichloroacetic acid **143** on treatment with iodine and pyridine in THF (20 °C, 12 h) afforded 4-(1-iodoalkyl)-2-trichloromethyl-5,6-dihydro-4*H*-1,3-oxazines **144** in 65%–90% yields.



143 144

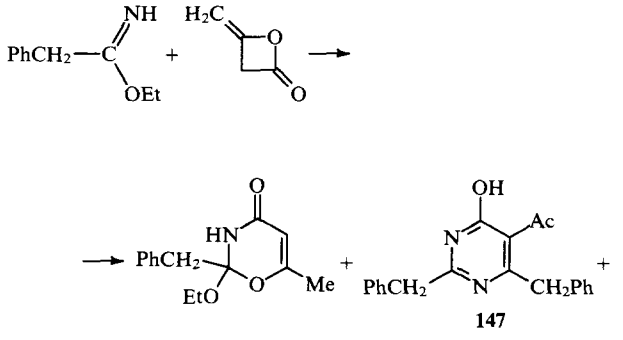
$R = R^2 = H, R^1 = Me$; $R = R^1 = H, R^2 = Et$;
$R = Me, R^1 = R^2 = H$.

A mixture of 2-ethoxy-6-methyl-2-phenyl-3,4-dihydro-2*H*-1,3-oxazin-4-one **145a** (yield 21.3%) and 6-methyl-2-phenyl-4*H*-1,3-oxazin-4-one **146a** (yield 16.0%) was obtained by the reaction of the benzoic acid iminoester with diketene in ether (refluxing for 5 h).[325] The authors note that, on refluxing in benzene, 2-ethoxy-3,4-dihydro-1,3-oxazin-4-one **145a** is converted qualitatively into the 1,3-oxazin-4-one **146a**.



145a **146a**

A mixture of 2-benzyl-2-ethoxy-6-methyl-3,4-dihydro-2*H*-1,3-oxazin-4-one (yield 54.6%), 5-acetyl-2,6-dibenzyl-4-hydroxypyrimidine **147** (yield 27%), and the (*N*-acetoacetyl)amide of phenyl-acetic acid is formed under similar conditions from the phenylacetic iminoester.[325]

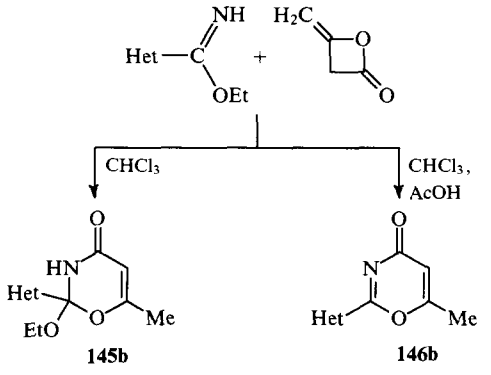


147

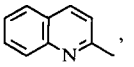
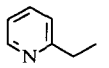
+ $PhCH_2CONHCOCH_2COMe$

On the other hand, the 4*H*-1,3-oxazin-4-one **146a** has been synthesised in 70% yield by refluxing (for 3 h) the benzoic acid iminoester with diketene (molar ratio 1:2) in benzene.[326]

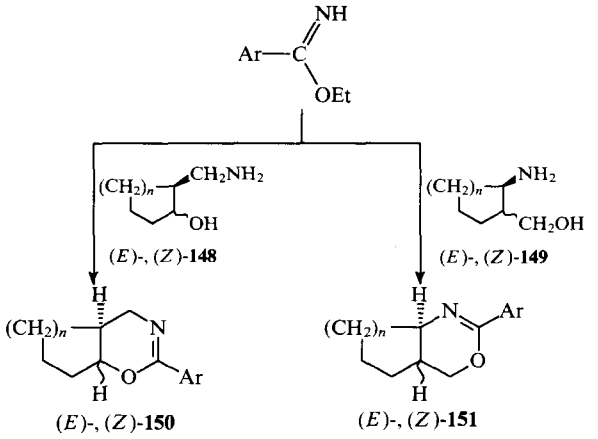
The interaction of the iminoesters of heterocyclic acids with diketene in chloroform in the presence of acetic acid (refluxing for 0.5–2 h) leads to 2-heteroaryl-6-methyl-4*H*-1,3-oxazin-4-ones **146b** in 13%–35% yield.[327] When the reaction is carried out in the absence of acetic acid (20–60 °C, 1–4 h), 2-ethoxy-2*H*-3,4-dihydro-1,3-oxazin-4-ones **145b** are formed in 33%–57% yield.



145b **146b**

Het = 2-Py, 3-Py, 4-Py,  ,  .

Hungarian investigators have studied in detail the condensation of the 4-chlorobenzoic acid iminoester with the stereoisomeric *cis*- and *trans*-2-aminomethylcycloalkanols **148** and 1-amino-2-hydroxymethylcycloalkanes **149**.[328,329] It was established that, when the reactants are heated in ethanol (for 24 h) in the presence of catalytic amounts of HCl, the (*E*)- and (*Z*)-5,6-tetramethylene- or (*E*)- and (*Z*)-5,6-pentamethylene-5,6-dihydro-4*H*-1,3-oxazines **150** are formed respectively in the case of the aminoalcohols **148**.

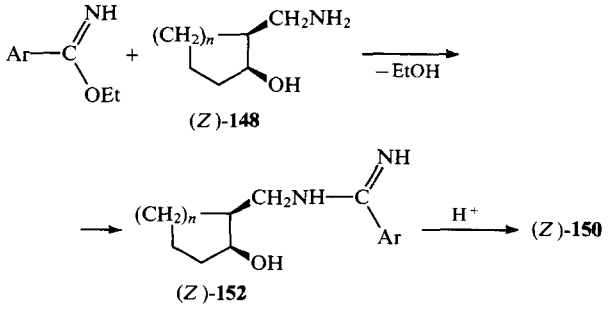


(*E*)-, (*Z*)-**150** (*E*)-, (*Z*)-**151**

$n = 2, 3$; $Ar = 4\text{-}ClC_6H_4$.

Condensation with the stereoisomeric aminoalcohols **149** leads respectively to the (*E*)- and (*Z*)-4,5-tetramethylene- or (*E*)- and (*Z*)-4,5-pentamethylene-4,5-dihydro-6*H*-1,3-oxazines **151** in 70% yield.

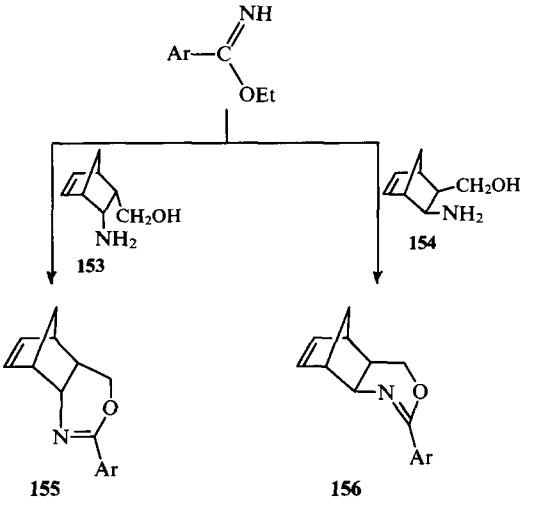
When the (*Z*)-isomers of the aminoalcohols **148** were refluxed (1.5 h) with the 4-chlorobenzoic acid iminoester in ethanol in the absence of an acid catalyst, the *N*-substituted amidines **152** were isolated in 70%–73% yields. On refluxing (for 12 h) in ethanol in the presence of HCl, the amidines are converted into (*Z*)-5,6-dihydro-4*H*-1,3-oxazines **150**.



(*Z*)-**148** (*Z*)-**152**

$Ar = 4\text{-}ClC_6H_4$

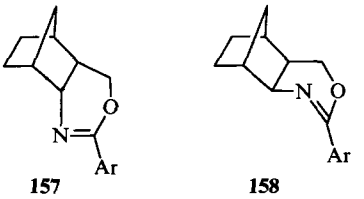
The interaction of equimolecular amounts of aromatic acid iminoesters and 3-*endo*-amino-2-*endo*-(hydroxymethyl)bicyclo-[2.2.1]hept-5-ene **153** or 3-*exo*-amino-2-*exo*-(hydroxymethyl)-bicyclo[2.2.1]hept-5-ene **154** in ethanol in the presence of catalytic amounts of HCl (refluxing for 6–10 h) affords a 32%–48% yield of 2-aryl-5,8-methano-4*ar*,5*t*,8*t*,8*ac*-tetrahydro-4*H*-3,1-benoxazines **155** and 2-aryl-5,8-methano-4*ar*,5*c*,8*c*,8*ac*-tetrahydro-4*H*-3,1-benzoxazines **156** respectively.[330–332]



155 **156**

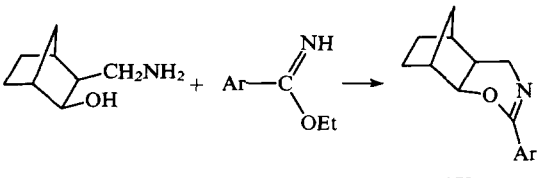
Ar = Ph, 3-ClC_6H_4, 4-ClC_6H_4, 4-MeC_6H_4.

2-Aryl-5,8-methano-4*ar*,5*t*,6,7,8*t*,8*ac*-hexahydro-4*H*-3,1-benzoxazines **157** (yield 34%–45%)[331,332] and 2-aryl-5,8-methano-4*ar*,5*c*,6,7,8*c*,8*ac*-hexahydro-4*H*-3,1-benzoxazines **158** (yield 27% to 38%)[330,332] were synthesised under similar conditions from 3-*endo*-amino-2-*endo*-(hydroxymethyl)bicyclo-[2.2.1]heptane and 3-*exo*-amino-2-*exo*-(hydroxymethyl)bicyclo-[2.2.1]heptane respectively.



157 **158**

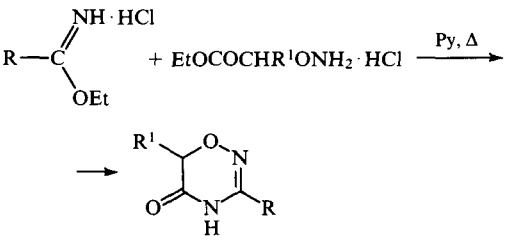
The condensation of aromatic acid aminoesters with *cis,exo*-3-(aminomethyl)bicyclo[2.2.1]heptan-2-ol under the conditions indicated above leads to 2-aryl-5,8-methano-4*ar*,5*c*,6,7,8*c*,8*ac*-hexahydro-4*H*-1,3-benzoxazines **159** in 51%–55% yield.[333]



159

6. Synthesis of 1,2,4-oxadiazine and 1,5,2-dioxazine derivatives

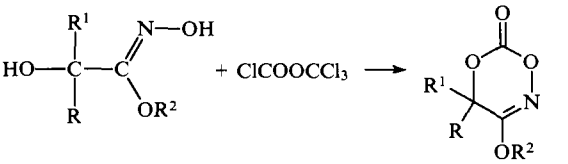
According to patent data,[334] derivatives of 1,2,4-oxadiazin-5-one **160**, which are effective herbicides and plant growth regulators, are formed in satisfactory yields when aromatic and heterocyclic acid iminoester hydrochlorides are refluxed with the hydrochlorides of *O*-substituted hydroxylamine in pyridine.



160

R = Ar, Het; R^1 = H, Me, Et, Ph.

The interaction of the (*E*)-isomers of the *N*-hydroxyiminoesters of carboxylic α-hydroxyacids **161** with trichloromethyl chloroformate at 20 °C leads to 3-alkoxy-4*H*-1,5,2-dioxazin-6-ones **162** in 70%–73% yields.[335]



161 **162**

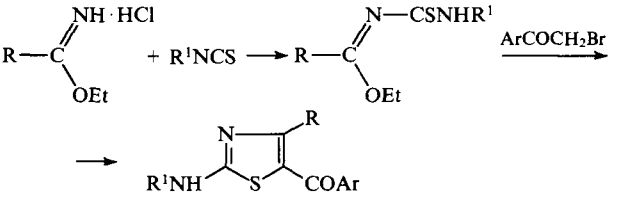
R, R^1 = H, Me, Ph; R + R^1 = $-(CH_2)_5-$; R^2 = Et, $PhCH_2$.

IV. Synthesis of five- and six-membered heterocycles containing nitrogen and sulfur atoms

1. Synthesis of thiazole, Δ^2-thiazoline, and benzothiazole derivatives

It was noted above that the interaction of the *N*-cyanomethyl-iminoesters **5** with hydrogen disulfide in pyridine results in the formation of 5-mercapto-1*H*-imidazoles (yield 20%–35%) together with 5-aminothiazoles (yield 10%–20%).[36]

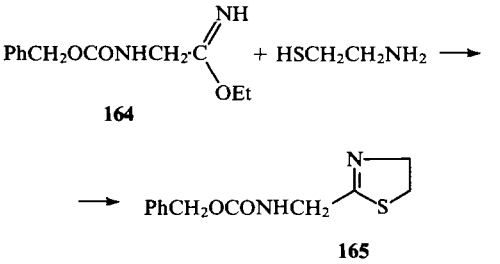
The reactions of aliphatic acid iminoesters with alkyl isothiocyanates lead to *N*-(alkylaminothiocarbonyl)iminoesters, which on treatment with 4-chloro-3-nitrophenylacyl bromide cyclise to 2-aminothiazole derivatives **163** — intermediates in the synthesis of pharmaceutical preparations.[336]



163

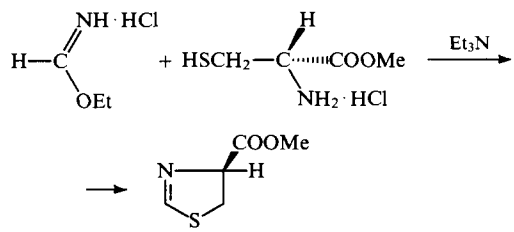
R, R^1 = Alk; Ar = 3-O_2N-4-ClC_6H_3.

The 2-substituted Δ^2-thiazoline **165**, which is a key compound in the synthesis of serine, threonine, allothreonine, and β-hydroxynorvaline, has been synthesised in 75% yield by condensing the *N*-acylated aminoacetic acid iminoester **164** with 2-aminoethanethiol in ethanol (35–50 °C, 3 h).[73]

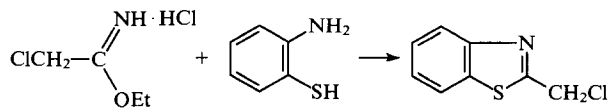


164 **165**

A chiral ester of (4*R*)-Δ^2-thiazoline-4-carboxylic acid has been obtained in 82%–85% yield by the reaction of the formic acid iminoester hydrochloride with the hydrochloride of the methyl ester of D-cysteine in the presence of triethylamine in methylene chloride (20 °C, 3 h).[337,338]

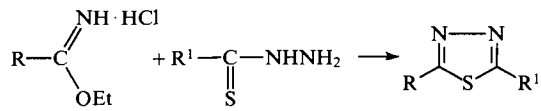


When the chloroacetic acid iminoester hydrochloride is refluxed with *o*-aminothiophenol in chloroform, 2-chloromethylbenzothiazole, which is an intermediate in the synthesis of biologically active substances[339] and functional derivatives of benzothiazole,[293] is formed in 70%–75% yield.[293,339]



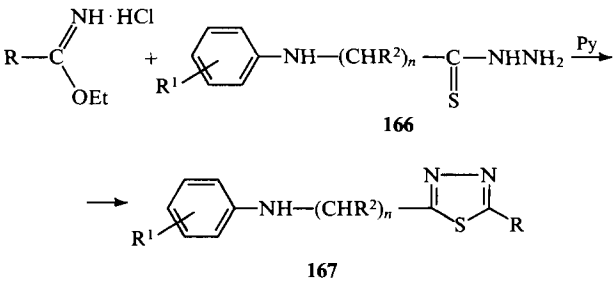
2. Synthesis of 1,3,4-thiadiazole derivatives

In 1963, Weidinger and Kranz[190] proposed a convenient method of synthesis of 2,5-disubstituted 1,3,4-thiadiazoles, which consists in condensing carboxylic acid iminoester hydrochlorides with carboxylic acid thiohydrazides. The reactions were carried out by refluxing equimolar amounts of the reactants in ethanol; under these conditions the yields of 1,3,4-thiadiazoles were 65%–78%.



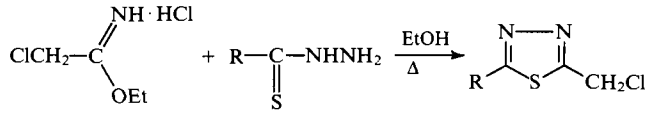
R = Me, Ar; R^1 = Ar.

The interaction of iminoester hydrochlorides with the thiohydrazides of *N*-substituted aminoacids **166** in pyridine leads to the 1,3,4-thiadiazoles **167**, which possess herbicidal properties.[340]



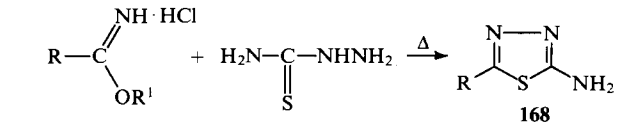
R = H, Me, cyclo-C_nH_{2n-1}, Ar; R^1 = Hal, Alk, AlkO, AlkHal
R^2 = H, Alk; n = 1, 2.

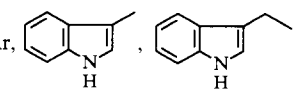
2-Chloromethyl-5-substituted 1,3,4-thiadiazoles, which are intermediates in the synthesis of preparations with an anticonvulsant activity, have been synthesised by the reaction of the chloroacetic acid iminoester hydrochloride with thiohydrazides.[341]



R = Ph, $PhCH_2$, 2-PhC_6H_4, 2-$PhOC_6H_4$, 2-$PhC_6H_4CH_2$.

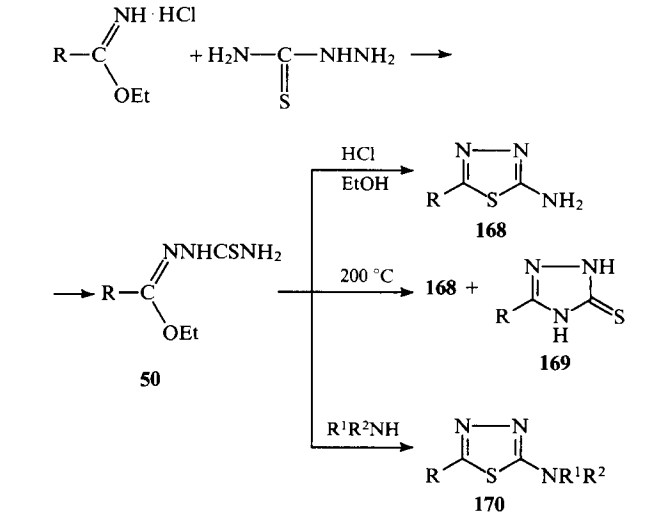
The condensation of carboxylic acid iminoester hydrochlorides with thiosemicarbazide leads to 2-amino-5-substituted 1,3,4-thiadiazoles **168**.[167,190,191,313,342–345] The reactions were carried out by refluxing the reactants in ethanol, dioxane, or pyridine [molar ratio (1–1.2):1; 1–4 h]; the yields of the 2-amino-1,3,4-thiadiazoles **168** were 34%–92%.



R = H, Alk, cyclo-C_6H_{11}, Ar,  ;
R^1 = Me, Et.

It had been noted earlier that the interaction of equimolar amounts of iminoester hydrochlorides and thiosemicarbazide in DMF at 20 °C (20 h) leads to the formation of carboxylic acid ester thiosemicarbazones **50** in 53%–74% yields.[188,189] Under certain conditions, the latter may cyclise to 2-amino-1,3,4-thiadiazoles. For example, 2-amino-5-substituted 1,3,4-thiadiazoles **168** have been synthesised in 31%–85% yields by refluxing the thiosemicarbazones in ethanol (1 h) in the presence of HCl (Scheme 4).

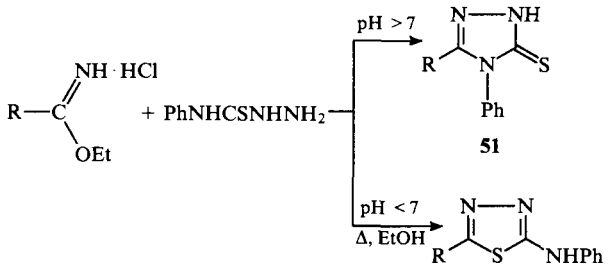
Scheme 4



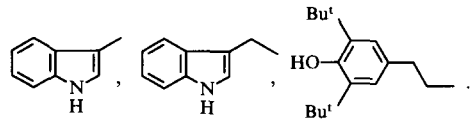
R = Alk, $PhCH_2$, Ar; R^1 = R^2 = Et;
R^1 + R^2 = $-(CH_2)_5-$.

Thermolysis of the thiosemicarbazones (200 °C, 20 min) leads to a mixture of the 2-amino-1,3,4-thiadiazoles **168** (yield 22%–74% and 3-substituted Δ^2-1*H*-1,2,4-triazoline-5-thiones **169** (yield 12%–25%).[188] Substituted 2-amino-1,3,4-thiadiazoles **170** have been obtained in 30%–35% yields by heating the thiosemicarbazone with secondary amines in DMF in a sealed tube (150 °C).[188]

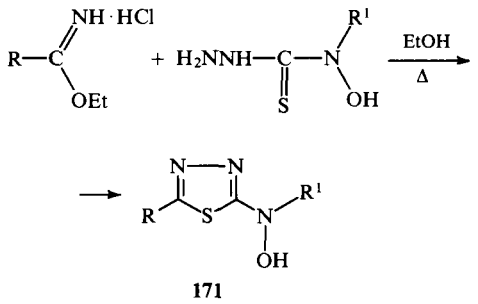
According to literature data,[89,167,190,191,342,343] the mode of the condensation of iminoester hydrochlorides with 4-phenylthiosemicarbazide is determined by the nature of the reaction mixture: in the presence of bases (pyridine, triethylamine, tripropylamine), 3,4-disubstituted Δ^2-1,2,4-triazoline-5-thiones **51** are formed, whereas in an acid medium the products are 2-phenylamino-5-substituted 1,3,4-thiadiazoles (yield 52%–85%).

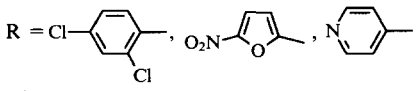


R = Ph, $Me_3SiCH_2CH_2$, $Et_2Si(Me)CH_2CH_2$,



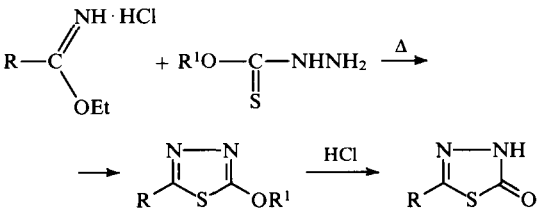
The interaction of equimolar amounts of iminoester hydrochlorides and 4-substituted 4-hydroxythiosemicarbazides in ethanol (refluxing for 0.5 h) leads to 2-hydroxyamino-1,3,4-thiadiazoles **171** in 40%–55% yields.[346]





R^1 = Me, Ar, All.

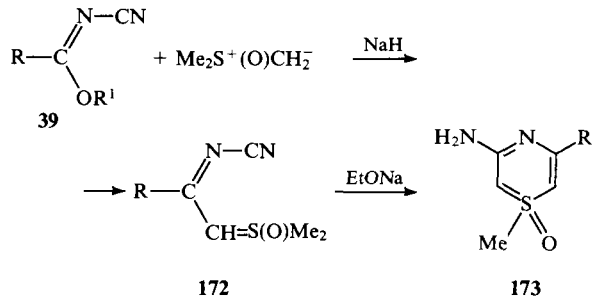
The synthesis of 2-alkoxy-5-substituted 1,3,4-thiadiazoles by the condensation of iminoester hydrochlorides with *O*-alkyl esters of thiocarbazinic acid in ethanol (refluxing for 0.5–1.5 h) has been described in a patent.[347] On treatment with hydrochloric acid, 2-alkoxy-1,3,4-thiadiazoles are converted into 3-substituted Δ^2-1,3,4-thiadiazolin-5-ones, which exhibit insecticidal, acaricidal and fungicidal activities.



R = H, Alk, CH=CH–C_nH_{2n+1} (n = 0–6), Ph;
R^1 = Me, Et, Bu.

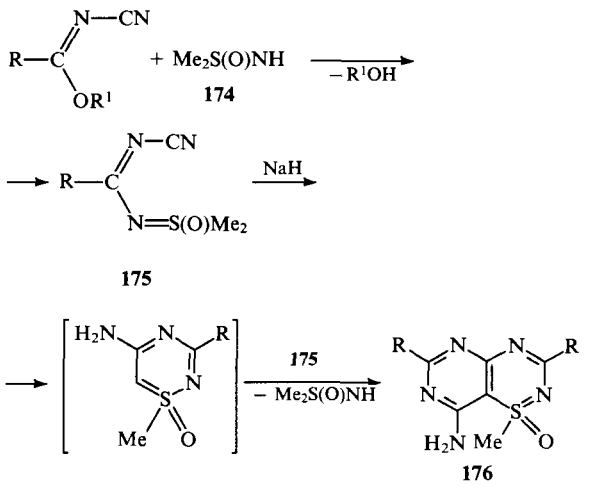
3. Synthesis of thiazine, thiadiazine, and thiatriazine derivatives

It has been reported[348] that the interaction of *N*-cyanoiminoesters with dimethyloxosulfonium methylide (20 °C, 24 h, molar ratio 1:1.2) in DMSO in the presence of sodium hydride leads to the formation of [1-R-2-(dimethyloxo-λ^6-sulfanylidene)ethylidene]cyanamides **172** in 83% yield. On refluxing (for 0.5 h) in ethanol in the presence of sodium ethoxide, the latter cyclise to 3-amino-1-methyl-5-R-1λ^4,4-thiazine 1-oxides **173** (yields 48%–82%).



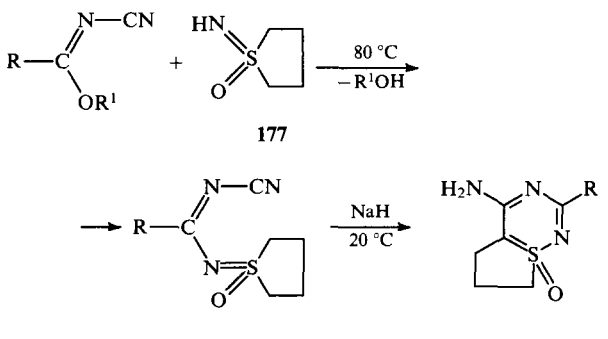
R = Ar,  ;
R^1 = Me, Et.

The condensation of *N*-cyanoiminoesters with the sulfoximide **174** (80 °C, 18 h) leads to *N,N*-disubstituted amidines **175** (yield 27%–91%), which are converted into 3,6-disubstituted 8-amino-1-methylpyrimido[4,5-*e*]-1λ^4,2,4-thiadiazine 1-oxides **176** (yield 39%–57%) on treatment with sodium hydride in DMSO (20 °C).[349]



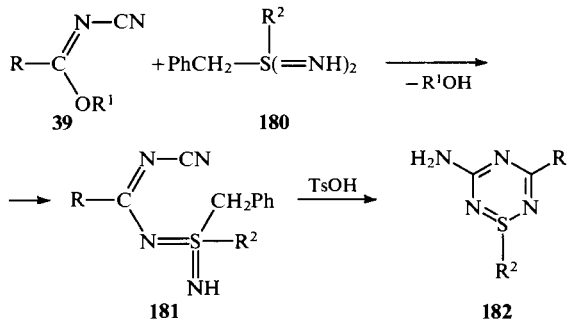
R = Me, Ar,  ,  ; R^1 = Me, Et.

The *N,N*-disubstituted amidines **178** have been obtained under similar conditions from the sulfoximide **177**. On treatment with sodium hydride, the amidines undergo intramolecular cyclisation to 2-substituted 4-amino-6,7-dihydro-5*H*-thieno-[2,1-*e*]-1λ^4,2,4-thiadiazine *S*-oxides **179** (yield 46%–74%).[349]



R = Me, Ph, 4-MeC_6H_4,  .

The reactions of equimolecular amounts of *N*-cyanoiminoesters and *S*-alkyl-*S*-benzylsulfodiimides **180** (60 °C, 16–48 h) afford 43%–90% yields of *N*-(alkylbenzylimino-λ^6-sulfanylidene)-N^2-cyanoamidines **181**.[350]



R = Ar,  ; R^1, R^2 = Me, Et.

On refluxing with toluene-*p*-sulfonic acid in ethanol, the *N,N*-disubstituted amidines **181** are debenzylated with simultaneous cyclisation to 1,5-disubstituted 3-amino-1λ⁴,2,4,6-thiatriazines **182** (yield 48%–71%).

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Heterogeneous free-radical reactions in oxidation processes

M Yu Sinev, L Ya Margolis, V N Korchak

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Abstract. The role of heterogeneous reactions of free radicals in oxidation processes of various types is analysed: homogeneous gas-phase, stabilised combustion, and heterogeneous-catalytic processes. It is shown that in all cases the observed kinetics and product compositions may be determined by the set of heterogeneous and homogeneous stages having the same nature, occurring in the systems simultaneously and as interdependent reactions. The possible mechanisms of the heterogeneous formation of free radicals and of their subsequent reactions are discussed. The methods for the investigation of heterogeneous radical reactions are examined. The bibliography includes 198 references.

I. Introduction

Oxidation processes (extensive and partial oxidation) are traditionally considered independently both in the theory of gas-phase reactions and in heterogeneous catalysis. There are a number of reasons for this, associated with the overall kinetic features, the mechanism of the activation of the reactants, and the chemistry of the elementary stages, which are different in homogeneous and heterogeneous processes. Furthermore, even the systems of concepts, terminology, and general approaches to the analysis and description of the processes in these two fields of chemical kinetics differ significantly.

There exist experimental facts and theoretical concepts according to which heterogeneous processes involving the reactor walls or the surface of solid packing can determine the characteristics of gas-phase oxidation processes. However, in heterogeneous-catalytic oxidation processes there is a possibility of the formation of species carrying an excess of free energy (the active and excited molecules, free atoms and radicals). The release of such species into the gas phase may lead to a homogeneous continuation of the process. Under these conditions, the reactions of the radical species play an especially important role. They are highly reactive in homogeneous processes and can also give rise to surface compounds which are intermediates in oxidation reactions.

Various aspects of the mechanisms and kinetics of heterophase processes involving free radicals have been surveyed in a number of publications.[1–13] The hypothesis of heterogeneous–homogeneous reactions, according to which chain carriers are initiated on the surface of the reaction vessel or catalyst, has been formulated in a review.[1] The release of these carriers into space leads to the continuation of the process in which the bulk-phase and surface reactions occurring simultaneously are closely interrelated and are independent.

The reactions including homogeneous and heterogeneous stages have been classified, the possible mechanisms of the heterogeneous formation of radicals have been analysed from the standpoint of thermochemistry, methods for the recording of active species and for the investigation of heterogeneous–homogeneous reactions have been described, and data concerning the mechanisms and kinetics of specific processes have been examined in a monograph.[2]

The possible variants of the combination of homogeneous and heterogeneous stages of a complex process have been discussed and examples of their occurrence in the oxidation reactions of substances belonging to different classes have been presented in a book.[3]

The differences in the description of gas-phase radical-chain processes have been analysed[4] within the framework of the traditional ideas of the chain theory, which do not take into account the possible participation of the surface in the chain propagation and branching stages, and also within the framework of the approach developed by the author, which does take into account such a possibility. It has been shown in relation to the hydrogen oxidation reaction that allowance for heterogeneous factors permits a more complete description of the phenomenology and kinetics of the process.

Analysis of the mechanism of the partial oxidation of methane showed that the formation of the methyl radical on interaction with an oxidative centre on the surface of the oxide catalyst represents the stage involving the activation of the CH_4 molecule in the catalytic process.[5,6] The selectivity of the process as a whole depends on the subsequent reactions of the $CH_3^{\cdot}$ radical both in the gas phase and in heterogeneous reactions.

The study of Driscoll et al.[7] was largely devoted to the employment of instrumental methods for the detection of free radicals formed in heterogeneous processes. Specfic procedures, which permit the application for this purpose of various modifications of mass-spectrometry, matrix isolation of radicals combined with measurement of IR and EPR spectra, photoelectron spectroscopy, and multiphoton and resonance ionisation methods, have been examined. Examples illustrating the role of free radicals in catalytic reactions have been presented.

Data on the generation of free radicals, obtained mainly by the 'freezing out' (or matrix isolation) of radicals in a matrix of

M Yu Sinev, L Ya Margolis, V N Korchak Laboratory for Heterogeneous Complex Catalysts, Semenov Institute of Chemical Physics, Russian Academy of Sciences, ul. Kosygina 4, 117977 Moscow, Russian Federation. Fax (7-095) 938 21 56

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reagents and reaction products with recording of EPR spectra, have been analysed in recent reviews.[8,9] It was shown that radicals form in many heterogeneous processes, including catalytic oxidation reactions.

Analysis of the reactions of the $OH^{\cdot}$ and $HO_2^{\cdot}$ radicals in the atmosphere showed that heterogeneous reactions of the radicals may be a significant factor determining the gas composition of the troposphere and the stratosphere.[10,11]

The kinetics of the catalytic reactions accompanied by the release of active species into space have been examined in two communications.[12,13] The conditions for the appearance of nonstationary regimes, the possible multistage mechanisms of such reactions, and the kinetic equations for the stationary and nonstationary conditions as a function of the nature of the reaction propagated in the gas phase, as well as the role of the mass transfer processes in the catalyst grain were analysed.

In recent years, the number of studies devoted to the heterogeneous reactions of free radicals has continued to grow. Some of the postulates formulated previously require rethinking in the light of the results. Unfortunately, a systematic consideration of the entire set of available data is not available in the literature. This has stimulated their survey and analysis from a single standpoint and the determination of the direction in which further progress in the understanding of the mechanisms of the oxidation processes may be attained.

II. Heterogeneous factors in homogeneous gas-phase oxidation processes

In the traditional theory of gas-phase radical-chain processes (RCP), the involvement of the surface (as a rule the walls of the reaction vessel or the surface of the packing introduced into the reactor) in the chain initiation and termination stages is considered.[14-16] The presence of a lower ignition pressure limit is associated with the decisive role of the heterogeneous termination. Within the framework of this approach, a significant feature is the regime in which the chain carriers are destroyed — in the diffusional or kinetic regime (in the latter case, an important factor is the probability of their destruction in collisions). On the other hand, the destruction itself is considered only as the disappearance of a species in the gas phase, no attention being devoted to the chemistry of the process and its detailed mechanism.

The need to take account of heterogeneous factors exists also when the chain initiation mechanism is considered. Since the work of van't Hoff,[17] the influence of the material and of the preliminary treatment and relative surface area of the reaction vessel walls on the kinetics of the oxidation processes in the gas phase has been frequently noted.

Considerable progress in the study of the role of the surface and radical-chain processes has been associated with the creation of a method for separate calorimetric measurements,[18] the essential feature of which consists in the measurement of the differences between the temperatures at different points in the reaction volume, for example near the walls and at some distance from them. Depending on the location of the process or of its individual stages, the magnitude and sign of these differences may differ. If heterogeneous stages are completely absent, heating takes place in the centre of the cylindrical vessel, and

$$\Delta T_v = \frac{Q_v}{4\pi\lambda},$$

where Q_v is the heat evolved in the volume reaction per unit time and λ is the thermal conductivity of the gas.

If the reaction takes place wholly on the surface of a cylindrical reactor having a radius R with a thermocouple-containing capillary having a radius r placed along the axis of the reactor, then

$$\Delta T_s = \frac{Q_s}{4\pi\lambda}\frac{r}{R+r}\ln\frac{R}{r},$$

where Q_s is the heat evolved in the heterogeneous reaction per unit time.

Finally, if the process takes place partially on the walls and partially in space, then

$$\Delta T = \frac{Q_v}{4\pi\lambda} + \frac{Q_s}{4\pi\lambda}\frac{2r}{R+r}\ln\frac{R}{r}.$$

Expressions similar to those quoted above may be obtained for fully homogeneous or fully heterogeneous reactions.[19]

In essence, the method involving separate calorimetric measurements has been the first direct experimental method for the investigation of heterogeneous–homogeneous processes. Numerous examples of its successful application to the study of the mechanisms of various processes, including gas-phase oxidation, have been quoted.[1,2,19] An evident limitation of the method is associated with the impossibility of using it to investigate the detailed mechanisms of the heterogeneous formation and subsequent reactions of active species. For this reason, until recently the principal conclusions concerning the mechanism of the heterogeneous stages have been reached on the basis of the analysis of the kinetics of the RCP (Radical Chain Process).

Thus the decrease in the effective activation energies for the thermal and oxidative pyrolysis of methane ($E_{ef} = 85-335$ kJ mol^{-1}) has been attributed to the involvement of the surface in the chain initiation.[20] It has been noted that, under conditions ruling out the influence of the surface (shock waves, adiabatic compression, and jets of a heated carrier gas), higher values of E_{ef} (>370 kJ mol^{-1}) are observed. If the primary step involves the chemisorption of methane, i.e.

$$[S] + H-CH_3 \rightarrow [H...S...CH_3], \qquad (1)$$

then the energy of the dissociation of the C–H bond and of the formation of the primary radicals $CH_3^{\cdot}$ diminishes. In a heterogeneous process involving a carbon surface (any initial surface under cracking conditions is of this kind), the energy E_{ef} decreases compared with its value in a purely homogeneous process approximately by 210 kJ mol^{-1} and approaches the experimental values.

There is serious evidence (see, for example, the study of Garibyan et al.[21]) in support of the heterogeneous chain initiation in the oxidation reactions of hydrogen and C_1-C_3 hydrocarbons in a quartz reactor. A break in the Arrhenius relation for the reaction

$$RH + O_2 \rightarrow R^{\cdot} + HO_2^{\cdot}, \qquad (2)$$

is observed in the temperature range 450–715 °C. The low-temperature section ($E_{ef} = 100$ kJ mol^{-1}) is attributed to a heterogeneous process, while the high-temperature section (200–240 kJ mol^{-1}) is attributed to a homogeneous process.

The possibility of the occurrence of heterogeneous chain branching, propagation, and transfer stages and not merely chain initiation and termination has been discussed.[15,22] This hypothesis makes it possible to explain many facts established in the study of the gas-phase oxidation processes (activation energies, nonlinear variation of the rate of reaction as the concentrations of the reactants are varied, dependence of the composition of the product on the coating of the reactor walls). Nevertheless, specific mechanisms involving heterogeneous stages in the reactions of specific radicals have been scarcely considered until recently in the RCP theory.

The analysis of the influence of heterogeneous factors on the rate of RCP was based on the following postulates:[23]

1. When the first ignition limit is stable and the kinetic curves for the variation of the concentrations of the components of the reaction mixture are reproducible, the rate coefficient for the heterogeneous radical destruction reaction is constant.

2. The heterogeneous chain carrier destruction reaction is a first order process.

3. The adsorption of chain carriers is identical with chain termination.

However, there are a whole series of characteristic features of the RCP kinetics which cannot be described without a more detailed allowance for the role of heterogeneous stages. These features include the following:[24] continued acceleration of the isothermal process after the concentrations or pressures of the reactants reach values below those characteristic of the first ignition limit; expansion of the range of self-ignition under the influence of species preadsorbed on the reactor walls; heterogeneous self-inhibition of the chain combustion; hysteresis phenomena; vibrational combustion regimes in a closed volume.

A series of studies, in which the new approach to the role of heterogeneous factors in gas-phase reactions has been developed, have been devoted to the analysis of these features.[23-38] It was shown that the kinetics of many processes, traditionally regarded as homogeneous, are determined by the presence of a feed-back between heterogeneous reactions and RCP in the gas phase. This is associated to a large extent with the involvement of heterogeneous stages not only (and not so much) in the initiation and destruction of chain carriers but also in the propagation and branching of chains. The reactor surface is regarded as a 'reservoir' providing a store of active species (or their precursors) in the reaction zone and ensuring their involvement in the process (in particular their influence on the branching stage).

One of the possible variants of such influence is the increase in the branching factor during the process as a result of the decrease in the effective rate of the heterogeneous destruction of the chain carriers.[25] This may be induced by a decrease in the probability of the destruction of the radicals in their interaction with the surface as the degree of coverage of the latter by various species increases during the reaction.[26] The fact that during the combustion of H_2 and CO the reaction does not stop when the concentration of the reactants falls below the first ignition limit, i.e. the observed degrees of conversion are much higher than might have been expected for a constant rate of chain termination, has also found an explanation.[23]

In certain cases, it has been possible to determine the nature of the active species concentrated on the surface and to put forward a mechanism of their influence on characteristic features of the process. In particular, it has been shown[29] that, under the conditions of the hydrogen oxidation reaction, the walls of the quartz reactor are capable of adsorbing considerable numbers of hydrogen atoms: one adsorbed hydrogen atom is formed per H_2 molecule converted into water, while at a reactor temperature of 450–650 K the coverage of the reactor wall may be 6.5×10^{13} atoms cm^{-2}.

Hydrogen atoms with similar properties, generated by an incandescent tungsten filament in a hydrogen atmosphere, are adsorbed on quartz. The lifetime of the hydrogen atoms on the surface under the conditions of reduced pressure at the reaction temperature (at least tens of minutes at ~500 °C) exceeds by several orders of magnitude the characteristic lifetimes (tens of seconds). However, when molecular hydrogen is supplied, the surface is rapidly cleaned.

The ability of oxygen to clean the surface by removing the adsorbed hydrogen atoms has been demonstrated in a study of the recombination of hydrogen atoms on the surface of a Chromel–Alumel thermocouple.[28] Whereas at 500 °C at a pressure of 3 Torr the stationary recombination temperature rise in a jet of atomic hydrogen was 2–5 °C, after the treatment of the thermocouple for 10 min with oxygen it rose to 30–50 °C.

The $-\rangle Si-OH$, $-\rangle Si-H$, and $SiH_x(OH)_{2-x}$ groups have been detected by IR spectroscopy during the oxidation of monosilane on a silica gel surface. In the absence of oxygen, they did not appear, i.e. these surface compounds are formed during oxidation and are intermediates.[34]

It has been postulated[23] that the stages involving the formation and reactions of the hydrogen atoms on the reactor surface play an important role in the mechanism of the oxidation of hydrogen. It is suggested (in contrast to the traditional point of view) that the collision of a hydrogen atom from the gas phase with the surface leads not to chain termination by recombination but to the formation of an adsorbed hydrogen atom (H_s), the reaction of which with molecular oxygen leads ultimately to chain branching.

$$H_s + O_2 \rightarrow HO_2, \quad (3)$$

$$H + HO_2 \rightarrow 2\,OH, \quad (4)$$

$$H + HO_2 \rightarrow H_2O + O, \quad (5)$$

$$O + HO_2 \rightarrow OH + O_2. \quad (6)$$

It is suggested that in the above scheme reaction (3) is heterogeneous whilst reactions (4)–(6) may be both heterogeneous, i.e. they proceed with participation of adsorbed atoms, and homogeneous.

In considering the possible mechanism of the heterogeneous chain self-ignition of SiH_4+O_2 mixtures, Azatyan and Aivazyan[35] suggested that, in addition to reactions (3)–(6), the following process leads to chain branching:

$$H_s + O_2 \rightarrow OH_s + O. \quad (7)$$

On the basis of the proposed scheme, it has been possible to construct a kinetic model and to obtain an equation describing the kinetics of the oxidation of hydrogen over a wide range of pressures of the reactants, including the conditions on either side of the lower ignition limit.[23, 32, 37]

Important evidence for the involvement of heterogeneous stages in chain propagation and branching is provided by nonstationary phenomena. The appearance of, for example, hysteresis phenomena and oscillatory regimes under static conditions without self-heating, detected in the oxidation reactions of CO and P_4 and SiH_4 vapours and also in the decomposition of NCl_3,[23] may be caused only by chemical factors, in particular by the reactions of the adsorbed chain carriers.[30-32, 34-36, 38] For example, in the oxidation of silane the propagation of the process as a function of time and also the variation of the first ignition limit are described by curves with hysteresis, which is associated with the reversible variation of the properties of the surface during combustion.[31]

The existence of decaying oscillations in the isothermal combustion of CO in a closed volume is due to the involvement in the reaction of adsorbed atoms and radicals:[29] repeated filling of the reactor containing MgO with a 'dry' $CO+O_2$ reaction mixture leads to a decrease in the number of pulsations, but, after the H_2+O_2 reaction has been carried out in the same reactor, the initial nature of the oscillations is restored.

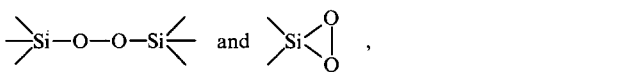
Repeated isothermal ignition in a closed volume has been observed also in the reaction of monosilane with oxygen. Azatyan and Aivazyan[38] were able to show that successive flashes occur at different distances from the reactor wall, have different spectral compositions, and correspond to different overall processes.

The results of kinetic analysis indicate[12] that the presence of several stationary states, including two unstable states responsible for the occurrence of autooscillations, may be associated with the reversible adsorption-desorption of radicals.

The studies considered above have not only created a new approach to the understanding of the kinetics of the RCP but have also posed the question of the chemical behaviour of the 'wall', which is important. Unfortunately, nothing has been said in the above communications concerning the nature of the surface centres of quartz responsible for the strong adsorption of hydrogen atoms and also the possibility of the occurrence of reaction (3), which is a key process in the chain branching induced by the surface.

The results of the study of the surface centres of oxides subjected to mechanical activation[39-45] and of 'reactive silica', obtained by the heat treatment of the large surface area of silica subjected to preliminary methoxylation,[46] have thrown some light on this question. Centres of various types are present on such surfaces and may be converted into one another and modified by means of special chemical treatment.

Centres of the paramagnetic and diamagnetic types, such as the $-\overset{|}{\underset{|}{Si}}^{\bullet}$, $-\overset{|}{\underset{|}{Si}}-O^{\bullet}$, and $-\overset{|}{\underset{|}{Si}}-OO^{\bullet}$, doubly coordinated silicon atoms $=Si:$, strained $-\overset{|}{\underset{|}{Si}}-O-\overset{|}{\underset{|}{Si}}-$ bridges, and the peroxide groups

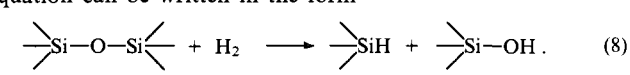


have been identified by EPR and optical spectroscopy. Their structures and reactivities have been investigated and it has been shown that some of them may induce the dissociation of the C–H and H–H bonds. Quantum-chemical calculations and comparison of the activation energies for the reactions of various surface centres of mechanically activated quartz with H_2, D_2, CH_4, C_2H_6, and C_3H_8 molecules have demonstrated the applicability of the Polanyi–Semenov correlation,

$$E = E_0 + \alpha|\Delta H| ,$$

to the reactions of surface centres with gas phase molecules.

It has been suggested[29] that the siloxane bonds are 'opened' under the influence of hydrogen atoms on the surface of quartz and hydroxy-groups are formed. Bystrikov et al.[40] were able to demonstrate by the NMR and IR spectroscopic methods and by the thermal desorption method in combination with quantitative chemical analysis that, when quartz is ground under a hydrogen atmosphere, $-\overset{|}{\underset{|}{Si}}H$ groups are formed, i.e. the overall reaction equation can be written in the form



(8)

According to the data obtained by Bobyshev and Radtsig,[44] the X–H bond dissociation energies in the surface compounds $-\overset{|}{\underset{|}{Si}}H$, $-\overset{|}{\underset{|}{Si}}OH$, and $-\overset{|}{\underset{|}{Si}}OOH$ are 419, 510, and 389 kJ mol^{-1} respectively. The first two values are comparable with the Si–O bond strength in quartz and, if analogous surface compounds are formed in the interaction of the surface of the quartz reactor with hydrogen atoms under the experimental conditions,[29] then the hydrogenation of the surface by hydrogen atoms is entirely probable. For such bond energies, the lifetime of the hydrogen on the surface should be extremely long even under evacuation at elevated temperatures. The probability of reaction (3) increases with decrease in the hydrogen bond energy. This question will be examined in greater detail below.

We shall consider specially the 'stabilised combustion' process, which will be understood (in accordance with Pfefferle and Pfefferle[47]) as gas-phase combustion occurring in the presence of a catalytically active surface of a solid. This makes it possible to carry out the process in 'weak' mixtures of a fuel with an oxidant at much lower temperatures, with a much lower yield of impurities contaminating the environment (in the first place nitrogen oxides), and with an increased efficiency of utilisation of the heat evolved under these conditions.[48]

Various catalysts, the macrokinetics of the processes, and the design of the reactors employed to achieve the stabilised combustion of various fuels (hydrocarbons, hydrogen, and CO) have been considered in a series of reviews.[47,49–51] Direct measurements of the concentrations of the active species (OH$^{\bullet}$ radicals[52–54] and oxygen atoms[55]) showed that, depending on the conditions and the nature of the surface, they can both decrease monotonically on moving away from the surface (in this case the process apparently proceeds as a heterogeneous reaction or is concentrated in the near-surface layer) and can pass through a maximum. The latter case probably indicates directly the occurrence in space of a chain process initiated by the reaction on the surface.

It is of interest that in the combustion of hydrogen the concentrations of the OH$^{\bullet}$ radicals ($\sim 10^{15}$ cm^{-3}) and the profiles of their concentrations along the normal to the surface are virtually identical for platinum and quartz at 1170 K.[47,52] For the combustion of methane[55] and ethane,[54] the oxygen atom concentration profiles depend on temperature in the case of the platinum catalyst: the concentration of oxygen atoms decreases monotonically on moving away from the surface below 1570 K (methane) and 1450 K (ethane), while at higher temperatures a concentration maximum ($\sim 10^{16}$ cm^{-3}) is attained at distances of 0.5–3.0 mm. In the case of a quartz surface, the concentration of oxygen atoms passes through a maximum, reaching $\sim 4 \times 10^{15}$ cm^{-3} (1580–1665 K, methane) and $\sim(1-2) \times 10^{15}$ cm^{-3} (1315–1560 K, ethane).

A wider range of metals has been investigated in the combustion of hydrogen.[56] The activity of the metals increases in the sequence Pt > Pd > Rh > Ir > Ni. With increase in pressure in the range 0.005–0.2 Torr in the temperature range 950–1300 K, the yield of the OH$^{\bullet}$ radicals passes through a maximum at 0.7 ± 0.1 Torr, but the maxima in the rate of reaction as a whole and in the rate of formation of the radicals may not coincide. The activation energies for the formation of radicals vary in the range from 1150 (Rh) to 172 (Pt) kJ mol^{-1} and are not correlated with the activities of the metals. The OH$^{\bullet}$ radicals are also formed in the reaction of hydrogen with a preoxidised metal in the absence of oxygen from the gas phase, i.e. they may be a product of the reaction of hydrogen with adsorbed oxygen atoms.

The data obtained in the above investigations[47–56] make it possible to return to the analysis of the influence of heterogeneous factors in gas-phase combustion processes at a new level. However, one should note yet again that even the early investigations (see, for example, Polyakov[1] and Gorokhovatskii et al.[2]) demonstrated in relation to the oxidation of hydrogen and hydrocarbons that the 'slow homogeneous' and explosive heterogeneous initiated oxidation processes obey the same rules. The results of the above investigations[47–56] show that the behaviour and role of the surfaces of the traditional 'wall-type' (quartz) and classical catalytic materials (Group VIII metals) in combustion processes may be similar.

III. Free radicals in heterogeneous-catalytic oxidation processes

It is clear from the preceding section that, whilst recognising the important role of the heterogeneous reactions of radicals in gas-phase oxidation processes, the RCP theory does not deal with the detailed mechanisms of these reactions, being restricted to a macrokinetic and in a number of instances a stoichiometric description. The details of the interaction of species with the surfaces of solids have been investigated traditionally in heterogeneous catalysis, resorting to data derived from solid state chemistry and surface science.

Out of the entire wide variety of processes in which both the surface of a solid and the surrounding bulk phase play a significant role, in heterogeneous catalysis one usually considers heterogeneous–homogeneous reactions which begin on the surface and pass to the surrounding space as a result of the release of active intermediate species into the gas phase, where the reactions involving them continue or are terminated.[13] In the present review, only processes with participation of radical species are considered, although there is a possibility that saturated molecules capable of reacting in the gas phase at a high rate[2] as well as molecules in an excited state[57] are released into space.

Generally speaking, the radicals formed in the heterogeneous stages may play yet another role in the process — they may be trapped by another active centre on the surface. In this case, the majority of the radicals are converted into the final reaction products within the catalyst grain or layer and only a small proportion of them, largely generated by the outer surface, may be detected experimentally in the free volume of the reactor.[58,59] There are also grounds for classifying these processes as heterogeneous–homogeneous because, firstly, the nature of the radical generation stage may be different in the two cases and, secondly, the radical may undergo reactions in homogeneous

stages between each generation on one centre and chemisorption on another, which again necessitates the joint consideration of heterogeneous and gas-phase processes. Furthermore, in the 'classical' heterogeneous – homogeneous catalysis it is likewise not permissible to rule out the possibility of a secondary interaction of the radicals with the surface, so that all the important stages in the chemical processes are of the same nature in both cases.

Thus all the reactions, the significant stages of which occur both on the surface and in space regardless of the role of these stages in the process as a whole (activation of the reactants, conversion of the intermediates, formation of the final products), should apparently be regarded as heterogeneous – homogeneous reactions.

This approach may prove to be too broad, but it makes it possible to consider related processes from single standpoints without emphasising the formal difference between them.

Before proceeding to the consideration of the individual stages of heterogeneous – homogeneous catalytic reactions, we shall consider general features. One may postulate that the probability of the formation of radicals should increase with decrease in the probability of the 'adhesion' of the reactant molecules to the catalyst surface, i.e. the heterogeneous – homogeneous character of the process should be more pronounced (a) in the oxidation of saturated molecules (hydrogen, alkanes) compared with alkenes, aromatic hydrocarbons, or organic compounds with functional group substituents, (b) in the case of compounds of one class — organic compounds with a smaller number of carbon atoms, (c) for oxide catalysts compared with metals, (d) for oxides without transition metal ions, and (e) at higher temperatures.[2]

Analysis of the literature data (Table 1) shows that the transfer of the reaction into space has been detected in a wide variety of processes with participation of compounds of different classes and molecular masses on catalysts of different nature. This is also indicated by the compilation of all the data presented by Gorokhovatskii et al.[2] Thus one may conclude that the presence of a homogeneous component in catalytic oxidation reactions is a common phenomenon. Despite the fact that the available literature data refer to catalytic systems and reactant conditions which are difficult to compare, in considering them it is possible to differentiate a series of common key aspects including common kinetics of heterogeneous – homogeneous catalytic reactions, a common mechanism of the formation of free radicals in heterophase processes, and common reactions of the radicals, including their interaction with the surface.

1. Kinetic features of heterogeneous – homogeneous catalytic processes

In a number of cases, the conclusion that heterogeneous-catalytic reactions undergo homogeneous propagation has been based on the analysis of the process kinetics (Table 1). Indeed, the presence of two reaction zones in a heterogeneous – homogeneous process may lead to the appearance of specific characteristics of the kinetics. In a number of cases, it is possible to differentiate the heterogeneous and homogeneous components.

The previously widely used kinetic method for demonstrating the heterogeneous – homogeneous nature of the process by varying the ratio of the surface of the catalyst or an 'inert' material to the free volume of the reactor (S/V) (see, for example, Refs 1, 2, 12, and 13) is based on the variation of the relative sizes of the reaction zones. Such demonstration is more reliable if the selectivity in the formation of various products varies simultaneously with the rate of the process as the S/V ratio is varied. For example, in the oxidation of propene on a bismuth – molybdenum oxide catalyst, it was demonstrated by this method[77] that epoxypropane is formed in a homogeneous process from the radicals released into space, while acrolein is formed in a process occurring on the surface. Similar experiments at higher temperatures have demonstrated that biallyl is a product of the homogeneous reactions of allyl radicals.[97]

The procedure used to demonstrate the involvement of radicals in the reaction, which consists in varying the direction of the flux of reactants in the presence of a large free volume along only one direction from the catalyst bed,[80] may be regarded as a variety of the method examined above. The nonadditivity of the rate of the oxidative dehydrogenation of propane in the free volume and on a thin bed of a V – Mg oxide catalyst has been demonstrated[80] and the observed proportions of the products have been accounted for by the occurrence of a chain reaction in the free volume.

The method involving the variation of the free volume has been used widely also at the present time, but, when applied to catalytic reactions, it can lead to erroneous conclusions. This is associated with the fact that, when the S/V ratio is varied, the rate and selectivity of the process may vary significantly only when the specific rates of the heterogeneous generation and destruction of the radicals are relatively low. Otherwise, the probability of the destruction of the radicals within the grain is close to unity (see the estimates made in a number of investigations[13,59,60]), the degree of conversion of the reactants on the catalyst is also high, and the homogeneous reaction occurring in the free volume does not contribute significantly to the process as a whole.

The nonmonotonic nature of the dependences of the reaction rates on the reactant concentrations has also been attributed to the heterogeneous – homogeneous course of process. Thus it has been assumed[61] that the extremum in the dependence of the rate of the catalytic oxidation of hydrogen on the concentration of oxygen cannot be accounted for within the framework of the equations obtained by the stationary concentrations and active surfaces methods. Since the maximum rate of reaction was attained with mixture compositions corresponding to the explosion limit, the observed features were accounted for by resorting to the concept that the hydrogen combustion is a chain reaction.

In a study of the oxidation of methane on MgO, an abrupt change in the composition of the products was observed when the contact time was varied.[98] The authors suggested that this can be accounted for by the difference between the concentrations of the methyl radicals in the gas phase and by the occurrence of their recombination reaction at higher concentrations (second order with respect to $CH_3^{\bullet}$ radicals) and of the addition of an oxygen molecule, i.e.

$$CH_3 + O_2 \Longleftrightarrow CH_3O_2,$$

at their lower concentration and subsequent formation of the extensive oxidation products (first order with respect to $CH_3^{\bullet}$ radicals).

A similar effect has been observed by other investigators[98,99] in the oxidation of methane on phosphate catalysts: a decrease in temperature and an increase in the oxygen concentration led to the preferential formation of formaldehyde, while the opposite change in conditions resulted in the growth of selectivity with respect to ethane. At a constant temperature, the overall selectivity with respect to $HCHO + C_2H_6$ remained almost unchanged, while the fraction of formaldehyde increased in proportion to the oxygen concentration, differing significantly on different catalysts. The authors postulate that this effect is due to a combination of the following factors: the dependence of the equilibrium position in the reaction involving the addition of oxygen to CH_3 on temperature and oxygen concentration and also the differences in the elementary interactions of the radicals with the surfaces of different catalysts.

The generalised formal kinetic models for heterogeneous – homogeneous reactions have been examined in a number of studies.[12,13,100] It was shown that, when the simplest multistage mechanisms operate, the forms of the kinetic equations for heterogeneous and heterogeneous – homogeneous nonchain reactions may be identical.[13]

Table 1. The release of species into the free volume in catalytic oxidation reactions.

Substance oxidised	Catalyst	Lower temperature limit of release into space/°C	Method of detection[a]	Ref.
H_2	$V_2O_5-MoO_3$	400	KA	60, 61
	Pt	500	LIF	62
	Pt	–	RFM	63
NH_3	Pt	525		64
CO	Pt	180	KA	65
	Pd	200	KA	66, 67
CH_4	SiO_2, Al_2O_3	650	KA, RFM	68
	MgO, Li/MgO, lanthanide oxides	500	RFM	69, 70
	metal oxides	500	KA	71
	K/Al_2O_3, Al_2O_3	550	RFM	59
	Sr/La_2O_3	700	PIMS	72
	MgO, Sm_2O_3	450	TAP	73
C_1-C_4	MgO	>25	IR, TPD	74
C_1-C_3	MgO, PbO, Bi_2O_3, $Bi_2O_3-MoO_3$	500	RFM	75
C_2-C_8	Al_2O_3, Cr_2O_3	400	SC	76
C_3H_6	$Bi_2O_3-MoO_3$	650	KA	77
	$Bi_2O_3-MoO_3$	450	RFM	78
	MgO, deposited Co and Mo oxides	450	RFM	60
C_3H_8	V_2O_5	570	KA	79
	V and Mo oxides	560	KA (SC)	80
C_6H_{12}	NaX zeolite	220	KA	81
	Pd	320	KA	82
C_6H_{14}	Pd	250	KA	83
$C_{11}H_{24}$	MgO	650	KA	84
C_6H_6	Pt	130	KA	85
	Pt	<80	KA	86
	Pd	220	KA	87
$C_6H_5CH_3$	Pt	180	KA	88
$C_6H_5CH=CH_2$	Pt	240	KA	89
CH_3OH	Ag	500	RFM	90, 91
C_3H_7OH	transition metal oxides	500	RFM	92
iso-$C_5H_{11}OH$	Ag	300	KA	93
HCHO	SiO_2, Al_2O_3	650	KA, RFM	68
ROH	Al_2O_3, Pt/Al_2O_3, transition metal oxides	315	RFM	94–96
RNH_2	transition metal oxides	350	RFM, MS	96

Note. Kiperman's data[13] were used in the compilation of the table.

[a] The following designations have been adopted: KA = kinetic analysis; IR = infrared spectroscopy; RFM = radical 'freezing out' (matrix isolation) method combined with measurements of EPR spectra; MS = mass spectrometry; SC = separate calorimetric measurements; TAP = temporal analysis of product; TPD = thermoprogrammed desorption; PIMS = photoionisation mass spectrometry; LIF = laser indiced fluorescence.

A more complex mechanism, postulating that the heterogeneous conversion of the surface compound into the reaction products takes place via a first order reaction and that the formation of radicals from this product is a second order process (chain branching, propagation, and quadratic termination reactions are possible in the gas phase), has been examined by Berman and Margolis.[12] Analysis of the kinetic equations describing the process shows that one or several stable stationary states with different contributions by the homogeneous component can exist. For other reactions orders, the stationary state becomes unstable and there is a possibility of the occurrence of auto-oscillatory regimes. It also follows from this analysis that smooth or abrupt changes in the reaction rate in the isothermal regime are possible when the reactant concentrations are varied monotonically.

The multiplicity of stationary states may be manifested by the appearance of hysteresis in the rate of reaction when the temperature is varied cyclically. This type of kinetics, observed in the oxidation of cyclohexane on the NaX zeolite, has been attributed to the partial transition of the reaction to the gas phase.[81]

Concluding the brief analysis of the kinetic features of heterogeneous–homogeneous catalytic processes, we may note that, on the basis of their analysis alone, it is impossible to reach a final conclusion concerning the presence or absence of the homogeneous component of the reaction. However, in certain cases such analysis may be fairly informative.

2. Methods for the investigation of heterogeneous–homogeneous radical reactions

The methods based mainly on the analysis of the kinetics and used in the investigation of heterogeneous–homogeneous reactions before the wide scale employment of various physical methods in chemical kinetics have been surveyed.[2] The majority of instrumental methods for the investigation of radical processes in the gas phase can be adjusted in principle to the study of heterogeneous radical reactions. Unfortunately, nowadays only a few of them are employed for such purposes, while in other cases it is still necessary to overcome significant technical difficulties. Here we shall describe briefly the characteristics of certain instrumental methods and new approaches without repeating, as far as possible, what has already been stated in the review[7] concerning the use of mass spectrometry, matrix isolation of radicals combined with measurement of IR and EPR spectra, photoelectron spectroscopy, and multiphoton and resonance ionisation for the study of the role of the free radicals in catalytic reactions.

3. Method involving separate calorimetric measurements

The separate calorimetric measurement method (SC method) was mentioned above when the role of heterogeneous factors in gas-phase reactions was considered. This method has also been employed in the study of the transfer of the reactions on heterogeneous catalysts into free space (see, for example, Ganieva et al.[76] and Nguyen and Kung[80]). One of the modifications of the SC method involves the carrying out of two series of experiments: in the first series, the catalyst in the form of a thin layer is deposited on the walls of the reaction vessel with a radius R, while in the second it is deposited on a capillary with a radius r in which a thermocouple is enclosed, the capillary being placed along the axis of a cylindrical reactor. The ratio of the heats evolved on the surface and in the reactor volume is defined by the relation[19,20]

$$\frac{Q_s}{Q_v} = \frac{\Delta T_2 - \Delta T_1}{2\Delta T_1 \ln(R/r)}.$$

As already mentioned, the limitation of the SC method consists in the impossibility of determining with its aid the nature of the species responsible for the bulk propagation of the process. Furthermore, in the study of processes occurring on granular porous catalysts the SC method makes it possible to differentiate only the fraction of the heat evolved in the free volume of the reactor and the latter may be very small even if the contribution of the volume reaction is high but the reaction itself is localised within the pores of the grain or in the space between the catalyst grains. More informative methods, permitting the direct detection of the active species and the determination of their form and concentration (or the rate of their generation), are therefore needed.

a. The method involving the 'freezing out' of radicals

The method in which the free radicals are isolated in a solid matrix from frozen reaction products, initial reactants, or substances specially added to the gas stream in order to form the matrix with subsequent measurement of the EPR spectra is used widely to investigate radical processes in the gas phase.[100] In the Russian literature, this method is referred to as the radical freezing-out method (RFM). Its description, scope, and specific examples of its application in the study of different processes, including heterophase processes, can be found in a series of reviews and monographs (see, for example, Refs 7–9 and 101). We shall consider only certain modifications of the method, which have given rise to fundamentally new possibilities.

It has been frequently noted (see, for example, Ermolaev et al.[97]) that, depending on the composition of the matrix and its temperature, the form of the EPR spectrum of the radicals frozen out may vary markedly, which hinders their identification. It is particularly difficult to distinguish the spectra of the $RO_2^{\bullet}$ radicals (R = hydrogen atoms or organic fragments) if their mixture is formed in the reaction and the matrix contains a large amount of water. In the presence of oxygen in the reaction mixture, the majority of the radicals are converted into $RO_2^{\bullet}$ in the cold part of the reactor or on the way to the freezing out trap. By employing liquid helium for cooling and argon as the matrix and by carrying out the process at low temperatures or in the absence of oxygen, the problem may be solved.[69,70,75] However, in most cases it is impossible to carry out the reaction under oxygen-free conditions and the use of liquid helium significantly complicates the technique.

A method has been proposed for the identification of radicals stabilised in a solid matrix involving their photolysis by UV light and the re-recording of the EPR spectrum.[95,97–99,102] The authors suggest (see the discussion of the paper of Ismagilov et al.[95]) that the photolysis involves the dissociation of the R–OO bond in the $RO_2^{\bullet}$ radical and that the $R^{\bullet}$ radical remains in the matrix. The spectra of the radicals $R^{\bullet}$ are more informative and the new radicals formed in the reaction can be identified in principle on their basis. This approach has been used in the study of extensive oxidation reactions of alcohols[97–99,102] and amines[96] on oxides and deposited platinum catalysts.

However, it is known that, when various peroxy-radicals $RO_2^{\bullet}$ (R = alkyl, allyl, vinyl, acyl, etc.) are irradiated, the primary step is the dissociation of the O–O bond and not of the C–O bond.[103] Furthermore, the reaction investigated leads to the formation of a mixture of radicals, so that the EPR spectrum obtained after photolysis is a result of the superposition of the spectra of all the paramagnetic species formed, which greatly complicates its analysis.

As already mentioned, in the gas-phase oxidation reactions, in catalytic processes, and in the chemistry of the atmosphere, the role of the stages involving the interaction of radicals with various surfaces is considerable. As a rule, the rate constants for these stages (or the probabilities of the reactions on collision of the radical with the surface) are high and methods with a high time resolution are needed for their investigation.

In the traditional RFM scheme when the entire gas stream is directed to the freezing out trap (direct sampling), the velocity of the gas jet is restricted by the considerable convective heat exchange which impairs the regime under which the matrix is frozen and the radicals are stabilised within it. As a result, the interaction of the radicals with the solid substance investigated,

deposited on the wall or placed along the axis of a cylindrical reactor, takes place in the diffusional regime.[104,105]

The time resolution can be increased by means of diffusional sampling,[106-108] in which the freezing out trap is placed in the vicinity of the axis of the gas stream but outside it, so that the gas should not heat it convectively. In order to increase the rate of the diffusional removal of radicals to the freezing out trap, helium is employed as the carrier gas. Since only a proportion of the radicals enter the matrix under the conditions of diffusional sampling, the sensitivity of the method is reduced by a factor of 5-6 compared with direct sampling. However, the velocity of the jet can then be increased to 30 m s^{-1} and the time resolution can be raised to $\sim 10^{-3}$ s, which renders the reactions of radicals with a surface, whose probability is close to unity, susceptible to measurement. This method has been employed to investigate the interaction of $HO_2^{\cdot}$ radicals with the surfaces of ice, carbon black, Al_2O_3, and various salts,[105] of the $CH_3^{\cdot}$ and $CH_3O_2^{\cdot}$ radicals with the surfaces of quartz and NaCl,[107] and of the $HO_2^{\cdot}$, $CH_3O_2^{\cdot}$, and $FO_2^{\cdot}$ radicals with the surface of quartz.[108]

b. Mass spectrometry

Repeated attempts to employ the mass-spectrometric (MS) method in the study of heterogeneous-homogeneous oxidation reactions have been made.[28,109-111] However, the problem is that in the usual method the fragments of saturated molecules generated on exposure to an ionising electron beam can give rise to the same peaks (m/z) in the spectrum as the radicals present in the system. The concentration of the latter is then usually several orders of magnitude lower, which virtually precludes their differentiation from the overall spectrum in practice.

The possibility of studying reactions involving free radicals increased sharply when photoionisation mass spectrometry (PIMS) was employed.[112] The ionisation thresholds of radicals are generally much lower than for the saturated molecules from which they are formed. Therefore the use of, for example, a UV radiation source with a set of filters designed for different light wavelength ranges or of lasers (multiphoton ionisation processes are then most often employed[113]) permits the selective ionisation of species (radicals) of one kind without ionising others (saturated molecules). This method has been used to investigate the generation of $CH_3^{\cdot}$ radical on the Sr/La_2O_3 catalyst for the oxidative condensation of methane (OCM)[72] and the interaction of these radicals with the surface.[114]

Time-of-flight mass spectrometry with multiphoton ionisation by laser radiation has been employed[115] for the detection of the methyl radicals formed in the OCM reaction on the Ca/Al_2O_3 and Sr/La_2O_3 catalysts. The use of mass spectrometry with chemical ionisation (MSCI) may also prove to be promising, but we are not aware of any examples of the application of this method in the study of heterogeneous-homogeneous processes.

A study has been published recently[73] in which the detection of radical species by mass spectrometry was combined with the TAP technique which make it possible to investigate processes on heterogeneous catalysts with a high time resolution.[116] This aspect is also extremely promising.

Hitherto it has been possible to consider the rates of reaction of radicals with a surface in only a small number of instances. The high sensitivity and selectivity ensured by the PIMS and MSCI methods make it possible to solve one of the most complex problems — the elucidation of the stoichiometry of heterogeneous radical reactions.

c. Molecular beams

The general term 'molecular beam method (or technique)' (MB) is usually understood as the set of methods for the investigation of the kinetics and mechanisms of reactions (both homogeneous gas-phase and heterogeneous reactions) in which the reactants and/or products are investigated and in which the directions of their velocities are rigorously specified (see, for example, the relevant reviews[117,118]). The methods for the generation and detection of the beam may be varied. For example, the distribution of the species with respect to different energy modes can be varied under these conditions from the Maxwell-Boltzmann equilibrium distribution to a fairly narrow distribution, which is different for different partner species. This makes it possible to investigate not only the reaction kinetics but also the dynamics of the energy transfer processes during collisions or the form of the potential energy surface for the system.

An additional advantage of the MB technique when applied to the study of heterogeneous processes is associated with the possibility of monitoring precisely the surface coverage and also of investigating the steric effects (the distribution of the species reflected by the surface or arising from it, the possibility of interaction as a function of the angle of incidence of the beam).[119] The combination of the MB technique with the methods for the simultaneous investigation of the surface and surface compounds (thermoprogrammed desorption and photoelectron spectroscopy,[120] IR spectroscopy with isotope substitution[121,122]) is particularly fruitful in the study of the reactions of radicals with various surfaces.

d. Laser induced fluorescence

The detection and the determination of the concentrations of species by the method based on the laser induced fluorescence (LIF) are based on the measurements of the emission by the excited species. The greatest advance in the application of fluorescence methods in the study of atoms and radicals was achieved when the excitation sources employed comprised pulsed or continuous broad-band and frequency-tunable dye-based lasers, which could be tuned to the narrow absorption bands of the test species.[123]

An advantage of the LIF method applied to heterogeneous-homogeneous processes is the possibility of measuring the concentration of species with a fairly high spatial resolution. This is in fact why it has been possible to determine the spatial profiles of the concentrations of $OH^{\cdot}$ radicals and O atoms in stabilised combustion processes.[52,55-57,124,125]

The use of the LIF method in the study of OCM process made it possible to demonstrate[126] that $OH^{\cdot}$ radicals are formed under the conditions of this reaction and also in the 'oxidation of water'.

e. Other methods

The method for the detection of species from the disappearance of a metallic mirror, used to confirm the involvement of radicals in the OCM reaction,[127] is based on the formation of volatile organometallic compounds in the interaction of, for example, thin films of metallic lead (a 'mirror' deposited beforehand on the reactor surface) with radicals (in the given instance tentatively identified with $CH_3^{\cdot}$). Although according to the data of Rice and Tweedell[128] certain mirrors (for example, tellurium or antimony mirrors) disappear only on exposure to radicals of a particular type ($CH_3^{\cdot}$, $C_2H_5^{\cdot}$), this method [as well as the low-temperature reduction of copper and tungsten oxides by hydrogen at a certain distance from the catalyst (Pd, Pt) employed in early investigations[129-131] and the disappearance of the glow in the gas under analogous conditions[132]] can serve as only a qualitative indication of the release of active species into the free volume.

Various modifications of IR spectroscopy have been employed to investigate the radical generation processes and the repeated interaction of the radicals with the surface of oxides.[74,133-136] However, one should note that only surface compounds (alkoxy- and hydroxy-groups), appearing as a result of the interaction of the active surface centres with hydrocarbons and with the radicals formed, were detected spectroscopically in the above investigations. Like other methods for the investigation of the surface and surface compounds, IR spectroscopy yields most information when it is combined with methods for the direct

detection of free radicals, as happens for example in the MB technique.

4. The mechanism of the heterogeneous formation of free radicals

As already mentioned, heterogeneous free radical formation reactions may play the role of chain initiation stages in RCP and of reactant activation stages in heterogeneous-catalytic processes. Therefore the elucidation of the mechanisms of such reactions is extremely important for the understanding of the process as a whole. Here we shall consider the energy relations of the interaction of reactant molecules with the active surface centres and the available data on the detailed mechanisms for these reactions.

a. Thermochemistry of the interaction of molecules with active surface centres

It follows from Table 1 that the propagation of heterogeneous-catalytic processes in the free volume occurs widely in the oxidation of substances of different classes. This indicates the existence of a universal cause which makes the formation of radicals in heterogeneous processes extremely probable.

Two cases in which the heterogeneous formation of radicals may become energetically more favourable than their homogeneous formation have been analysed.[2]

1. In the dissociative adsorption of a molecule with subsequent desorption of one of the adsorbed fragments:

$$AB + 2Z \rightarrow ZA + ZB, \quad (9)$$

$$ZA \rightarrow Z + A^{\cdot} \quad (10)$$

2. In the binding to the surface of only one of the fragments of the activated molecule (the second fragment escapes into the free volume under these conditions).

$$AB + Z \rightarrow ZB + A^{\cdot}. \quad (11)$$

In the first case, the bond dissociation energy in the initial molecule decreases more the higher the energy of the bond between its fragments and the surface centres Z; however, under these conditions the activation energy for the abstraction of a radical from the surface increases.

In the second case, the bond dissociation energy diminishes less, but there is no need for additional energy consumption on the abstraction of a radical from the surface. According to the authors,[2] the formation of radicals via the second mechanism in one stage is more probable.

On the other hand, when one considers the probability of the release of radicals into the free volume in a particular reaction, then a different assessment must be made, namely one must compare the energy relations for the formation of radicals in the interaction of various molecules with the surface of the solid with the energy relations for other possible types of interaction leading to the activation of the reactants. Such analysis may be performed on the basis of the available thermochemical literature data (see, for example, Refs 137–139).

Table 2 presents estimates of the energy expenditure ($\Delta H + E_{st}$, where ΔH is the overall enthalpy change and E_{st} is the energy evolved in the stabilisation on the surface of an activated molecule or its fragment) in the following processes leading to the activation of certain molecules in catalytic reactions on the surface: (1) abstraction of a hydrogen atom from the RH molecule by a powerful oxidative centre on the oxide surface $[O]_s$ or by a surface metal atom [M] with formation of a radical $R^{\cdot}$:

$$[O]_s + RH \rightarrow [OH]_s + R^{\cdot}, \quad (12)$$

$$(\Delta H_1 + D_{O-H}) = D_{R-H},$$

Table 2. Energy expenditure (kJ mol^{-1}) on the activation of molecules via different mechanisms.

Molecule	Energy expenditure in processes			
	12 (or 13)	14	15	16
H_2	431	1668	1668	1484
CH_4	431	1630	1308	1250
C_2H_6	410	1584	1183	1120
C_3H_8	398	1609	1162	1078
n-C_4H_{10}	393	1605	1154	1037
iso-C_4H_{10}	389	1601	1120	1016
C_2H_4	435	–	1275	1012
C_3H_6	322	1421	1033	936
C_6H_6	427	–	1258	886
CH_3OH ($R = CH_2OH$)	385	–	1099	1049
HCHO	314	–	1195	1045
NH_3	439	1630	1463	991

or

$$[M] + RH \rightarrow [M-H] + R^{\cdot}, \quad (13)$$

$$(\Delta H_1 + D_{M-H}) = D_{R-H};$$

2) Heterolytic dissociation with abstraction of a proton from a strong basic centre $[O^{2-}]_s$ with formation of an anion R^-:

$$[O^{2-}]_s + RH \rightarrow [O^{2-}...H^+]_s + R^-, \quad (14)$$

$$\Delta H_2 + Q_{H^+} + Q_{R^-} = D_{R-H} + I_H - I_{R-R^-};$$

(3) Heterolytic dissociation into a hydride ion, which is bound to the cation $[M^{n+}]_s$ and the cation R^+:

$$[M^{n+}] + RH \rightarrow [M^{n+}...H^-]_s + R^+, \quad (15)$$

$$\Delta H_3 + Q_{R^+} + Q_{H^-} = D_{R-H} + I_R - I_{H-H^-};$$

4) Ionisation of the molecule with formation of a molecular ion RH^+, whereupon

$$\Delta H_4 + Q_{RH^+} = I_{RH}. \quad (16)$$

In the above equations, ΔH_i represents the enthalpy changes in the corresponding processes, D_{R-H} is the energy of the homolytic association of the R–H bond, I_j represents the ionisation potentials of the species, and Q_j are the heats of adsorption of the species.

It is easy to demonstrate that in all these processes the sign and magnitude of the heat change depend on the compensation of the energy by binding the fragments of the activated molecule to the surface centres. The energy which has to be compensated is as a rule minimal for the first process. For example, in the case of oxide catalysts one may expect that the energy of the O–H bond formed in this process is comparable to the energy expenditure on the homolytic dissociation of the R–H bond, i.e. its compensation does not require the binding of the second fragment. In the heterolytic dissociation of bonds [reactions (14) and (15)], the energy expenditure is so large that its compensation requires the binding of both fragments, which must occur synchronously in a single reaction step, i.e. the activation of the molecule requires the presence of paired centres with unusual configurations and energy relations. For process (12) [or (13)], it is sufficient to have single oxidative centres.

The above analysis shows that the formation of free radicals in the interaction of molecules of substances of various classes with the surfaces of metals and oxides may prove to be energetically preferable compared with other mechanisms of their activation. Furthermore, this process requires only one type of single centres and it takes place in a single stage. The combination of these factors may render such a process the most

favourable. This conclusion is the opposite of that arrived at by Gorokhovatskii et al.,[2] but it is based on quantitative thermochemical data. It may be that this in fact explains the more common employment of the approach based on the homogeneous propagation of oxidative heterogeneous-catalytic reactions (Table 1).

b. Generation of free radicals in catalytic reactions

The considerable progress in the study of heterogeneous–homogeneous radical reactions in recent years has been due to the considerable attention devoted by investigators to the catalytic oxidative condensation of methane (OCM) to higher hydrocarbons on oxide catalysts, which proved to be a convenient model in the study of such reactions.[5–8]

The formation of radicals in the presence of OCM catalysts under catalytic conditions (or close to such conditions) has been demonstrated by means of a whole series of methods (Table 1). The rates of formation of the radicals are close to the rates of reaction of the reactants.[59] According to current ideas, the overall mechanism of this reaction is the same on all oxide catalysts. The primary OCM product (ethane) is formed as a result of the recombination of the methyl radicals generated by the oxide surface. The differences between the catalysts, which determine their different efficiencies, are themselves determined by the properties and concentrations of the radical-generating active centres and also by the specific surface, porosity, and morphology, on which the relative rates of the secondary heterogeneous and homogeneous radical reactions depend. Results important for the understanding of the mechanisms of the generation and secondary reactions of the radicals in heterogeneous processes have in fact been obtained precisely in the study of the OCM process (the discussion below is based mainly on these results).

One of the mechanisms of the formation of free radicals in oxidation processes on oxide catalysts most frequently discussed in the literature presupposes the homolytic dissociation of the bond in the RH molecule when it collides with a strong oxidative surface centre $[O]_s$ with the simultaneous formation of a free radical and a surface hydroxy-group $[OH]_s$ in a single stage:[59,60,69–71,74,75]

$$[O]_s + RH \rightarrow [OH]_s + R^{\cdot} \qquad (17)$$

There exists an alternative point of view, according to which the process proceeds via dissociative adsorption and the key factor is the presence on the oxide surface of strong basic centres $[O^{2-}]_b$, which ensure the heterolytic dissociation of a C–H bond in the hydrocarbon molecule:[140–146]

$$[O^{2-}]_b + RH \rightarrow [O^{2-}...H^{+}] + (R^{-})_{ads} . \qquad (18)$$

The conversion of the anion R^{-}_{ads} produced into a radical requires that it should lose an electron on interaction with an electron-accepting (hole) centre $[h^{+}]$:

$$[h^{+}] + (R^{-})_{ads} \rightarrow [h^{0}] + R^{\cdot}_{2}. \qquad (19)$$

A model of the heterolytic dissociation of the C–H bond was initially formulated for the activation of alkenes and aromatic hydrocarbons in their partial oxidation reactions; subsequently it was transferred to the activation of methane.[140,147,148] This was based on the presence in many catalysts of the OCM process of alkali, alkaline earth, and lanthanide ions. In certain cases, the efficiency of the catalyst increases after the introduction of an alkaline modifying agent.

It follows from the data in Table 2 that the heterolytic bond dissociation in lower alkanes is energetically extremely unfavourable. It has been suggested that the role of the basic centres $[O^{2-}]_b$ actually consists in compensating for the energy expenditure on the dissociation of the C–H bond by binding the proton. If the energy of the interaction of these centres with Lewis acids (proton, CO_2) is adopted as a measure of the basicity, then its increase would entail an increase in the efficiency of the catalyst.

The rates of formation of the OCM products on different oxide catalysts (M/Al_2O_3 and M/MgO, where M = Li, Na, K, Cs, Pb, or Nd) have been compared[149,150] with the numbers of active centres and their strengths, which were determined from the adsorption of CO_2 by programmed thermal desorption and calorimetric methods. There is no direct correlation between the rate of formation of the OCM product and the basicity, but in a number of cases (the Pb/Al_2O_3 and Nd/MgO catalysts with different contents of the deposited component and MgO–alkali metal cation systems) an inverse correlation has been observed between the rate and the heats of adsorption. The introduction of alkaline components into oxide systems apparently leads not only (or even not so much) to an increase in their basicity but also to the modification of the oxidative properties of the lattice oxygen.[151]

Indeed, it has been shown[150] that an increase in the Na content in the Li/MgO and and Nd/MgO catalysts leads to an increase in the concentration of the oxidative centres. At the same time the rate of formation of the OCM product increases. Similar results have been obtained also for other oxide catalysts.[151–153] Furthermore, the interaction of oxide systems containing strong oxidative centres with methane leads to the formation of OCM products even in the absence of oxidants from the gas phase.[115,152–158]

Thermochemical studies have shown[153,157] that the relation between the activation energy for the formation of C_2 hydrocarbons in the interaction of methane with these oxides and the O–H bond energy in the hydroxy-group formed simultaneously corresponds to the Polanyi–Semenov relation obtained for the homolytic abstraction of a hydrogen atom from a methane molecule by various species in the gas phase:

$$CH_4 + X^{\cdot} \rightarrow CH^{\cdot} + XH , \qquad (20)$$

where X = F, OH, H, CH_3, O, Cl, Br, I, HO_2, CH_3O, CH_3O_2, etc.

Data concerning the applicability of the Polanyi–Semenov relation to the dissociation of the C–H and H–H bonds in hydrocarbon and hydrogen molecules on the active centres arising in the mechanical treatment of quartz and aerosil were presented above.[42,43] Although the formation of free radicals was not recorded directly in the above investigations, analysis of the kinetic isotope effects and the characteristics of the formation and reactions of the surface compounds, which according to the authors are products of radical capture, enabled them also to drawn an analogy between heterogeneous and the gas-phase reactions of type (12) [or (13)] and (20).

Similar conclusions concerning the mechanisms of the processes under consideration were reached in a study of the interaction of various molecules with irradiated (in the visible, UV, X-ray, and γ-ray ranges) oxides – MgO,[74,159,160] TiO_2,[161–163] and others,[164,165] as well as SiO_2 and Al_2O_3, modified by vanadium, molybdenum, and tungsten ions.[161,166–168] Irradiation, which leads to the formation of hole O^{-} centres with powerful oxidative properties, induces a sharp increase in the reactivity of the oxides. As a result, in the reaction of methane, for example, it is possible to detect the formation of ethane even at room temperature.[162] According to Kotova's data,[165] the process proceeds via the homolytic dissociation of a C–H bond with formation of excited surface OH groups. The presence of molecular hydrogen in the system inhibits the reaction of methane.

Thus the combination of the available data on the mechanism of the interaction of hydrocarbons and hydrogen with oxides confirms the conclusion reached earlier on the basis of thermochemical data that free radicals may be formed as a result of the homolytic dissociation of R–H bonds under the influence of oxidative surface centres. We may add only that the oxygen ions bound to the readily reducible cations,[115,155] the radical-ions $O^{\cdot -}$,[69,70,74,75,169,170] the surface oxygen ions O^{2-}_{LC} with a lower coordination,[70] and peroxide ions O^{2-}_{2} [156–158,170,171] are included in the literature among the centres possessing such properties.

However, one cannot rule out the possibility that at elevated temperatures all these types of active oxygen are converted into a single type, most probably the radical-ion $O^{\cdot -}$.[170,172-174]

$$O^{2-} + [h^+] \text{ (or } M^{n+}) \rightarrow O^{\cdot -} + [h^0] \text{ [or } M^{(n-1)+}], \quad (21)$$

$$O_2^{2-} \rightarrow 2\ O^{\cdot -}. \quad (22)$$

The results of quantum-chemical calculations[175-180] confirm the high probability of the formation of methyl radicals in the interaction of methane with $O^{\cdot}$ surface centres. On different oxide systems (MgO, MoO_3, $CuMoO_4$), the $O^{\cdot -}$ centres are equally active and have similar properties regardless of the pathways leading to their formation (their appearance as a consequence of the nonstoichiometry of the oxide or as a result of electron transfer under the influence of radiation).[181] Hole centres, having similar electronic properties but present in other systems (for example N^{2-} and AlN), possess also a similar activity in relation to the generation of radicals.[182]

Hitherto we have dealt with the mechanism of the formation of radicals in the interaction of the molecules of the substances being oxidised with the surface centres of catalysts. However, the available experimental data show that, apart from such 'primary' radicals which are products of the abstraction of a hydrogen atom from the RH molecule, and $RO_2^{\cdot}$ radicals, species can also be detected in the gas phase the products of which must be a series of far reaching consecutive transformations of the initial molecules.

As regards the $OH^{\cdot}$ radicals and oxygen atoms formed in stabilised combustion processes,[47,52-57] the available data are insufficient to consider the mechanism of their formation. In particular, it has been suggested[57,124,125] that $OH^{\cdot}$ radicals are formed on recombination of the oxygen and hydrogen atoms adsorbed on the metal surface, but one cannot rule out also their formation in secondary homogeneous reactions. On the other hand, according to some data, in the OCM reaction the generation of secondary $OH^{\cdot}$ radicals is important for the dynamics of the active centres of the catalysts.[128] We shall therefore consider their generation in greater detail.

In one of the first studies devoted to the formation of radicals in the OCM reaction,[69] it was shown that, when molecular oxygen is used as the oxidant, the rate of generation of radicals in the presence of the Li/MgO catalyst is constant, whilst in the case where N_2O is employed it decreases monotonically. The differences in the occurrence of the OCM in the presence of O_2 and N_2O are also indicated by the results obtained on the Sm_2O_3 catalyst:[183] and replacement of O_2 by N_2O lowers significantly the rate of the process.

Studies of the kinetic isotope effect occuring when CH_4 is replaced by CD_4 showed that, in the oxidation by oxygen, one cannot postulate the existence of a single stage determining the rate of the process,[184] whilst in the oxidation by N_2O such a stage is the reoxidation of the catalyst active centres.

The study of the oxidation–reduction properties of the Li/MgO catalyst showed that its reduction by hydrogen-containing reductants is not accompanied by the evolution of water, or at least that the dehydration of the reduced surface is a very slow process.[153,185] However, when oxygen is supplied to a specimen reduced by hydrogen or hydrocarbons, a rapid evolution of water is observed. When N_2O is introduced, the specimen is reoxidised at temperatures below 700 °C solely by the molecular oxygen formed to a small extent in the catalytic decomposition of N_2O. This led to the conclusion that the traditional mechanism of the oxidation-reduction processes, according to which stage (17) is followed by the dehydroxylation stage

$$2\ [OH]_s \rightarrow [O^{\cdot -}]_s + [O]_s + H_2O, \quad (23)$$

and the oxygen vacancies $[O^{\cdot -}]$ formed are filled as a result of the chemisorption of oxidants from the gas phase, i.e.

$$[O^{\cdot -}]_s + \tfrac{1}{2}O_2 \rightarrow [O]_s, \quad (24)$$

or

$$[O^{\cdot -}]_s + N_2O \rightarrow [O]_s + N_2, \quad (25)$$

does not operate in oxide systems with a high lattice oxygen $[O]_s$ bond energy because stage (23) is reversible and the equilibrium is greatly displaced to the left. This conclusion has been confirmed by thermochemical data.[186] Naturally, in the absence (or at a very low concentration) of oxygen vacancies, the reoxidation via reaction (24) or (25) is impossible. However, molecular oxygen is nevertheless capable of reoxidising a surface coated by hydroxy-groups via the overall reaction

$$4\ [OH]_s + O_2 \rightarrow 2\ H_2O + 4\ [O]_s. \quad (26)$$

According to the data of Sinev et al.,[185] this unusual 'oxidative dehydrogenation' of the catalyst active centres can proceed via the following stages:

$$[OH]_s + O_2 \rightarrow [O]_s + HO_2^{\cdot}, \quad (27)$$

$$[OH]_s + HO_2^{\cdot} \rightarrow [O]_s + H_2O_2, \quad (28)$$

$$H_2O_2 \rightarrow 2\ OH_2^{\cdot}, \quad (29)$$

$$[OH]_s + OH^{\cdot} \rightarrow [O]_s + H_2O. \quad (30)$$

The sum of stages (27)–(30) gives rise to the oveall equation (26). Among the heterogeneous stages leading to the reoxidation of the active centres, stage (27) is slowest. Its rate constant is higher the lower the O–H bond energy in $[OH]_s$.

The modelling of the reoxidation process via the proposed mechanism using the rate constants for stages (27), (28), and (30), estimated from Sinev's thermochemical data,[187] and the known rate constant for the homogeneous decomposition of hydrogen peroxide demonstrated a satisfactory agreement with experimental kinetic data.[186] There is so far no direct evidence that the reoxidation proceeds via the proposed mechanism. However, the data[126] indicating the presence of $OH^{\cdot}$ radicals in the gas phase may serve as indirect evidence for the validity of the mechanism (27)–(30) and hence for the heterogeneous–homogeneous radical nature of the reoxidation of the reduced oxide surface.

It is important to note that reaction (27), which is of key importance in the mechanism (27)–(30), is stoichiometrically identical with reaction (3), which, according to Azatyan,[23] is responsible for many of the characteristics of the RCP involving the oxidation of various hydrogen-containing compounds or mixtures (see Secion II). This confirms yet again the close relation between heterogeneous processes (in the given instance, the transformation of the active surface centres on oxide catalysts) and radical reactions.

In conclusion of this Section, we may note that there are numerous publications in the literature devoted to the mechanism of the formation of radicals under the conditions of oxidation reactions on oxide catalysts. Unfortunately, this cannot be said about metallic catalysts, although fairly extensive factual data on the release of radicals from the surfaces of metals into the free volume have accumulated.

5. The mechanism of the interaction of radicals with the surface of a solid

One can postulate that the subsequent fate of the radicals formed in particular heterogeneous reactions depends in the general case on the relation between the number of collisions of the radicals in the gas phase and with the surface and also on the nature and reactivity of the surface centres.

The reactions of radicals in the gas phase have been investigated widely by various methods and for many of them reliable kinetic data have been obtained and have been treated systematically in numerous monographs, reviews, and data banks (see, for example, Refs 188–190). Unfortunately, this cannot be said about the heterogeneous reactions of radicals, for which, as already mentioned, it is frequently difficult to specify even their stoichiometry. On the other hand, if the catalyst pores are

sufficiently narrow and tortuous and the species diffuse in them in Knudsen or transitional regimes, then the number of collisions of the radicals with the surface is large and the contribution of these reactions to the overall formation of the catalytic reaction products and to the process selectivity may be decisive.

The influence of the porosity on the heterogeneous radical destruction processes has been investigated.[191] The radicals ($CH_3O_2^{\bullet}$, $C_4H_9O_2^{\bullet}$, $C_3H_5^{\bullet}$, and $C_3H_5O_2^{\bullet}$) were generated in the first part of a two-section reactor and were then directed to SiO_2 and Al_2O_3 specimens having different specific surfaces and porosities. The peroxy-radicals proved to be more reactive than the corresponding hydrocarbon radicals. An increase in pore radius leads to an increase in the rate of destruction of the radicals, which indicates easier permeation of the radicals into the grain and an increase in the effective area of the surface on which their destruction takes place. The recapture of the radicals formed from C_1-C_4 hydrocarbons on irradiated MgO [74] leads to the surface alkoxy-groups $[OR]_s$. Their decomposition under the conditions of programmed thermal desorption results in the formation of the corresponding alkenes from the C_2-C_4 alkanes:

$$[OC_nH_{2n+1}]_s \rightarrow [OH]_s + C_nH_{2n}, \quad (31)$$

and of CO and H_2 from methane:

$$[OCH_3]_s \rightarrow CO + \tfrac{3}{2}H_2. \quad (32)$$

In view of the unusual importance of the heterogeneous radical reactions for the OCM process, numerous studies have been devoted to the interaction of methyl radicals with various oxides. The types of reactions of the $CH_3^{\bullet}$ radicals on different surfaces are apparently determined by the differences between the properties of the active centres and in the first place the surface oxygen. Depending on the electronic properties of the oxide and on the cation in the coordination sphere of which the oxygen ion is present, the probability of the formation of methoxy-groups and their reactivity may vary greatly.

The kinetics of the accumulation and consumption of the $[OCH_3]_s$ groups formed on recapture of the methyl radicals by the oxidised Al_2O_3, CaO, and BaO surfaces have been investigated[133-136] by the IR spectroscopy of surface electromagnetic waves and by reflection-absorption IR spectroscopy. The activation energy for the formation of methoxy-groups from methane varied in the range from 63 (BaO) to 126 (Al_2O_3) kJ mol^{-1}, while the activation energy for their subsequent conversion into formate groups was 21 – 33 kJ mol^{-1}.

Quantum-chemical calculations for the interaction of $CH_3^{\bullet}$ radicals with MoO_3 showed [175,176] that methoxy-groups of two different types may be formed: with $O-CH_3$ bond energies of ~38 and ~272 kJ mol^{-1}. The methoxy-groups of the first type may be formed when the radicals are captured by the O^{2-} or O^- ions formed on irradiation. The presence of stable (chemically generated) O^- ions on the surface was responsible for the strong binding of the radicals and the formation of stable methoxy-groups (second type).

The study of the reactivities of various oxides in the relation to the $CH_3^{\bullet}$ radicals generated catalytically in the CH_4+O_2 reaction showed that the typical OCM catalysts (MgO, Li/MgO) are almost 'transparent' towards the radicals, while the catalysts for the extensive (ZnO, NiO, CeO_2) and partial (MoO_3/SiO_2) oxidation capture them effectively.[192,193] An electron is transferred when the $Mo^{6+} \rightarrow Mo^{5+}$ transition takes place in the interaction of the methyl radical with MoO_3/SiO_2; in the case of CeO_2, an electron is transferred to an adsorbed oxygen molecule with formation of $O_2^{\bullet}$. The methoxy-group is successively converted into a formate group, which ultimately leads to the formation of carbon oxides.

A similar investigation but with azomethane as the source of radicals and a Knudsen cell as the reactor showed that at 650 °C the probability of the capture of $CH_3^{\bullet}$ radicals by the surfaces of typical OCM catalysts (La_2O_3, Li/MgO, Sr/La_2O_3) in the absence of oxygen from the gas phase is ~10^{-7}, increases to ~10^{-6}, and remains unchanged at $P_{O_2} = (1-18) \times 10^{-4}$ Torr.[194] The absence of a dependence of the probability of capture on the oxygen pressure in this range shows that the species interacting with the surface is the $CH_3^{\bullet}$ radical and not $CH_3O_2^{\bullet}$, the concentration of which increases in proportion to P_{O_2}. On ZnO and CeO_2, the probability of capture in the absence of oxygen is close to 10^{-5}, diminishing somewhat with increase in P_{O_2} from 0 to 1.8×10^{-3} Torr. The introduction of N_2O into the gas phase does not affect the process. The activation energy for the capture of the radicals on different oxides is 13 – 33 kJ mol^{-1}.

An attempt has been made[195] to determine the types of the reactions of the $CH_3^{\bullet}$ radicals obtained by irradiating different oxides under a methane atmosphere. In the absence of a catalyst, the formation of any kind of product has not been detected; on the other hand, in the presence of catalysts ethane and CO appear, the rates and selectivities of the formation on different oxides differing significantly and depending on the preliminary treatment. The authors suggest that irradiation promotes the generation of $CH_3^{\bullet}$ radicals and their capture by the surface oxygen ions leads to the formation of methoxy-groups, which decompose with evolution of CO and H_2.

Whereas the capture of methyl radicals by the surfaces of the OCM or extensive oxidation catalysts leads to the formation of carbon oxides, in the case of vanadium, molybdenum, and possibly tungsten oxides the conversion of the methoxy-groups into partial oxidation products has been postulated.[161] This has been demonstrated[196] by direct experiments involving the interaction of the $CH_3^{\bullet}$ radicals, obtained as a result of the decomposition of azomethane, with the MoO_3 and MoO_3/SiO_2 catalysts. In the presence of water vapour, the authors observed the formation of methanol, while under a dry atmosphere formaldehyde was formed, which confirms the possibility of the partial oxidation of methane on MoO_3-containing catalysts via the formation and recapture of a surface methyl radical:

$$Mo^{VI}O^{2-} + CH_3^{\bullet} \rightarrow Mo^{V}OCH_3^{-}. \quad (33)$$

Depending on the presence or absence of water in the gas phase, either the hydrolysis of the methoxy-groups with formation of methanol or their decomposition with formation of formaldehyde may take place.

There are also data showing that the methoxy-groups can themselves be a source of methyl radicals.[197,198] In particular, the formation of methyl radicals has been observed in the temperature range 525 – 650 K on programmed heating of a molybdenum single crystal, on the (110) face of which initially oxygen (0.15 – 0.50 of a monolayer) and then methanol (at 120 K) are adsorbed.[197] This may indicate the reversibility of reaction (33) and the validity of the quantum-chemical calculations.[175,176]

The results of studies on the interaction of $CH_3^{\bullet}$ radicals with clean and oxidised metal surfaces have been published recently.[120-122] The molecular beam method combined with methods involving the simultaneous investigation of the surface and surface compounds were employed in these studies.

On the oxygen-modified (100) face of a molybdenum single crystal, the adsorption of radicals is observed even at room temperature.[120] If the surface coverage by oxygen is incomplete, then the dehydrogenation and disproportionation of the methyl fragments take place on heating with evolution of methane and hydrogen into the gas phase and the formation of surface carbon, which reacts in its turn with the oxygen present on the surface, affording CO. The maximum rates of evolution of methane, hydrogen, and CO are attained at ~500 K; the CO evolution curve has a second maximum at 950 K. If no free metal atoms (not coated by oxygen) remain on the surface, then the second CO evolution peak is absent and the rate of evolution of methane diminishes, tending to a constant value on the surface the composition of which corresponds to MoO_2. Hence it follows that the dehydrogenation and disproportionation processes takes place more vigorously on a metal surface than on an oxide surface.

Programmed thermal desorption and reflection-absorption IR spectroscopic methods have been used[121] to investigate the interaction of methyl radicals with the (111) face of a platinum single crystal. The formation of the $Pt-CH_3$ and Pt_3CCH_3 groups (at a much lower concentration) was observed at 150 K. On heating, the liberation of ethene is observed, but ethane is not formed. The authors suggest that the methyl fragments dissociate partially to CH_2 and, tentatively, that ethene is formed in the course of one of two reactions:

$$CH_3 + CH_2 \rightarrow C_2H_5 \rightarrow C_2H_4 + H, \quad (34)$$

$$CH_2 + CH_2 \rightarrow C_2H_4. \quad (35)$$

Hall et al.[122] investigated the interaction of methyl radicals with the clean and oxidised (100) and (111) faces of a nickel single crystal. If the surface contains hydrogen or a preadsorbed hydrocarbon (for example, ethane), then methane is rapidly evolved when radicals are introduced. The adsorption of radicals on the (100) face and subsequent heating lead to the recombination of the methyl fragments with the hydrogen atoms and the evolution of methane at 220 K. On the (111) face, this process is much more vigorous. It has been shown in experiments that isotope-substituted molecules that at 240 K the methyl groups abstract a hydrogen atom from the adsorbed species and no longer from the surface. The oxidation of the surface alters completely the type of reactions: at temperatures of about 300 K, the adsorbed methyl fragments recombine with formation of ethane and the desorption of $CH_3^{\bullet}$ radicals is also observed.

Overall, one has to conclude that, although the reactions of the radicals with the solid surface are extremely important in both homogeneous gas-phase and heterogeneous-catalytic oxidation processes, their kinetics and mechanisms have not yet been investigated adequately.

IV. Conclusion

Analysis of the literature data shows that it is difficult to find examples of purely homogeneous oxidation processes in the gas phase, which are not influenced by heterogeneous factors. On the other hand, the reactions on heterogeneous catalysts are frequently accompanied by the release of free radicals into the gas phase and this is not a side process in relation to the main reaction pathway in the adsorbed layer but is an essential stage leading to the formation of the final products in homogeneous or secondary heterogeneous stages.

Taking into account the data obtained in recent years in the course of intensive investigations of the OCM and stabilised combustion processes, one may ask the question what is the meaning of the expression 'proportion of the reaction occurring in the free volume (or on the surface)' if the heterogeneous and homogeneous stages are equally inseparable components of the conversion of the reactants into products?

Another question also arises: how fundamental is the difference between the 'gas-phase' reactions, on the one hand, and 'heterogeneous–homogeneous catalytic' reactions, on the other, if in either case both the rates of the elementary processes in the gas phase and the entire set of factors determining the rates of heterogeneous processes (the chemical nature and morphology of the solid, the surface area, the purity of the surface, etc.) are equally important?

In the light of the above analysis, these differences are completely indeterminate. Refraining from more wide scale generalisations, we may venture to express the view that the boundary between the gas-phase and heterogeneous-catalytic oxidation is arbitrary and its existence is associated mainly with the fact that the studies in these two fields developed almost independently for decades. Such isolation had to some extent also a positive aspect, since it made it possible to concentrate on the 'main' process and to differentiate and investigate the characteristic features of the elementary reactions in the gas phase or on the surface of a solid, refraining from dealing with 'side' factors. However, the combination of the efforts of specialists dealing with the study of the kinetics and mechanisms of reactions in the gas phase, heterogeneous catalysis, solid state chemistry, and surface phenomena appears extremely promising. The greatest progress is to be expected in this connection as regards the development and adaptation of highly sensitive methods for the study of radical processes in heterogeneous reactions, the creation of kinetic models of complex heterophase processes, and ultimately a deeper understanding of the mechanisms of the oxidation reactions and the possibility of controlling them.

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Polymers with arylenedicarbadodecaborane fragments in the chain

S V Vinogradova, P M Valetskii, Yu A Kabachii

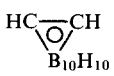
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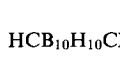
Abstract. The results of studies on polymers with arylene dicarbadodecaborane fragments in the chain are surveyed. The characteristic features of the formation of these polymers, their properties, and their unusual thermal behaviour are examined. The mechanism of the thermal transformations of polyarylenedicarbadodecaboranes is discussed. The probable usefulness of the radical arylation of dicarbadodecaboranes(12) is demonstrated. Certain aspects of the practical employment of dicarbadodecaborane-containing polymers are considered. The bibliography includes 135 references.

I. Introduction

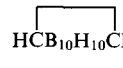
Communications appeared in 1962–1964 about the synthesis of new organoboron compounds having the empirical formula $C_2B_nH_{n+2}$ and, in particular, the compound $C_2B_{10}H_{12}$ – dicarba-*closo*-dodecaborane(12) (its trivial names are 'carborane' or 'barene'),[1–10] for which three isomeric forms are known:



1,2-Dicarba-*closo*-dodecaborane(12) (*o*-carborane)†



1,7-Dicarba-*closo*-dodecaborane(12) (*m*-carborane)



1,12-dicarba-*closo*-dodecaborane (12) (*p*-carborane)

The first dicarbadodecaborane-containing polymers were also obtained almost at the same time.[10,11] A large number of various heterochain and carbochain polymers with 1,2-, 1,7-, and 1,12-dicarbadodecaborane fragments in the chain have been synthesised since that time and data on these polymers have been described in numerous review-type communications.[12–28]

The introduction of dicarbadecaborane-containing fragments into the polymer chain appeared attractive, since investigators hoped to obtain polymers with improved thermal characteristics, because dicarbadodecaboranes are thermally stable: 1,2-dicarbadodecaborane withstands heating under an inert atmosphere to 475 °C, after which it isomerises to the more stable 1,7-dicarbadodecaborane;[29] when 1,2-dicarbadodecaborane is heated at 700 °C, a mixture of 1,7- and 1,12-dicarbadodecaboranes is obtained;[30] prolonged heating of 1,7-dicarbadodecaborane at 615 °C afforded 1,12-dicarbadodecaborane.[31]

At the same time, in the first stages investigators encountered difficulties in the preparation of high-molecular-mass polymers from bifunctional dicarbadodecaborane derivatives [for example, 1,2- and 1,7-bis(hydroxymethyl)dicarbadodecaboranes, 1,2- and 1,7-bis(carboxymethyl)dicarbadodecaboranes, and their derivatives].[12,24–27,32] It was suggested[12,23,25,27] that this is due to the specific properties of dicarbadodecaborane, which constitutes a strongly electron-accepting group, and also the structural characteristics and the associated steric hindrance in the reactions involving the synthesis of the polymers. However, by virtue of the development and the determination of the principal characteristic features of the polymer formation reactions and in particular polycondensation, the difficulties in achieving high molecular masses in the synthesis of dicarbadodecaborane-containing polymers were overcome and true high-molecular-mass polymers were obtained.

Dicarbadodecaborane-containing monomers with functional groups directly attached to the dicarbadodecaborane nucleus [1,7- and 1,12-dicarbadodecaborane-dicarboxylic acid, 1,7- and 1,12-dicarbadodecaboranylenediamines, and 1,2- and 1,7-bis-(hydroxymethyl)dicarbadodecaboranes] have been widely used in the synthesis of dicarbadodecaborane polymers. Diverse heterochain polymers have been obtained from these starting materials: polyesters, polyamides, polybenzimidazoles, polyoxadiazoles, polybenzoxazoles, polyimides, and many others.[12,19–27,32–34] However, the search for methods of synthesis of polymeric systems with enhanced thermal characteristics led to the conclusion that the use of functional aromatic derivatives of dicarbadodecaborane is promising for the synthesis of dicarbadodecaborane-containing polymers. Since the end of the 1960s, the chemistry of dicarbadodecaborane-containing polymers began to develop successfully. The results of studies in this field are examined and surveyed in the present review.

† Unless otherwise stated, henceforth dicarba-*closo*-dodecaborane(12) will be abbreviated to dicarbadodecaborane (Translator).

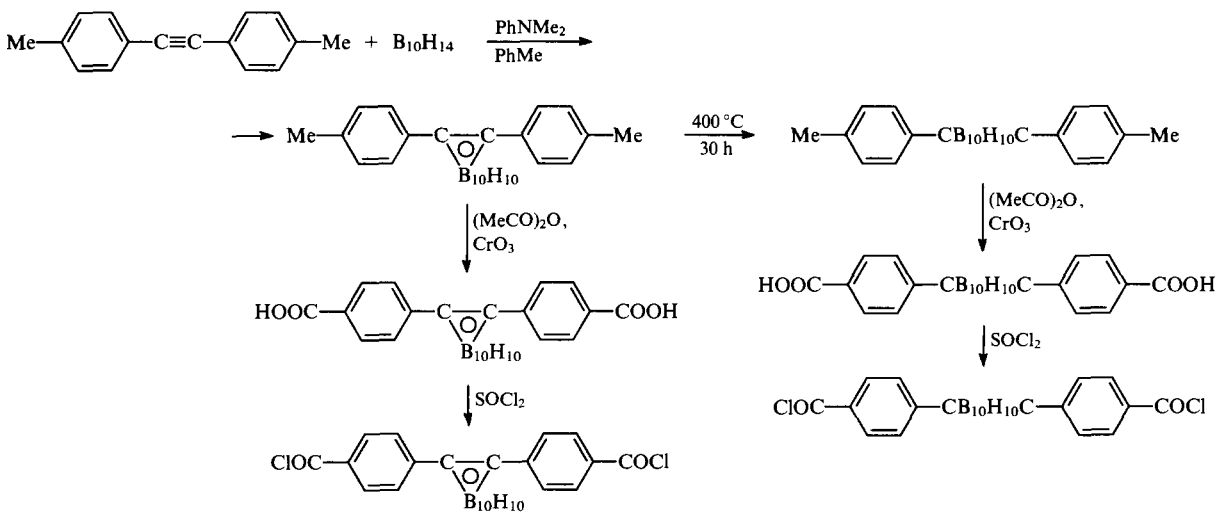
S V Vinogradova Heterochain Polymer Laboratory, Nesmeyanov Institute of Organoelement Compounds, ul. Vavilova 28, 117813 Moscow, Russian Federation. Fax (7-095) 135 50 85. Tel. (7-095) 135 61 78
P M Valetskii, Yu A Kabachii Polymer Synthesis Laboratory, Nesmeyanov Institute of Organoelement Compounds, ul. Vavilova 28, 117813 Moscow, Russian Federation. Fax. (7-095) 135 50 85

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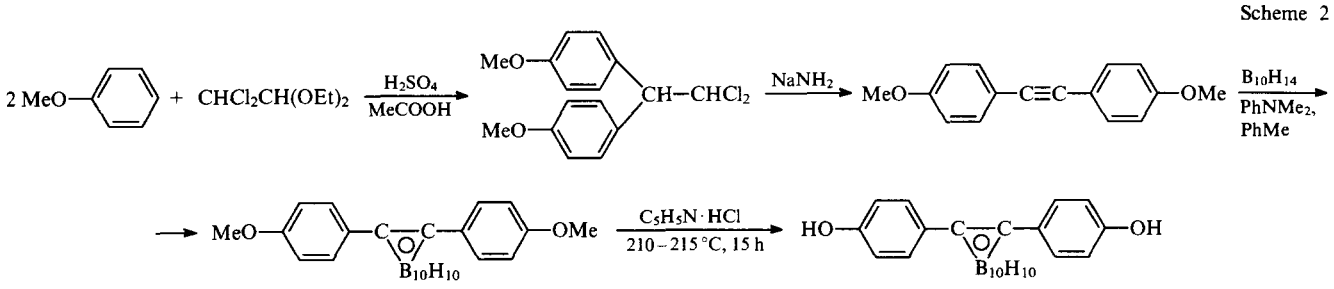
II. Synthesis of aromatic bifunctional derivatives of dicarbadodecaborane(12)

Synthesis of polymers with diarylenedicarbadodecaborane fragments in the macromolecule requires functional aromatic derivatives of dicarbadodecaborane with the corresponding structure. At the beginning of studies in this field, there was no information in the literature about the synthesis of di- and tetrafunctional aromatic derivatives of dicarbadodecaborane. Therefore, in the first stage of this research, much attention was devoted to the chemistry of these monomers. This led to the development of methods of synthesis of compounds such as 1,2- and 1,7-bis(4-carboxyphenyl)dicarbadodecaboranes, their chlorides, and their dihydrazides, 1,2-bis(4-hydroxyphenyl)-dicarbadodecaborane, the dianhydrides of 1,2- and 1,7-bis-(3,4-dicarboxyphenyl)dicarbadodecaboranes, etc.[35-39] Schemes for the synthesis of some of them are presented below as examples.

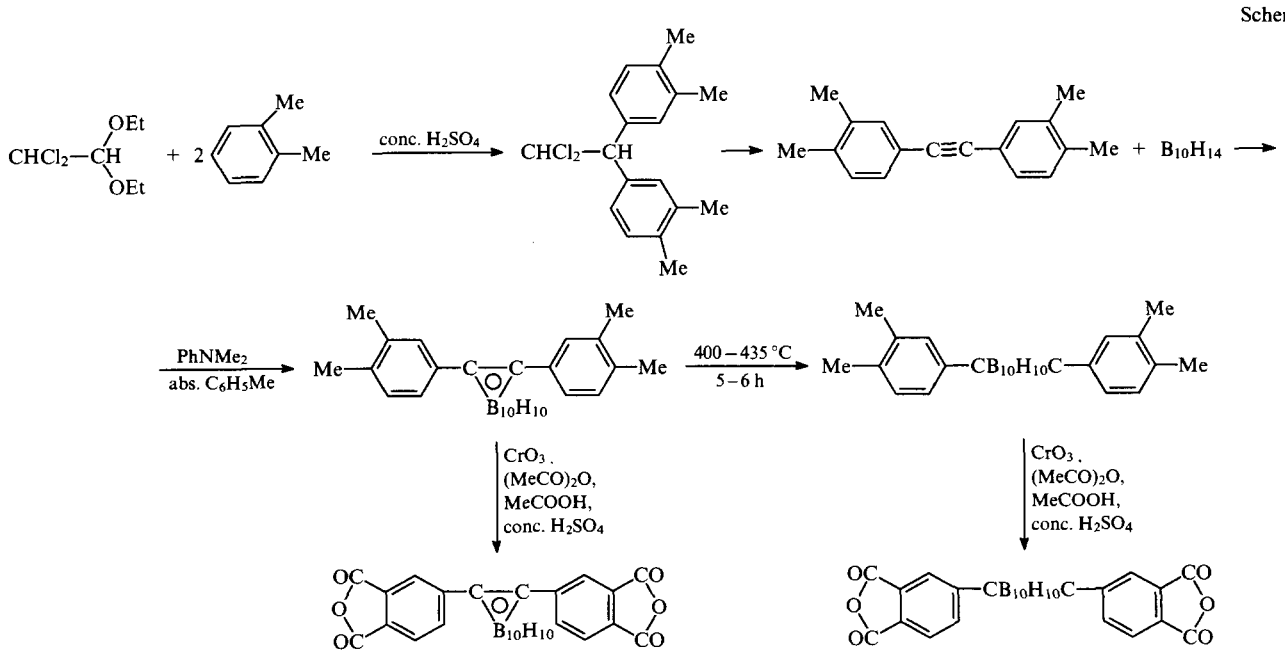
Scheme 1



Scheme 2



Scheme 3



Thus 1,2- and 1,7-bis(4-carboxyphenyl)dicarbadodecaboranes were obtained by oxidising the corresponding ditolyl derivatives of 1,2- and 1,7-dicarbadodecaboranes with chromium trioxide.[35] Scheme 1 illustrates the synthesis of these dicarboxylic acids and their chlorides. 1,2-Bis-(4-hydroxyphenyl)-dicarbadodecaborane was synthesised in accordance with Scheme 2.[36]

The dianhydrides of 1,2- and 1,7-bis(3,4-dicarboxyphenyl)-dicarbadodecaborane were obtained in accordance with Scheme 3.[37,38] The tetramethyltolane required for this purpose was synthesised both by the reaction of asymmetric dichlorodisilylethanes with $NaNH_2$ in aromatic hydrocarbons and by the dehydrochlorination of the same compounds with the aid of KOH in dimethyl sulfoxide.

A fairly large set of the initial functional diarylenedicarbadodecaboranes made it possible to synthesise a wide variety of linear aromatic dicarbadodecaborane-containing heterochain polymers, including polymers with heterocycles in the chain: polyarylates, polyesterketones, polyamides, poly-1,3,4-oxadiazoles, polyimides, polyazophenylenedicarbadodecaboranes, as well as thermoreactive polymers of the type of polyphenylene, and phenol-formaldehyde and epoxide polymers.

III. Linear heterochain polymers with diarylenedicarbadodecaborane fragments in the chain

Polyarylates, polyesterketones, aromatic polyamides, poly-1,3,4-oxadiazoles, polyimides, and polyazophenylenedicarbadodecaboranes with diarylenedicarbadodecaborane fragments in the chain are considered in this section.

1. Polyarylates

The synthesis of dicarbadodecaborane-containing polyarylates with diarylene-dicarbadodecaborane fragments in the chain was achieved by the high-temperature or acceptor-catalytic [in the presence of triethylamine (Schemes 4–6)] polycondensation in three versions:

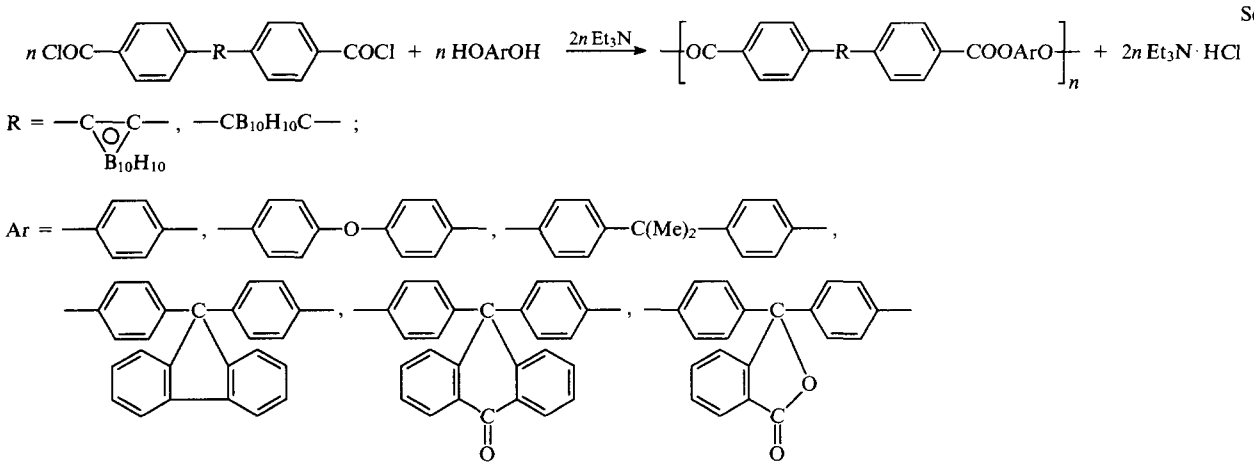
(1) by the reaction of the chlorides of 1,2- and 1,7-bis-(4-carboxyphenyl)dicarbadodecaboranes with various dihydric phenols;

(2) From 1,2-bis(4-hydroxphenyl)dicarbadodecaborane (phenolcarborane) and the chlorides of various aromatic dicarboxylic acids;

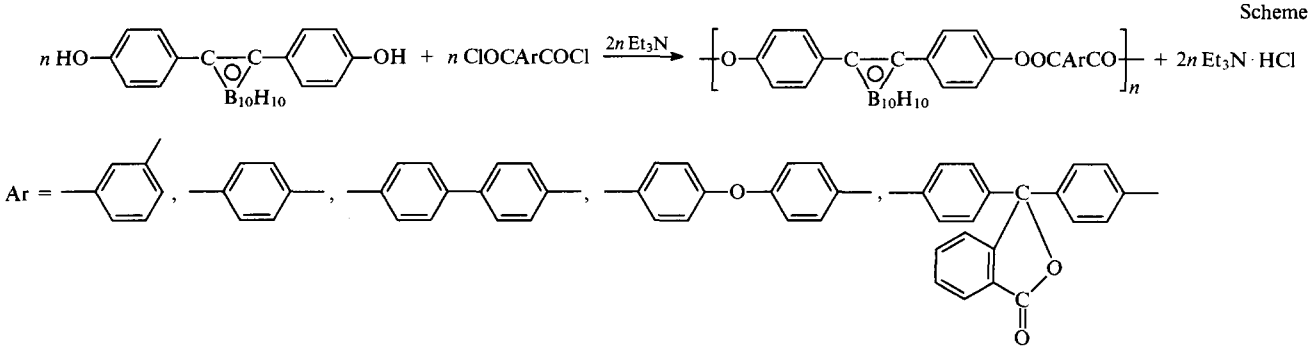
(3) By the reaction of 1,2-bis(4-hydroxyphenyl)dicarbadodecaborane with the chloride of 1,2-bis(4-carboxyphenyl)dicarbadodecaborane.

The characteristics of formation of these polymers and their properties have been examined in a series of studies.[21,25,40–60]

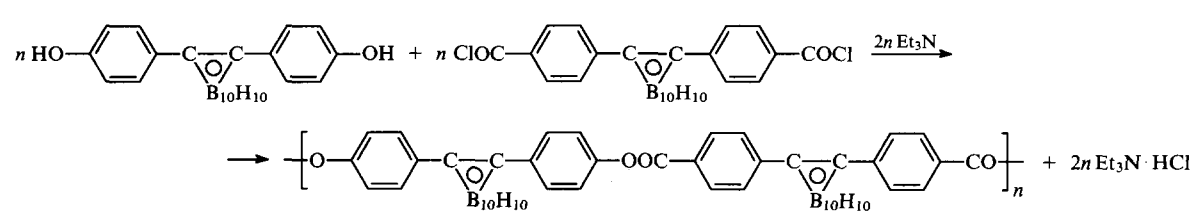
Scheme 4



Scheme 5



Scheme 6



In order to find ways of synthesising high-molecular-mass polyarylates derived from 1,2- and 1,7-bis(4-carboxyphenyl)-dicarbadodecaborane, a series of characteristics of the synthesis of these polymers under the conditions of acceptor-catalytic and high-temperature polycondensation in solution have been investigated in relation to the polycondensation of the chlorides of these acids with 9,9-bis(4-hydroxyphenyl)fluorene (phenol-fluorene). The influence of the nature of the solvent, the concentrations of the starting materials, the reaction temperature, the reaction time, and the method used to introduce the monomers on the molecular mass and yield of the polymers were studied. It was found that both procedures can be successfully employed to synthesise high-molecular-mass polymers (Table 1).

In the acceptor-catalytic polycondensation, polymers with a high molecular mass are obtained when the process is carried out in acetone at 45–50 °C for 1 h with a solid acid chloride introduced into a solution of the bisphenol and triethylamine.

The study of the polycondensation occurring on heating in high-boiling solvents showed that the molecular mass of the dicarbadodecaborane-containing polyarylates is influenced significantly both by the nature of the solvent and by the concentrations of the initial compounds. The most suitable solvent proved to be Sovol (chlorinated biphenyl) and α-chloronaphthalene. The optimum concentrations of the starting materials were 1–2 M. The polycondensation was carried out at 220 °C for 10–16 h. The yields of the dicarbadodecaborane-containing polyarylates [of 1,2- and 1,7-bis(4-carboxyphenyl)dicarbadodecaboranes] were nearly quantitative both in the acceptor-catalytic and in the high-temperature polyesterification. Table 2 presents certain properties of the polyarylates derived from 1,2- and 1,7-bis(4-carboxyphenyl)dicarbadodecaboranes.

The interesting influence of the bulky cardo-group on the structure of the dicarbadodecaborane-containing polyarylates under consideration is noteworthy.[40] Thus the polyarylates derived from 1,2-bis(4-carboxyphenyl)dicarbadodecaborane and dihydric phenols containing bulky groups of the cardo-type (phthalide, fluorene, and anthrone) possess a crystallinity with an average degree of order according to X-ray diffraction data.

Table 1. The reduced viscosities (η_{red}) and molecular masses (M_w) of polyarylates obtained from the acid chlorides of 1,2- (**A**) and 1,7-bis-(4-carboxyphenyl)dicarbadodecaboranes (**B**) and various dihydric phenols by acceptor-catalytic (1) and high-temperature (2) polycondensation.

Initial components in the synthesis of polyarylates		η_{red}/dl g^{-1}		$10^{-3} M_w$	
		1	2	1	2
dihydric phenol	acid chloride				
Hydroquinone	**A**	0.6	0.3	–	–
	B	0.6	0.9	–	–
Bis(4-hydroxyphenyl) ether	**A**	0.6	0.9	116	107
	B	2.0	1.9	94	132
2,2-Bis(4-hydroxy-phenyl)propane	**A**	0.9	–	110	–
	B	0.6	2.3	22	–
9,9-Bis(4-hydroxy-phenyl) fluorene	**A**	0.9	2.3	99	80
	B	1.3	1.2	50	27
9,9-Bis(4-hydroxy-phenyl)-10-anthrone (phenolanthrone)	**A**	0.9	0.5	66	52
	B	1.1	0.7	76	–
Phenolphthalein	**A**	1.2	–	–	–
	B	2.0	2.4	–	–

Note. η_{red} was obtained for a 0.5% solution of the polymer in tetrachloroethane at 25 °C; M_w was determined by light scattering in chloroform.

On the other hand, an amorphous or a weakly ordered structure is characteristic of dicarbadodecaborane-containing polyarylates based on dihydric phenols such as hydroquinone, di(4-hydroxyphenyl) ether, and 2,2-bis(4-hydroxyphenyl) propane.

The polyarylates obtained from the more symmetrical 1,7-isomer and dihydric phenols of the type of hydroquinone

Table 2. The properties of polyarylates obtained from the acid chlorides of 1,2- (**A**) and 1,7-bis(4-carboxyphenyl)dicarbadodecaboranes (**B**) and various dihydric phenols by acceptor-catalytic polyesterification.

Initial components in the synthesis of polyarylates		Softening temperature[a]/°C	Properties of film[b]		Temperature of onset of decrease in mass[c]/°C	Coke residue on heating (%)	
			σ/kgf cm^{-1}	ε(%)		up to 900 °C[d]	at 400 °C[d]
dihydric phenol	acid chloride						
Hydroquinone	**A**	320	Brittle film		380	88	94
	B	320	"		380	85	91
Bis(4-hydroxyphenyl) ether	**A**	290	500	23	390	85	90
	B	280	990	10	390	81	85
2,2-Bis(4-hydroxyphenyl) propane	**A**	290	570	4	400	62	96
	B	320	650	2	420	50	86
9,9-Bis(4-hydroxyphenyl) fluorene	**A**	350	680	4	420	60	95
	B	360	1050	5	400	58	90
9,9-Bis(4-hydroxyphenyl)-10-anthrone	**A**	350	470	–	410	70	96
	B	340	920	4	400	–	98
Phenolphthalein	**A**	350	570	2	400	78	98
	B	340	1100	7	400	80	98

[a] The temperature corresponding to the point of intersection of the tangents to the thermomechanical curve in the region of the onset of flow was adopted as the softening temperature; the load applied to the specimen was 0.8 kgf cm^{-2} and the heating rate was 70 K min^{-1}.
[b] σ is the tensile strength of a nonoriented film and ε is the relative elongation at break.
[c] Determined from the thermogravimetric curve at a heating rate of 4.5 K min^{-1} in air.
[d] Determined under isothermal conditions in air in the course of 3 h.

or 2,2-bis(4-hydroxyphenyl)propane have a more ordered structure than those derived from the 1,2-bis(4-carboxyphenyl)-dicarbadodecaborane.[42] According to X-ray diffraction data, the former polyarylates have a fairly high degree of order. The polyarylates derived from 1,7-bis(4-carboxyphenyl)dicarbadodecaborane and dihydric phenols with a cardo-group differ little as regards the degree of order from the analogous polymers based on the 1,2-dicarbadodecaborane-containing monomer. On passing to the polyarylates based on the 1,7-isomer, only a slight tendency towards the formation of an amorphous structure may be noted.[42]

The softening temperatures of the polyarylates based on the 1,2- and 1,7-isomers of bis(4-carboxyphenyl)dicarbadodecaborane and dihydric phenols having the same structure are similar for the same phase state. The highest softening temperatures (340–360 °C) are characteristic of the polyarylates derived from dihydric cardophenols.

The polyarylates derived from both isomers of bis(4-carboxylphenyl)dicarbadodecaborane dissolve in many organic solvents, including aromatic hydrocarbons.[42] The study of the hydrodynamic properties of the solutions and of the molecular mass distribution (MMD) of polyarylates based on 1,2- and 1,7-bis(4-carboxyphenyl)dicarbadodecaboranes led to the discovery of the specific nature of the interaction with the solvent of the polyarylates containing 1,2- and 1,7-dicarbadodecaborane fragments in the chain.[43] Whilst the molecular masses of the polyarylates with the 1,7-diphenyldicarbadodecaborane fragments in the chain are similar, the latter have significantly higher specific viscosities than the analogous polymers with the 1,2-diphenyldicarbadodecaborane fragments regardless of the method of synthesis. This made it possible to postulate that the polyarylates based on 1,2-bis(4-carboxyphenyl)dicarbadodecaborane exists in solution as denser macromolecular coils than can be accounted for by both steric factors and by the greater influence of the dipole moment in the case of the polyarylates with the 1,2-dicarbadodecaborane groups.

The parameters K and a in the Mark–Houwink equation have been determined for the polyarylate obtained from 1,7-bis-(4-carboxyphenyl)dicarbadodecaborane and bis(4-hydroxyphenyl) ether.[43] In chloroform and tetrahydrofuran (THF), $K = 4.74 \times 10^{-4}$ and 2.7×10^{-4}, while $a = 0.71$ and 0.70 respectively. The polydispersity coefficient for the polymer under consideration, synthesised by acceptor-catalytic polyesterification, is 1.35, indicating its comparatively narrow MMD.[43]

The mechanisms of the relaxation processes in the polyarylates based on 1,2- and 1,7-bis(4-carboxyphenyl)dicarba-dodecaboranes have been investigated by dielectric proton magnetic resonance spectrometry and by the thermodepolarisation and radiothermoluminescence methods over a wide temperature range (from −196–300 °C).[44,45,50,58] This led to the establishment of the existence of two regions where the resonance line becomes narrower, one of which (the high-temperature region) is near the glass points of the polymers and is due to the segmental motion of the polymer chain, while the other (the low-temperature region −50 to 150 °C) is induced by the local mobility of the dicarbadodecaborane chain frag-ments. The temperature corresponding to the 'unfreezing' of the segmental mobility depends significantly on the chemical structure of the dihydric phenol and depends little on the structure of the diphenyldicarbadodecaborane fragments incorporated in the chain.

It has also been shown that the vibrations of the 1,2-dicarbadodecaborane nucleus are hindered compared with the 1,7-isomer both by the appreciable conjugation of the 1,2-dicarbadodecaborane fragment with the aromatic rings and due to steric effects. This is reflected in the relaxation processes in the dicarbadodecaborane-containing polyesters, the results of the study of which indicate an increase in the rigidity of the macrochain on passing from the 1,7- to the 1,2-dicarbadodecaborane-containing polymers.[44,58]

Colourless films, the strength parameters of which are listed in Table 2, are obtained from the 1,2- and 1,7-bis(4-carboxyphenyl)dicarbadodecaborane-based polyarylates by casting the latter from solution.

A series of studies have been carried out on the thermal properties of the 1,2- and 1,7-bis(4-carboxyphenyl)dicarba-dodecaborane-based polyarylates in air and under an inert atmosphere — under both dynamic and isothermal conditions.[21,25,40–42,46–49,51,59] It was found that the initial polymer degradation temperature is 20–60 °C higher than for the usual polyarylates and, furthermore, the polyarylates have greater 'coke' residues (50%–90% relative to the initial mass on heating in air to 900 °C), whereas the usual polyarylates derived from terephthalic acid and 1,9-bis(4-hydroxyphenyl)fluorene are fully combusted at 650–700 °C. Table 2 shows that, after heating in air at 400 °C for 3 h, the mass of dicarbadodecaborane-containing polymers diminishes by 2%–15%, whereas the 1,9-bis-(4-hydroxyphenyl)fluorene polyterephthalate begins to decompose even before 400 °C and its degree of decomposition after 3 h is 35%. Analysis of the gaseous products of the degradation of the dicarbadodecaborane-containing polyarylates under consideration demonstrated the presence in them of a lower content of carbon oxides and an appreciable content of hydrogen.[21,25,48,49]

The survey of the data obtained established that the dicarbadodecaborane nuclei in the polymer chain have a stabilising effect on the thermal stability of the ester linkage, increasing thereby the thermal stability of the polymer. It has been suggested that this stabilising effect of 1,2-dicarbadodecaborane groups is associated with their conversion into dicarbaundecaborate groups.[48]

A comparative study of the thermal behaviour of the polyarylates obtained by the reaction of 9,9-bis(4-hydroxyphenyl)fluorene with 1,2-bis(4-carboxyphenyl)dicarbadodecaborane and terephthalic acid revealed an interesting feature:[47] in vacuo, gel formation in the 1,2-dicarbadodecaborane-containing polyarylates begins sooner than in polyfluoreneterephthalate [poly(9,9-fluorenylenediphenyl terephthalate)? (translator)] and reaches a maximum at 350 °C, whilst the gel content in the case of polyfluoreneterephthalate is only 2.7%. Under oxidation conditions, the dicarbadodecaborane-containing polyarylate is already fully cross-linked at 275 °C, whereas polyfluoreneterephthalate contains only 30% of the gel at 350 °C.

A study has been made of the structural-chemical transformations of 1,2- and 1,7-dicarbadodecaborane-containing polyarylates during isothermal heating in the temperature range 225–325 °C (at 25 °C intervals) in vacuo and in the presence of oxygen by means of IR spectroscopy and sol-gel analysis.[59] Analysis of the results led to the conclusion that, during vacuum heating and under oxidation conditions, the dicarbadodecaborane fragments participate in the cross-linking of the polymer chain of the dicarbadodecaborane-containing polyarylates, forming inorganic intermolecular B–O–B linkages. In terms of their ability to form three-dimensional structures, the 1,7-dicarbadodecaborane-containing polyarylates are superior to the 1,2-dicarbadodecaborane polymers.

The electrical conductivities of the solid pyrolysis products formed on heat treatment of the polyarylate obtained by the reaction of 1,7-bis(4-carboxyphenyl)dicarbadodecaborane and bis(4-hydroxyphenyl) ether for 1 h in vacuo (10^{-3} Torr) at 600, 900, and 1200 °C have been investigated by electronic spectroscopy.[60] The aromatic rings in the polymer chain of this polyarylate are separated (apart from the dicarbadodecaborane fragments) also by ester groups, which do not transmit π-conjugation along the chain, as a result of which the degree of conjugation of the initial system is low and the system does not exhibit semiconducting properties. The comparatively small changes in the electrical conductivities and activation energies for the specimens heated to 600 °C indicate a low degree of reorganisation of the internal structure of the polymer, leading to the formation of condensed polynuclear systems in the solid pyrolysis products. The electrical conductivity at 150 °C of the specimen heated to 900 °C increases by approximately

twelve orders of magnitude compared with the initial polymer and the electrical conduction process becomes nonactivated ($E \approx 2.89$ kJ mol^{-1}). In terms of the absolute value of the electrical conductivity, this pyrolysis product is at the boundary between semiconductors and metals. The observed change in electrical conductivity is due to the formation of highly conjugated polynuclear systems in the pyrolysis product.

The absolute values of the electrical conductivities of the specimens heated to 1200 °C increase slightly compared with the electrical conductivity of the specimen heated to 900 °C, but, after heating at 1200 °C, a negative temperature coefficient of the resistance, $\alpha = -0.12$ K^{-1} is observed, i.e. with increase in temperature the electrical conductivity of the specimens does not increase, as in typical semiconducting materials, but actually diminishes, which is characteristic of materials with the metallic type of conductivity. Consequently heat treatment of the specimens at 900–1200 °C is accompanied by a significant reorganisation of the internal structure. The thermal e.m.f.'s of the specimens obtained at 900 and 1200 °C are respectively 9.3 and 6.8 μVK^{-1} at 100 °C. The sign of the thermal e.m.f. shows that the principal electric current carriers are electrons. Thus the pyrolysis of the dicarbadodecaborane-containing polyarylate leads to the formation of an extended region of aromatic ring systems cross-linked in space by the residual dicarbadodecaborane fragments.

As noted above, 1,2-bis(4-hydroxyphenyl)dicarbadodecaborane has been used to synthesise polyarylates with diphenyldicarbadodecaborane fragments in the chain.[21,54–56] 1,2-Bis(4-hydroxyphenyl)dicarbadodecaborane was subjected to acceptor-catalytic and high-temperature polycondensation with dicarboxylic acid chlorides (see Scheme 5). A number of characteristic features of these processes have been investigated in relation to the polycondensation of 1,2-bis(4-hydroxyphenyl)dicarbadodecaborane with isophthalic acid chloride: influence of the nature of the solvent, temperature, concentrations of initial substances, and the order in which they are introduced into the reaction sphere, on the reduced viscosities of the solutions of the polymers obtained and their structures.

It was found that, when the acceptor-catalytic polyesterification is carried out in acetone (heterogeneous conditions), changes in the process temperature, in the concentrations of the starting materials, and in the order in which they are introduced into the reaction zone did not lead to the formation of polymers with a high reduced viscosity of the solution. A positive result was not obtained either when the acceptor-catalytic polycondensation was carried out under homogeneous conditions (in dichloroethane, tetrahydrofuran, dioxane, and benzene) and also when the synthesis was performed by high-temperature polycondensation in Sovol and α-chloronaphthalene at 220 °C. In all cases, polymers with low reduced viscosities of the solutions (0.07–0.31 dl g^{-1} in tetrachloroethane) were obtained. The molecular mass of a polymer with a reduced viscosity of 0.07 dl g^{-1}, determined by the light scattering method in tetrahydrofuran, was 8600. The reason for the formation of polymers with low molecular masses is their limited solubility in the reaction medium due to the crystallisation of the polymers during their formation.[55]

The tendency of the 1,2-bis(4-hydroxyphenyl)dicarbadodecaborane-based polyarylates to form highly ordered and sparingly soluble systems is manifested to an even greater extent in the polycondensation of 1,2-bis(4-hydroxyphenyl)-dicarbadodecaborane with terephthalic and biphenyl-4,4′-dicarboxylic acid chlorides. Such polyarylates, obtained by high-temperature polycondensation, have a highly ordered crystal structure according to X-ray diffraction data and do not dissolve in any of the solvents known for polyarylates even such as trifluoroacetic and sulfuric acids. Polymers with a lower degree of order are formed in the acceptor-catalytic polycondensation, but in this case too the terephthalic acid-based polyarylates are insoluble.[55]

Attempts have been made to obtain the above polyarylates by high-temperature polycondensation using finely dispersed magnesium as the catalyst and also by the rapid heating of the initial components in a high-boiling solvent to 250–340 °C with subsequent polycondensation at these temperatures for 1 h and rapid cooling of the initial solution to room temperature. In this case, the poly[1,2-bis(4-hydroxyphenyl)dicarbadodecaborane terephthalate] dissolved immediately after synthesis in a mixture of tetrachloroethane and phenol, but it soon precipitated and then no longer dissolved.[55]

On the other hand, under conditions where the polymers formed are amorphous and readily soluble, it is possible to attain high molecular masses. This occurs in the polycondensation of 1,2-bis(4-hydroxyphenyl)dicarbadodecaborane with the chlorides of oxybis(benzene-4-carboxylic)acid and bis(4-carboxyphenyl)-phthalide. In the former case, it was possible to obtain a polymer with a reduced viscosity in tetrachloroethane (TCE) of 0.92 dl g^{-1} (molecular mass 140 × 10^3), while in the latter the reduced viscosity was 0.62 dl g^{-1} (molecular mass 93 × 10^3). Both polymers are soluble in chloroform, tetrachloroethane, tetrahydrofuran, and benzene.

Since one of the ways of disturbing the order in the polymer is copolycondensation, a series of mixed polyarylates based on isophthalic (or terephthalic) acid, 1,2-bis(4-hydroxyphenyl)-dicarbadodecaborane, and phenolphthalein were obtained.[55] It was found that, for a relatively high content of phenolphthalein residues in such copolymers, the degree of order in the copolymer formed diminishes, which improves its solubility and the reduced viscosity is fairly high. For example, the copolymer obtained from 1,2-bis(4-hydroxyphenyl)dicarbadodecaborane, phenolphthalein, and terephthalic acid chloride in molar proportions of 0.5 : 0.5 : 1 has a crystal structure with a relatively low degree of order, is soluble in chloroform, tetrachloroethane, and tetrahydrofuran, and its reduced viscosity in tetrachloroethane is 1.53–1.67 dl g^{-1}. With increase in the content of 1,2-bis(4-hydroxyphenyl)dicarbadodecaborane residues in the mixed polyarylates, the degree of order in the latter increases, while the reduced viscosity and the solubility diminish.

Mixed 1,2-bis(4-hydroxyphenyl)dicarbadodecaborane and chloro- or methylhydroquinone polyterephthalates have been synthesised recently by acceptor-catalytic polycondensation. The possibility of obtaining them from organoelement liquid-crystal polymers has been investigated.[41,52,53] The liquid-crystal properties of such dicarbadodecaborane-containing copolyarylates are indicated both by the composition of the copolymer and by its microstructure. For example, with increase in the molar proportion of the 1,2-bis(4-hydroxyphenyl)dicarbadodecaborane residues in the copolyarylate derived from 1,2-bis(4-hydroxyphenyl)dicarbadodecaborane and chlorohydroquinone from 0.4 to 0.6, the temperature range corresponding to the existence of the mesophase expands from 245–400 °C to 230–400 °C. In all cases the 1,2-bis(4-hydroxyphenyl)dicarbadodecaborane-based homo- and copolyarylates were obtained in high yields (85%–95%).

Table 3 presents data on certain properties of the 1,2-bis(4-hydroxyphenyl)dicarbadodecaborane-based polyarylates. Comparison of the data in Tables 2 and 3 permits the conclusion that the softening temperatures of the polyarylates are hardly influenced by the presence between the 1,2-dicarbadodecaborane group with hydroxy- or carboxy-phenyl residues. Thus, whereas the softening temperature of the amorphous polyarylates derived from 1,2-(4-hydroxyphenyl)dicarbadodecaborane and oxybis(benzene-4-carboxylic) acid is 275–285 °C, that of the isomeric amorphous polyarylate derived from 1,2-bis(4-carboxyphenyl)dicarbadodecaborane and bis(4-hydroxyphenyl) ether is 280–290 °C. On the other hand, comparison of the melting points of the crystalline polyarylates derived from 1,2-bis(4-hydroxyphenyl)dicarbadodecaborane and terephthalic and isophthalic acids (~400 and 245 °C respectively) with those of the crystalline polyesters of 1,2-bis(4-hydroxymethyl)dicarbadodeca-

Table 3. Certain properties of 1,2-bis(4-hydroxyphenyl)dicarbadodecaborane polyarylates obtained by acceptor-catalytic (I) and high-temperature (II) polycondensation.

Acid chloride	Methods of synthesis	η_{red}/dl g^{-1} (TCE, 25 °C)	Structure[a]	Softening temperature[b]/°C	Temperature of onset of mass loss/°C		Coke residue at 900 °C (%)	
					in air[c]	in helium[d]	in air[c]	in helium[d]
Isophthalic	I	0.31	Crystalline, low	245				
	II	0.20	degree of order	240	350	360	70	90
Terephthalic	I	–	Crystalline, high	~400				
	II	–	degree of order	>400	380	380	82	88
Biphenyl-4,4'-dicarboxylic	I	0.20	Crystalline, moderate degree of order	~400				
	II	–	Crystalline, high degree of order	>400	370	370	85	85
Oxybis(benzene-4-carboxylic)	I	0.92	Amorphous	275				
	II	0.46	"	285	380	400	75	88
Of bis(4-carboxyphenyl)phthalide	I	0.62	"	330	400	410	77	85
	II	0.28	"	300				

[a] X-Ray diffraction data. [b] See footnote to Table 2. [c] See footnote to Table 2. [d] Heating rate 5 K min^{-1}.

borane and terephthalic and isophthalic acids[61] (221 and 88 °C respectively) clearly demonstrates that it is desirable to introduce the dicarbadodecaborane groups into the polymer chain in the form of diphenyldicarbadodecaborane fragments in order to create heat-resistant polymers.

As can be seen from Table 3, the 1,2-bis(4-hydroxyphenyl)-dicarbadodecaborane-based polyarylates are thermally stable and give rise to high amounts of coke residue on heating to 900 °C both under an inert atmosphere and in air.

A polyarylate with an increased content of diphenyldicarbadodecaborane fragments, the chain of which contains only 1,2-diphenyldicarbadodecaborane fragments together with the ester groups, has been synthesised by the high-temperature polycondensation of 1,2-bis(4-hydroxyphenyl)dicarbadodecaborane with the acid chloride of 1,2-bis(4-carboxyphenyl)dicarbadodecaborane in α-chloronaphthalene at 220 °C for 15–18 h (Scheme 6).[56] This polymer had the most crystalline structure (degree of crystallinity 55%) and was soluble only in tetrahydrofuran. The synthesis of polyarylates by acceptor-catalytic polycondensation in acetone or by high-temperature polycondensation in Sovol with rapid heating of the solution of the starting materials to 320 °C and the maintenance of the reaction mixture at this temperature for 1 h with subsequent rapid cooling to 0 °C gives rise to specimens with a lower degree of crystallinity. In the last case, the polymer is soluble not only in tetrahydrofuran but also in cyclohexanone. None of these polymers melt below 400 °C. Above this temperature, their thermal degradation begins.

However, it was observed that this dicarbadodecaborane-containing polyarylate can be converted into an amorphous form by reprecipitating the polymer from solution in tetrahydrofuran in cooled water or methanol. The specimens, converted into an amorphous form, dissolve in chloroform, tetrachloroethane, and even in benzene, softening at 260–290 °C. The amorphous specimen can be reconverted into a crystalline form by heating a 3% solution of the polymer in tetrachloroethane (from which the polymer begins to precipitate during the crystallisation process) or by slow (over a period of several days) evaporation of the polymer solution in chloroform. The specimens obtained in this way do not melt below 400 °C.

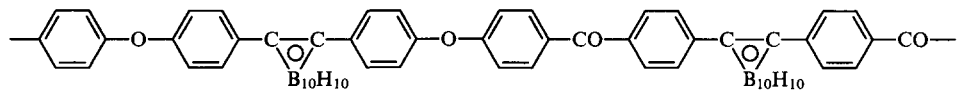
The degree of crystallinity of the polyarylates with 1,2-diphenyldicarbadodecaborane units can be altered also by heat treatment. Thus successive heating of the same specimen with a degree of crystallinity of 55% at 230, 290, and 330 °C in air for 30 min reduces the degree of crystallinity to 26%, 22%, and 16% respectively. On the other hand, when the specimen is heated at 450 °C, its degree of crystallinity falls to 5%–8%.

Thus, by manipulating the conditions in the synthesis or in the subsequent treatment of the polymer, it is possible to alter specifically the structure of this diphenyldicarbadodecaborane-containing polyarylate and hence its heat resistance.

The study of the characteristic features of the thermal and thermooxidative degradation of the polyarylates derived from 1,2-bis(4-hydroxyphenyl)dicarbadodecaborane and 1,2-bis(4-carboxyphenyl)dicarbadodecaborane[56,57] revealed a difference in the behaviour of the crystalline specimen and the specimen converted into an amorphous form on heating, which may be due to the difference between the molecular mobilities in the temperature range 280–380 °C.[57] It was established that the thermal stability of the amorphous polymer is higher. Thus the mass of a specimen of the latter does not change up to ~650 °C, whereas crystalline specimens exhibit a decrease in mass at 400 °C.[56]

The structural transformations of the polyarylate derived from 1,2-bis(4-hydroxyphenyl)dicarbadodecaborane and 1,2-bis-(4-carboxyphenyl)dicarbadodecaborane and, for comparison, the polyarylate obtained from 4,4'-dihydroxybiphenyl and 4,4'-dicarboxybiphenyl on heat treatment (for 1 h) in vacuo (10^{-3} Torr) in the temperature range 300–1200 °C have been investigated and the characteristic regions corresponding to the thermal transformations of the polymers have been determined.[62] The temperature range corresponding to the existence of the EPR absorption for the dicarbadodecaborane-containing polyarylate is much wider (400–1200 °C) than for the usual polyarylate (400–700 °C). The maximum concentration of paramagnetic centres is attained at 800 °C for the dicarbadodecaborane-containing polyarylate and at 600 °C for the usual polyarylate.

It was found that heating of the dicarbadodecaborane-containing polyarylate at 300 °C induces hardly any changes in the crystalline polymer specimen, while the amorphous specimen becomes crystalline under similar conditions. An increase in temperature to 400 °C leads to the complete disruption of the crystal structure of the polymer and to its conversion into an amorphous form. After heating to 500 °C, considerable chemical transformations take place and an appreciable amount of boric acid is formed. This may indicate the interaction of the dicarbadodecaborane groups and the products of their thermal transformations with the oxygen



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bound chemically in the polymer and in its reaction products. At 600 °C, the polymer structure is fully disrupted and at 700 °C small amounts of graphite particles are formed. A further increase in temperature up to 1000 °C does not lead to significant changes in the structure of the specimen. The latter remains porous and the amount of graphite increases. According to the results of dynamic thermogravimetric analysis (DTGA) in helium at a heating rate of 5 K min^{-1}, specimens of the dicarbadodecaborane-containing polyarylate do not exhibit a region of vigorous decomposition up to 900 °C. The decrease in mass virtually ceases towards 750 °C and the rate of change of the mass in the temperature range 700–750 °C is only 0.01%–0.02% when the temperature is altered by 1 K.

Comparison of the results of X-ray diffraction and of the EPR spectra of the heat-treated polymers (the dicarbadodecaborane-containing and usual polymers) permits the conclusion that the principal difference between the polyheteroarylenedicarbadodecaboranes and their usual organic analogues is the displacement of the extensive decomposition processes and of the rearrangement of the initial structure to higher temperatures and also the specific interaction of the dicarbadodecaborane groups or the products of their thermal transformation with the chemically bound oxygen.[62]

2. Polyesterketones

Brief data have been published recently concerning simple aromatic polyesterketones in which the 1,2-, 1,7-, and 1,12-dicarbadodecaborane groups and phenylene units are joined via oxygen or CO groups (for example, as in a type **1** polymer).[63] These polymers are obtained by the interaction of diphenylenedicarbadodecaboranedicarboxylic acids having the corresponding structure and diphenoxyphenyl derivatives of the dicarbadodecaborane.

The polymers generally have an amorphous structure and a glass point of 180–220 °C and form films from solutions in methylene chloride and chloroform. According to DTGA data, the polymers begin to lose mass at 350–400 °C without fusion, the overall mass loss at 1000 °C amounting to about 10%–15%. This enabled the authors to postulate that the pyrolysis of such polymers under an inert atmosphere can lead to the formation of a ceramic boron carbide residue dispersed in the graphite matrix.

3. Polyamides

Polyamides with diphenylenedicarbadodecaborane fragments in the chain have been obtained by the reaction of the acid chlorides of 1,2- and 1,7-bis(4-carboxyphenyl)dicarbadodecaboranes with aromatic diamines (Scheme 7) under the conditions of low-temperature polycondensation in solution or by polycondensation in an organic solvent–water–hydrogen chloride acceptor mixture.[21,64–67]

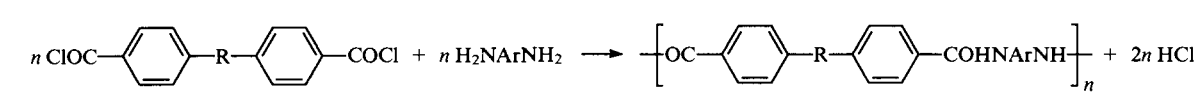
In order to discover the most favourable conditions of synthesis, certain features of the formation reactions of the polyamides (the nature of the solvent, reaction temperature, concentrations of the initial components, etc.) were investigated in relation to the polycondensation of the acid chloride of 1,2-bis(4-carboxyphenyl)dicarbadodecaborane with *m*-phenylenediamine and 1,2-bis(4-carboxyphenyl)dicarbadodecaborane with 9,9-bis(4-aminophenyl)fluorene. It was found that, in the case of the low-temperature synthesis of the polyamide, the polymers with the highest reduced viscosity are obtained when the process is carried out in dimethylacetamide at −30 °C (synthesis for 1 h at −30 °C and maintenance at room temperature for 1–2 h) at a concentration of the starting materials of 1.0 M.

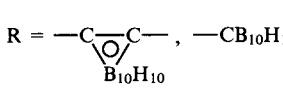
When the polycondensation was carried out in an organic solvent–water system, best results were obtained when tetrahydrofuran and a concentration of the starting material of 0.3 M were employed. In this case, $NaHCO_3$ was used as the hydrogen chloride acceptor. The process was carried out at room temperature for 20 min with vigorous stirring of the reaction mass. Both methods can be used successfully to obtain high-molecular-mass dicarbadodecaborane-containing polyamides.

As an example, Table 4 presents the intrinsic viscosities of 0.5% solutions of the polymers in *N*,*N*′-dimethylacetamide at 25 °C and their molecular masses determined by the light scattering method in *N*-methyl-2-pyrrolidinone.

Outwardly the aromatic polyamides derived from 1,2- and 1,7-bis(4-carboxyphenyl)dicarbadodecaboranes are white fibrous or powdered substances. Many of them are soluble not only in amide solvents but also in tetrahydrofuran, cyclohexanone, a mixture of tetrachloroethane with phenol, and tricresol. The polyamide obtained from 1,4-phenylenediamine and 1,2-bis-(4-carboxyphenyl)dicarbadodecaborane is an exception. It does not dissolve in the solvents listed above and is insoluble even in sulfuric acid. The polyamides synthesised are also insoluble in tetrachloroethane.

Scheme 7





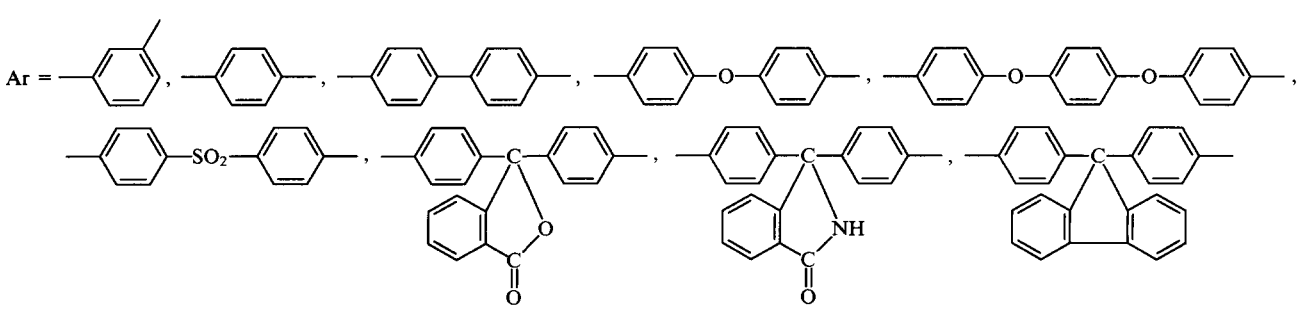


Table 4. The reduced viscosities and molecular masses of the polyamides obtained from various diamines and the acid chlorides of 1,2- (**A**) and 1,7-bis(4-carboxyphenyl)dicarbadodecaboranes (**B**) by low-temperature polycondensation in *N,N*-dimethylacetamide.

Initial components in the synthesis of polyarylates		η_{red}/dl g^{-1} (10^{-3} M_w)
diamine	acid chloride	
1,3-Phenylenediamine	**A**	0.74 (106)
	B	0.60
1,4-Phenylenediamine	**A**	Insoluble
	B	0.66
4,4′-Diaminobiphenyl	**A**	0.50
	B	1.05
Bis(4-aminophenyl) ether	**A**	0.91 (160)
	B	0.79
Bis(4-aminophenyl) ether of hydroquinone	**A**	0.81
	B	–
Bis(4-aminophenyl)sulfone	**A**	0.40 (19)
	B	0.40
9,9-Bis(4-aminophenyl)-fluorene	**A**	0.75 (70)
	B	1.50 (70)
Bis(4-aminophenyl)phthalide	**A**	0.75 (67)
	B	0.70
Bis(4-aminophenyl)phthalimide	**A**	0.50
	B	–

Strong films are formed from solutions of the diphenyldicarbadodecaborane-containing amides. For example, nonoriented films of the polyamides obtained by the reaction of 1,2-bis(4-carboxyphenyl)dicarbadodecaborane with anilinephthalein and the bis(4-aminophenyl) ether of hydroquinone have tensile strengths of 750 and 760 kgf cm^{-2} and relative elongations at breaks of 5% and 30% respectively. The tensile strength of the film obtained from the polyamide derived from 1,7-bis-(4-carboxyphenyl)dicarbadodecaborane and anilinefluorene is 940 kgf cm^{-2} with a relative elongation at break of 20%. At 300 °C, the film of this polymer retains a high strength (370 kgf cm^{-2}) and its relative elongation at this temperature is 111%.

The majority of the polyamides considered are amorphous. The polyamides obtained from anilinefluorene and both bis-(4-carboxyphenyl)dicarbadodecaborane isomers and also the polymer obtained by the reaction of benzidine and 1,7-bis-(4-carboxyphenyl)dicarbadodecaborane, which has a crystalline structure with a low degree of order, are exceptions.

Table 5 presents the thermal properties of aromatic polyamides based on 1,2- and 1,7-bis(4-carboxyphenyl)dicarbadodecaboranes. Evidently high softening temperatures are characteristic of these polyamides. The polyamides derived from benzidine, 1,4-phenylenediamine, and diamines with cardo-groups have the highest softening temperatures (370–400 °C). Comparison of the results of a thermomechanical study of aromatic polyamides derived from 1,7-bis(4-carboxyphenyl)dicarbadodecaborane [64] and 1,7-dicarbadodecaboranedicarboxylic acid [69] permits the conclusion that the use of aromatic bifunctional derivatives of 1,7-dicarbadodecaborane leads to much more heat-resistant polyamides. For example, whereas the softening temperatures of the polyamides obtained by the reaction of 1,7-dicarbadodecaboranedicarboxylic acid with 1,4-phenylenediamine, benzidine, and bis(4-aminophenyl) ether are 210, 250, and 220 °C (in all cases with decomposition), the softening temperatures of the analogous polyamides based on 1,7-bis(4-carboxyphenyl)dicarbadodeca-borane are 380, 400, and 300 °C respectively.

The thermal and thermooxidative behaviour of dicarbadodecaborane-containing aromatic polyamides have been investigated in a number of studies. [64–66, 68, 70, 71]

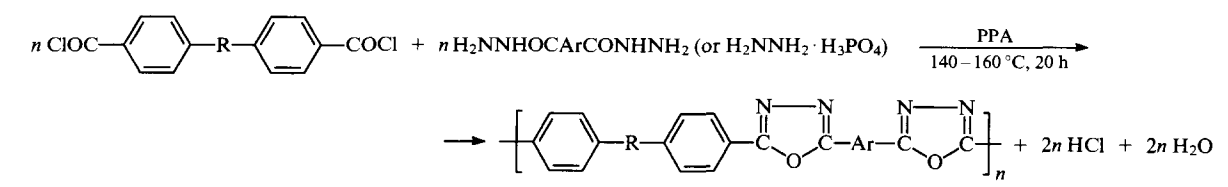
Table 5 (over) shows that the temperature of the onset of a change in mass is in the range 370–435 °C (in air) and 380–450 °C (in an inert medium) for diphenyldicarbadodecaborane-containing polyamides under the conditions of DTGA. [65] The overall rate of degradation of the dicarbadodecaborane-containing polyamides considered is appreciably lower than for the usual aromatic polyamides. On heating to 900 °C in air and especially under an inert atmosphere, the polyamides based on both isomers of bis(4-carboxyphenyl)dicarbadodecaborane give rise to a large amount of a coke residue (up to 30%–60% in air and up to 82%–96% in helium), whereas polyamides based on the reaction of terephthalic acid with cardo-diamines give rise to 13%–16% of coke residue (in air) and 48%–53% (in helium) (Table 5). [65] The nature of the thermal degradation of polyamides with 1,2- and 1,7-diphenyldicarbadodecaborane fragments is close to that of the degradation of polyamides based on 1,7-dicarbadodecaboranedicarboxylic acid, but the onset of vigorous decomposition is displaced towards higher temperatures. The amide groups in the dicarbadodecaborane-containing polyamides possess a greater hydrolytic stability compared with those in the usual polyamides. It is also noteworthy that the 1,2-dicarbadodecaborane groups stabilise the amide linkage in polyamides to a greater extent than the 1,7-dicarbadodecaborane groups. One of the reasons for the increase in the mass of the polyamidodicarbadodecaboranes when the latter are heated in air is believed to be the oxidation of the dicarbadodecaborane nucleus by atmospheric oxygen with formation of involatile oxygen-containing boron compounds. [68]

The electrophysical properties of polyamides based on 1,2- and 1,7-bis(4-hydroxyphenyl)dicarbadodecaboranes and anilinefluorene as well as their molecular mobility have been investigated. [72] It has been noted that the replacement of the 1,2-dicarbadodecaborane nucleus by the 1,7-dicarbadodecaborane nucleus is accompanied by a decrease in the rigidity of the macrochains.

4. Poly-1,3,4-oxadiazoles

For the synthesis of homogeneous and mixed poly-1,3,4-oxadiazoles with diphenyldicarbadodecaborane fragments in the chain, use has also been made of 1,2- and 1,7-bis-(4-carboxyphenyl)dicarbadodecaboranes. [73–75] The study of the characteristic features of this synthesis showed that, even after prolonged interaction of 1,2- and 1,7-bis(4-carboxyphenyl)-

Scheme 8



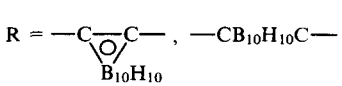


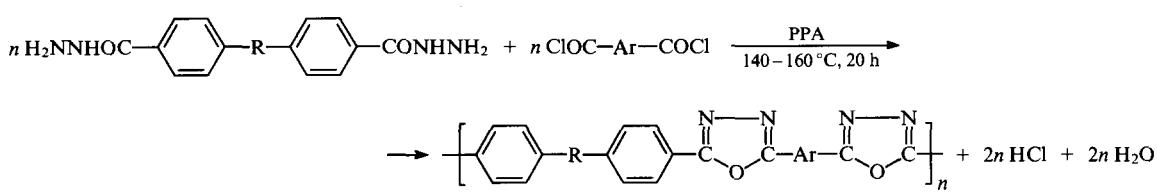
Table 5. Thermal properties of the polyamides obtained from the acid chlorides of 1,2- (**A**) and 1,7-bis(4-carboxyphenyl)dicarbadodecaboranes (**B**), terephthalic acid (**C**), and various diamines.

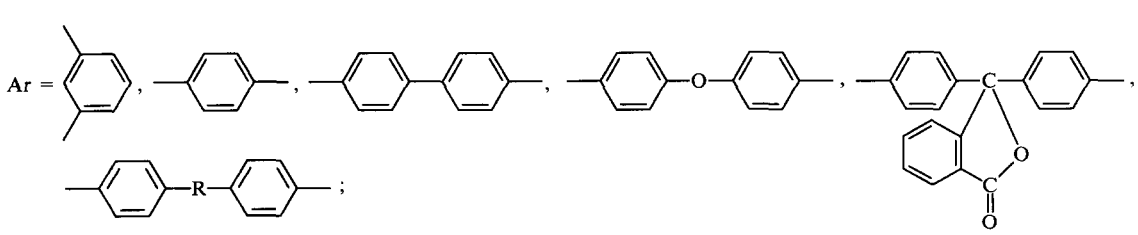
Initial components in the synthesis of polyarylates		Softening temperature[a]/°C	Temperature of onset of change in mass/°C		Maximum increase in mass of specimen in air (%)	Temperature of attainment of maximum increase in mass[b]/°C	Temperature range of intense decomposition in helium/°C	Coke residue at 900 °C (%)	
Diamine	Acid chloride		in helium	in air				in helium	in air
1,3-Phenylene-diamine	**A**	310	420	410	14.9	520	470–580	96	67
	B	320	410	420	9.0	520	420–560	92	66
1,4-Phenylene-diamine	**A**	360	420	410	7.9	490	435–550	94	47
	B	380	410	420	4.0	500	440–550	91	62
4,4′-Diamino-biphenyl	**A**	350	400	400	4.4	530	440–550	96	45
	B	400	410	420	4.0	500	470–560	89	52
Bis(4-amino-phenyl) ether	**A**	325	410	410	12.7	460	420–560	92	49
	B	300	400	380	–	–	420–560	90	33
Bis(4-amino-phenyl) ether of hydroquinone	**A**	280	–	–	–	–	–	–	–
Bis(4-amino-phenyl)sulfone	**A**	305	380	410	9.0	490	400–570	87	45
	B	320	380	370	–	–	440–520	82	60
9,9′-Bis(4-amino-phenyl)fluorene	**A**	370	415	420	2.2	–	440–540	87	30
	B	370	450	420	–	–	460–580	89	47
	C	–	410	390	–	–	450–620	53	13
Bis(4-amino-phenyl)phthalide	**A**	380	400	400	–	–	450–580	87	36
	B	390	435	435	–	–	450–560	85	45
	C	–	360	380	–	–	440–600	48	16
Bis(4-amino-phenyl)-phthalimide	**A**	385	–	–	–	–	–	–	–

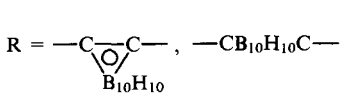
[a] See footnote to Table 2. [b] The range between the two points of intersection of the tangents to the corresponding branches of the S-shaped thermogravimetric analysis curve was adopted as the temperature range.

dicarbadodecaboranes with hydrazine phosphate or dicarboxylic acid dihydrazides in polyphosphoric acid (PPA) at 180–200 °C, the corresponding poly-1,3,4-oxadiazoles are not formed. It was not possible to obtain the polymers also by the interaction of the dihydrazides of 1,2- and 1,7-bis(4-carboxyphenyl)dicarbadodecaboranes with dicarboxylic acids. However, when one begins with the dichlorides of dicarboxylic acids, it is possible to synthesise homogeneous and mixed dicarbadodecaborane-containing poly-1,3,4-oxadiazoles with a fairly high molecular mass. In this case, the process proceeds in accordance with Scheme 8 or 9 and under comparable conditions leads to products differing appreciably in molecular mass and, in the case of 1,2-bis(4-carboxyphenyl)dicarbadodecaborane derivatives, in composition.

Scheme 9

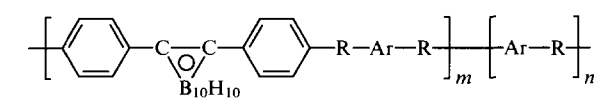


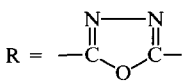




Thus the polymers obtained from the dihydrazides of the dicarbadodecaborane-containing dicarboxylic acids (Scheme 9) have lower reduced viscosities (0.10–0.70 dl g^{-1}) in a 3:1 (by weight) tetrachloroethane–phenol mixture than the products obtained in accordance with Scheme 8 (0.50–3.10 dl g^{-1}). The composition of the mixed poly-1,3,4-oxadiazoles based on 1,2-dicarbadodecaborane derivatives corresponds to the molar ratio of the starting materials only when one of them is the dihydrazide of 1,2-bis(4-carboxyphenyl)dicarbadodecaborane (Scheme 9). In the synthesis in accordance with Scheme 8, the corresponding polymers have a reduced content of the 1,2-bis-(4-carboxyphenyl)dicarbadodecaborane residues compared with the molar ratio of the starting materials. Presumably one of the causes of the formation of polymers with a lower molecular mass via Scheme 9 is the decrease in the reactivity of the NH_2 groups of the dihydrazides of the dicarbadodecaboranedicarboxylic acids caused by the presence in them of the dicarbadodecaborane nucleus and by its electron-accepting nature.

The high-temperature polycyclisation in polyphosphoric acid involves the homopolycondensation of the dicarboxylic acid dihydrazides with formation of poly-1,3,4-oxadiazoles. This process can take place simultaneously with the main one and can lead to the enrichment of the polymer in the aromatic dicarboxylic acid residues, incorporated in the polymer chain in the form of blocks of the corresponding homopoly-1,3,4-oxadiazoles.





The structure of the 1,7-bis(4-carboxyphenyl)dicarbadodecaborane derivatives, which are sterically more favourable, makes it possible to obtain from them mixed poly-1,3,4-oxadiazoles with a composition which is determined by the molar ratio of the starting materials (Scheme 8).[74]

The presence of dicarbadodecaborane groups, especially of the 1,2-dicarbadodecaborane group, in the polyoxadiazoles impart to the latter a high solubility in organic solvents. The softening temperatures of these polymers are in the range 260–350 °C depending on the chemical structure. The homopolyoxadiazoles based on the 1,2- and 1,7-bis(4-carboxyphenyl)-dicarbadodecaboranes and the mixed polyoxadiazole obtained from 1,7-bis(4-carboxyphenyl)dicarbadodecaborane and terephthalic acid have the highest softening temperatures (330–350 °C). Compared with the cardo-polyoxadiazoles based on bis(4-carboxyphenyl)phthalide (softening temperature 390 °C), the dicarbadodecaborane-containing homopolyoxadiazoles soften at a temperature lower by 40–50 °C, which is apparently associated with the fact that the 1,2- and 1,7-dicarbadodecaborane groups weaken the intermolecular interactions of the polymer chains to a greater extent than the phthalide groups.

Strong transparent films, which in a number of instances give rise to an appreciable elongation at break, were obtained from solutions of the polymers (for example, from solution in a tetrachloroethane–phenol mixture). For example, the tensile strength of the polyoxadiazole obtained from 1,7-bis-(4-carboxyphenyl)dicarbadodecaborane and isophthalic acid is 1140 kgf cm^{-2} and the relative elongation at break is ~200%.[74] The majority of the polymers obtained are amorphous or have an amorphous structure with signs of crystallinity. According to DTGA data, the mass of diphenyldicarbadodecaborane-containing polyoxadiazoles changes in air in the temperature range 380–440 °C. For the majority of the polyoxadiazoles with dicarbadodecaborane groups, an increase in mass is observed in air at a temperature of about 500 °C. On heating to 900 °C, the coke residue amounts to more than 90% in a number of instances [for example the coke residues produced by the polyoxadiazoles based on 1,2- and 1,7-bis(4-carboxyphenyl)dicarbadodecaboranes are 98% and 97% respectively].

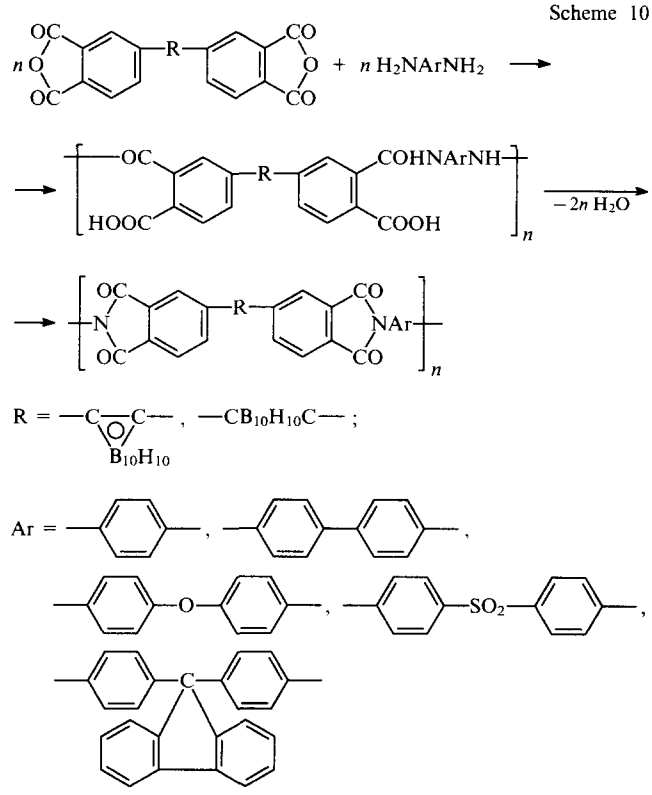
The study of the thermal degradation of polyoxadiazoles and the corresponding model systems led to the conclusion that at relatively low temperatures (300–400 °C) processes involving the hydrolytic decomposition of the oxadiazole ring becomes dominant whilst, with increase in temperature the role of the homolytic reactions is enhanced. The presence of 1,2- and 1,7-dicarbadodecaborane nuclei in the polyoxadiazoles hinders the occurrence of heterolytic decomposition reactions.[75]

5. Polyimides

The development of a method of synthesis of 1,2- and 1,7-bis(3,4-dicarboxyphenyl)dicarbadodecaboranes, presented in Scheme 3, led to the possibility of obtaining from these compounds and various aromatic diamines and of investigating polyimides with diphenyl-1,2- and diphenyl-1,7-dicarbadodecaborane fragments in the chain.[76–81]

Both two-stage and single-stage high-temperature polycondensations in solution have been used to synthesise dicarbadodecaborane-containing polyimides.[77] Scheme 10 presents the structures of the polyimides synthesised.

Scheme 10



In connection with the two-stage method of synthesis, a study was made of the influence on the formation of polyamidoacids in dimethylacetamide of various low-temperature polycondensation conditions: the concentrations of the reactants (0.3–0.7 M or 10 mass%–30 mass%), the basicity of the initial diamines, the reaction temperature (0–50 °C), and the reaction time (1.5–3.5 h).[77] Polyamidoacids with the maximum reduced viscosities (up to 1.84 dl g^{-1} in dimethylacetamide) were obtained in the case of the most basic diamine (benzidine); on passing from benzidine to bis(4-aminophenyl) ether and then to bis(4-aminophenyl) sulfone, the values of η_{red} diminish appreciably, which, incidentally, has been observed also for the usual polyamidoacids. In the experimental range, changes in reaction temperature and reaction time hardly affect the results of the synthesis. The

optimum conditions for the synthesis of 1,2- and 1,7-dicarbadodecaborane-containing polyamidoacids proved to be as follows: concentration 0.7 M for the 1,2-isomer and 0.3 M for the 1,7-isomer, temperature 20–25 °C, reaction time 1.5 h.

The single-stage polycyclisation method and the two-stage polycondensation method with thermal or chemical cyclisation in the second stage, known in connection with the preparation of the usual polyimides, have been used to synthesise polyimides with diphenyl-1,7-dicarbadodecaborane fragments in the chain. In the two-stage method of synthesis, higher-molecular-mass polyimides with diphenyl-1,7-dicarbadodecaborane fragments in the chain are obtained in the case of the chemical cyclisation. The reduced viscosities of the 0.5% solutions in dimethylacetamide are 1.24–1.70 dl g^{-1}; the molecular mass of the polyimide based on bis(4-aminophenyl) ether with η_{red}= 1.7 dl g^{-1}, determined by the light scattering method in dioxane, is 115 × 10^3.

It was observed that the 1,2-dicarbadodecaborane group in the dianhydride of 1,2-bis(3,4-dicarboxyphenyl)dicarbadodecaborane and in the macromolecules of the polyimides is unstable in relation to the action of aprotic dipolar solvents of the type of *N,N*-dimethylacetamide, *N,N*-dimethylformamide, and *N*-methylpyrrolidinone and also of the cyclising mixture in chemical cyclisation, being converted into derivatives of the dicarbaundecaborate anion. An increase in the pyridine content in the cyclising mixture shortens the cyclisation time, promoting simultaneously an increase in the yield of the dicarbaundecaborate derivative. In the case of the 1,2-bis(3,4-dicarboxyphenyl)-dicarbadodecaborane, the degradation of the dicarbadodecaborane nucleus was also observed in the single-stage method of synthesis, evidently under the influence of the initial diamine.[77] However, it was nevertheless found that polyimides with diphenyl-1,2-dicarbadodecaborane fragments can be synthesised successfully by single-stage polycondensation in a high-boiling solvent (nitrobenzene, *p*-chloronitrobenzene, *p*-nitrotoluene) at 170–190 °C in the presence of hydrogen chloride as the catalyst, provided that the basicity of the amino-group in the aromatic diamines is reduced by employing *N,N*-diacyl derivatives as the starting materials. Among the acyl derivatives of aromatic diamines with HCO, MeCO, PhCO, and CF_3CO groups, the first two are the most reactive.[78] This method makes it possible to avoid the degradation of the 1,2-dicarbadodecaborane nucleus during the synthesis and hence to achieve successfully the synthesis of polyimides with unaffected diphenyl-1,2-dicarbadodecaborane fragments in the chain. Polyimides with 1,2-dicarbadodecaborane groups can be synthesised also by the two-stage polycondensation with thermal cyclisation in the second stage.

Outwardly the dicarbadodecaborane-containing polyimides are powdered or fibrous yellow or greyish-white substances. According to X-ray diffraction data, these polymers are amorphous with the exception of polyimides based on bis(4-aminophenyl) sulfone, which show certain signs of crystallinity.

Polyimides with diphenyl-1,2- and diphenyl-1,7-dicarbadodecaborane fragments in the chain, which generally possess properties characteristic of aromatic polyimides (high heat resistance, satisfactory mechanical and electrical properties of films produced from them) are readily soluble in a wide range of solvents by virtue of the specific influence of the dicarbododecaborane groups. Among the dicarbadodecaborane-containing polyimides obtained, the highest solubility is shown by the polyimides based on bis(4-aminophenyl) ether and anilinefluorene, which are soluble even in dioxane and tetrahydrofuran. Strong films can be obtained by casting from a solution of these dicarbadodecaborane-containing polyimides. For example, the strength of the film obtained from the polyimide based on 1,7-bis-(3,4-dicarboxyphenyl)dodecaborane and bis(4-aminophenyl) ether by the two-stage method with chemical cyclisation of the polyamidoacid is 980 kgf cm^{-2} and their elongation at break is 88%.[77]

According to the results of thermomechanical tests, the dicarbadodecaborane-containing polyimides based on benzidine do not soften on heating. Among the remaining polyimides, polymers based on 1,7-bis(3,4-dicarboxyphenyl)dicarbadodecaborane with *p*-phenylenediamine and anilinefluorene exhibited the highest heat resistance, their softening temperatures being ~375 and ~380 °C respectively.

The characteristics of the molecular motion in dicarbadodecaborane-containing polyimides have been investigated by electron spectroscopic methods and it has been shown that the intramolecular relaxation process observed in the temperature range 160–180 °C is associated with the vibrations of the heterocyclic fragments adjoining the dicarbadodecaborane groups via the aromatic ring. It has been established that the rigidity of the chain increases on passing from 1,7- to 1,2-dicarbadodecaborane-containing polymers.[80]

The relative permitivities of 1,7- and 1,2-diphenyldicarbadodecaborane-containing polyimides are the same (3.8 at 23 °C and a frequency of 1 MHz) and hardly change in the temperature range from −170 to 270 °C. Numerically this value is close to the dielectric permitivity of polyimides not containing a dicarbadodecaborane fragment. The tangent of the dielectric loss angle at a frequency of 1 MHz is 1.4 × 10^{-3} at 23 °C for the 1,2-dicarbadodecaborane-containing polyimide based on bis-(4-aminophenyl) ether and 2.0 × 10^{-3} for the 1,7-dicarbododecaborane-containing polymer.[79]

According to DTGA data, dicarbadodecaborane-containing polyimides begin to undergo a change in mass in air and in an inert medium at higher temperatures than other polyheteroarylenes with diphenyldicarbadodecaborane fragments and their decomposition reaction is slower. In air, the mass of 1,2-dicarbadodecaborane-containing polyimides begin to change in the temperature range 430–450 °C and that of their analogues with 1,7-dicarbadodecaborane groups begins to change at 450–470 °C and the process takes place with some absorption of oxygen (~1%–9% relative to the initial mass). On heating under an inert atmosphere, the mass of dicarbadodecaborane-containing polyimides begins to change at 500–510 °C; it decreases by only 5%–7%, which is 8–10 times smaller than for the usual polyimides.[81] On heating to 900 °C, the coke residues from dicarbadodecaborane-containing polyimides are in most cases 92%–97% under an inert atmosphere.

On heating under isothermal conditions in air (4 h at 400 °C), the molecular mass of the polyimide based on 1,7-bis(3,4-dicarboxyphenyl)dicarbadodecaborane and *p*-phenylenediamine does not change. The polyimides containing dicarbaundecaborate anions in the chain begin to lose mass at low temperatures; the amounts of their coke residues at 900 °C are also fairly large (78%–95%).[77]

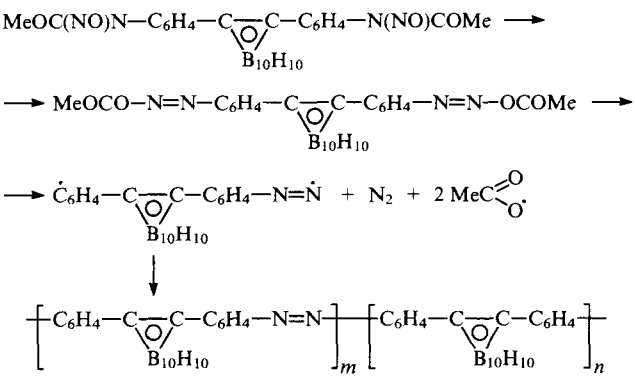
The pyrolysis at 1000 °C of the polyimides obtained from 1,2- and 1,7-bis(3,4-dicarboxyphenyl)dicarbadodecaboranes with bis-(4-aminophenyl) ether or anilinefluorene and, for comparison, also the polyimides based on the dianhydride of oxybis(benzene-dicarboxylic)acid and bis(4-aminophenyl) ether under an argon atmosphere was investigated.[81] Analysis of the pyrolysis products demonstrated an appreciable difference between the dicarbadodecaborane-containing and the usual polyimides. This is manifested by an increased content of hydrogen, carbon monoxide, methane, and benzene in the pyrolysis products and by the absence of products such as aniline and benzonitrile characteristic of the pyrolysis of the usual polyimides. The formation of methane is a consequence of secondary reactions resulting from the increased content of hydrogen in the volatile pyrolysis products. It has been suggested that the absence of a very small amount of decomposition products containing nitrogen derived from the imide ring may be evidence for the binding of these products in the involatile residues, the yield of which is fairly high under the pyrolysis conditions. The products of the decomposition of the diphenyldicarbadodecaborane or diphenyl ether fragments apparently also remain in the carbonised matrix. These results suggested that the section of the polymer chain of the dicarbadodecaborane-containing polyimides most subject to homolytic decomposition is the diphenyldicarbadodecaborane

fragment with the adjacent imide ring, the primary products of the decomposition of which may in fact be hydrogen (from the dicarbadodecaborane nucleus), carbon monoxide, benzene, and also mono- and di-phenyldicarbadodecaboranes.[81]

6. Polyazophenylenedicarbadodecaborane

The synthesis and certain properties of polyazophenylene-1,2-dicarbadodecaborane have been described.[82,83] 1,2-Bis(*N*-nitrosoacetamidophenyl)-1,2-dicarbadodecaborane was used as the initial monomer. The recombination of the phenyl and azophenyl products of its decomposition actually leads to the formation of a dicarbadodecaborane-containing polyazophenylene (Scheme 11).

Scheme 11



The polyazophenylenedicarbadodecaborane was obtained in a suspension of cyclohexane in water in which the proportions of the two phases were 1:2. The monomer concentration was 7.5 g litre^{-1}, the temperature was 50 °C, and the reaction time was 4 h. The yield of the polymer was nearly quantitative. Outwardly, the polymer consisted of a pale-brown powder. It was readily soluble in chloroform, benzene, dimethylformamide, tetrahydrofuran, and, partially, in methanol and acetone. The molecular mass of its low-molecular-mass fraction (30%) was 820 and that of the higher-molecular-mass fraction (70%) was 1560. The presence of an EPR signal with an intensity of 3.3×10^{17} spins g^{-1} and the absorption in the long-wavelength part of the electronic spectrum indicated the presence of a conjugated bond system in this polymer.[82,83]

The polyazophenylenedicarbadodecaborane exhibits high thermal and thermooxidative stabilities. On isothermal heating in helium at 400 °C, a decrease in mass to 9% is observed initially, after which it hardly changes for 3 h. According to DTGA data (heating rate 4.5 K min^{-1}), the dicarbadodecaborane-containing polyazophenylene is stable up to 350 °C in air, after which an increase in the mass of the specimen is observed, amounting to approximately 30% at 600 °C. This apparently occurs owing to the addition of oxygen to the B–H bonds. The amount of the coke residue at 800 °C is ~90% of the initial mass.

It has been suggested that the ability of the dicarbododecaborane units of the polymer to combine with oxygen at high temperatures with formation of inactive products is of interest for the employment of such a polymer as a stabiliser[57] and for the inhibition of the thermooxidative degradation of thermally stable polymers.[82,83]

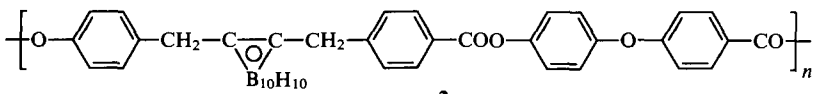
It has also been noted that 1,2-bis(*N*-nitrosoacetamidophenyl)-1,2-dicarbadodecaborane can be used for the synthesis of dicarbadodecaborane-containing copolymers by combining the processes involving the recombination of its decomposition products with those involving the radical polymerisation of various monomers.[82,83] For example, the copolymers of polyazo(hydroxyphenyl)dicarbadodecaborane with styrene, containing from 4 mass% to 38 mass% of polyazophenylenedicarbadodecaborane fragments, have been synthesised by emulsion copolymerisation. The introduction of polyazo(hydroxyphenyl)dicarbadodecaborane into polystyrene macromolecules significantly increases the thermal stability of the latter. Thus intense degradation of polystyrene begins at 300 °C, while that of the copolymer of styrene containing only 4% of polyazophenylenedicarbadodecaborane takes place at 350–360 °C.

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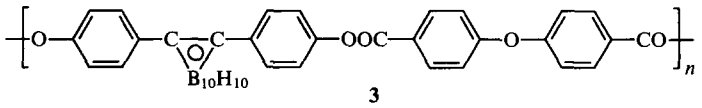
Summarising the foregoing, one should note that the development of new di- and tetra-functional aromatic derivatives of 1,2- and 1,7-dicarbadodecaboranes and the study of the characteristics of the formation of polymers from them have made it possible to obtain various new classes of linear heterochain polymers — polymers with diphenyldicarbadodecaborane fragments in the chain and a high molecular mass. These polymers possess a set of valuable properties and their thermal characteristics and in many cases also their solubilities are significantly superior to those of the usual organic analogues.[83] The introduction of dicarbadodecaborane groups into the polymer chain in the form of diphenyldicarbadodecaborane fragments increases significantly the heat resistance of such polymers compared with polymers based on bifunctional aliphatic derivatives of dicarbadodecaborane.

The study of the behaviour of linear polyheteroarylenedicarbadodecaboranes of the type of the polyarylates **2**–**5**, the polyamides **6** and **7**, and the polyimides **8** and **9** (see over) during the sorption process in the vapour of an effective solvent (THF) showed that structural changes take place in the amorphous polymers with formation of a thermodynamically improved structure.[85] It was found that the temperature for the onset of gel formation depends little on the isomerism of the dicarbadodecaborane nucleus and the framework surrounding it and depends more on the medium in which the heat treatment has been carried out. In air, the temperature for onset of gel formation is 15–20 °C lower than in vacuo. In the cardo-analogues (the polymers **10**–**12**), the gel fraction appears at temperatures higher by 50 °C. After the gel formation point (~280 °C) has been passed, the subsequent structure formation takes place much faster in the polymers with the 1,7-dicarbadodecaborane fragments in the chain, which may be due both to the greater segmental mobility of these polymers and to the smaller extent of the purely degradative reactions occurring simultaneously.

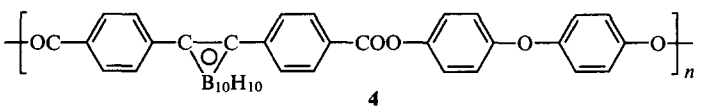
The significant difference between the behaviour of polyheteroarylenedicarbadodecaboranes and that of the usual organic analogues, both as regards the position of the initial gel formation point and the rate of accumulation of the gel fraction, suggested that intermolecular bonds are formed in the experimental temperature range (250–350 °C) mainly with participation of the dicarbadodecaborane groups. This is most characteristic of polymers with 1,7-dicarbadodecaborane fragments and has been confirmed by the fact that a nearly quantitative yield of the gel fraction is observed in these polymers at temperatures below that of the onset of gel formation in the polymers not containing dicarbadodecaborane groups.[85]



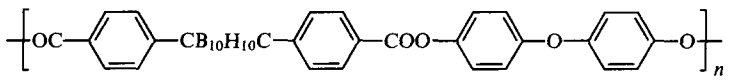
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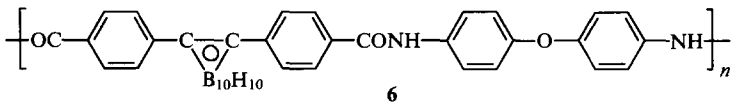
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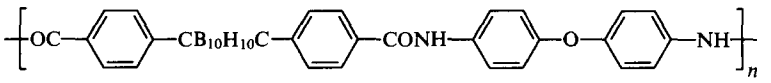
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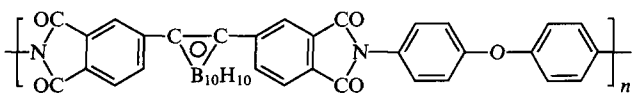
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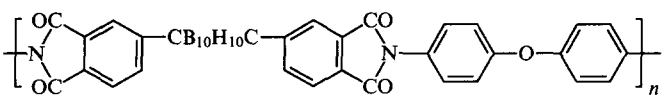
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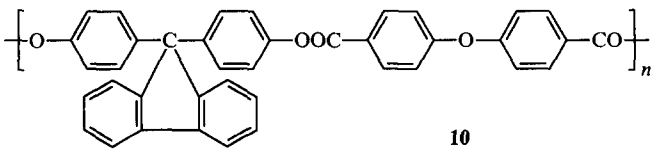
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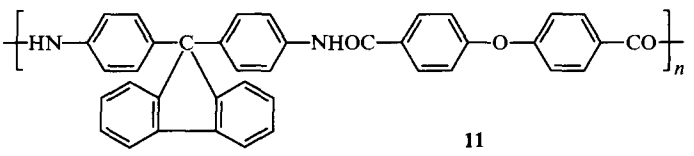
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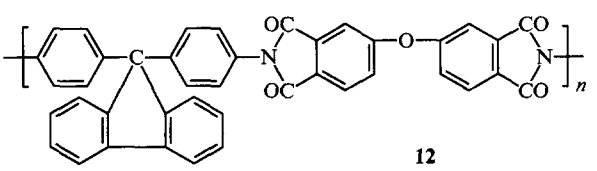
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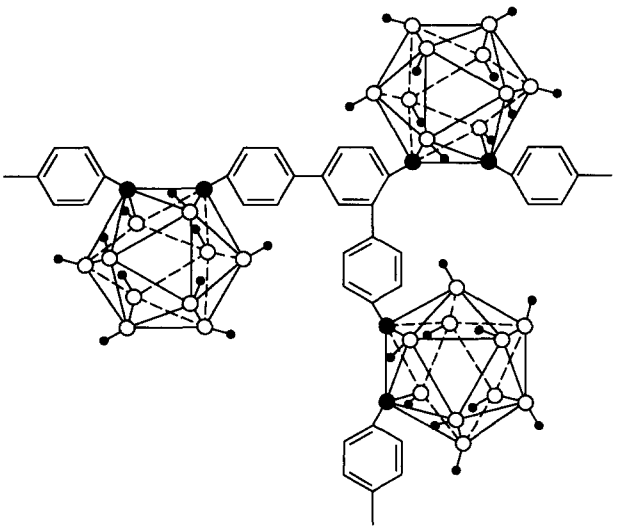
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IV. Phenylenedicarbadodecaborane-containing polymers of the thermoreactive type

The study of linear polyheteroarylenedicarbadodecaboranes of the type of polyarylates, polyamides, polyoxadiazoles, polyimides, etc. showed that the specific difference between these polymers and their usual organic analogues is their ability to form already in the temperature range 250–270 °C three-dimensional thermally stable polymers in which the inorganic networks are evidently combined with organic network molecules. It therefore appeared promising to employ this specific property of the aromatic derivatives of dicarbadodecaborane(12) in polymers of the thermoreactive type, containing reactive functional groups together with the dicarbadodecaborane groups. It might have been expected that, as a result of the introduction of dicarbadodecaborane groups into such systems, the properties of the thermoreactive and dicarbadodecaborane-containing polymers would be usefully mutually supplemented, in the first place in those applications, traditional for thermoreactive oligomers and polymers, where, together with the simplicity of processing, a high thermal stability and the formation of secondary coking products are required.

We shall now deal with phenylenedicarbadodecaborane-containing polymers of the polyphenylene, epoxide, phenolformaldehyde, and polycyanurate types.

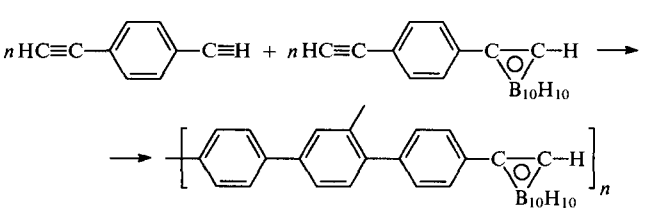
The 1,2-dicarbadodecaborane-containing oligophenylenes, obtained from diphenyl-1,2-dicarbadodecaborane, are presented below.



The polycondensation of diphenyl-1,2-dicarbadodecaborane was carried out in the presence of Lewis acids ($AlCl_3$, $MoCl_2$, etc.) and oxidising agents (MnO_2, $CuCl_2$, etc.) at 120–220 °C.[86,87] The oligomers have a molecular mass of 1300 and a softening temperature of about 300 °C. They do not melt up to 350 °C and are readily soluble in organic solvents (chloroform, benzene, acetone, etc.) According to DTGA data, the decrease in their mass in air is 1.6% at 600 °C and 11.6% at 900 °C.

The preparation of polydicarbadodecaboranephenylenes by the reaction of 1,7-$Cu_2C_2B_{10}H_{10}$ with *m*-$C_6H_4I_2$ in 1:1 molar proportions has been mentioned.[63] Together with the formation of a polymeric product, there is a possibility in this instance of the formation of macrocyclic systems in which the 1,7-dicarbadodecaborane fragments are linked to 1,3-disubstituted phenylene rings. When *m*-$C_6H_4I_2$ is replaced by 1,3- or 2,6-disubstituted pyridines, macrocyclic systems in which the 1,7-dicarbadodecaborane fragments are linked to pyridine rings are formed together with the polymeric product.

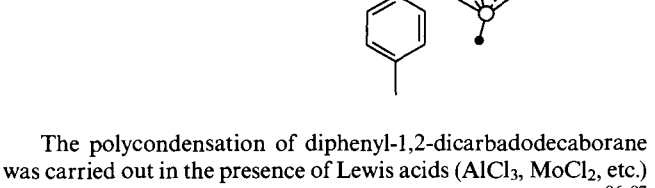
The synthesis of *p*-[1-(1,7-dicarbadodecaboranyl)]phenylethyne has been achieved by the reaction of diethynylbenzene with decaborane in the presence of dimethylaniline in toluene.[88] Dicarbadodecaborane-containing polyphenylenes were obtained by the joint polycyclotrimerisation of this dicarbadodecaborane-containing ethyne with diethynylbenzene (taken in equal proportions) in the presence of the $NiCl_2.2PPh_3.2NaBH_4$ system.



For an equimolecular ratio of the starting materials, fully soluble copolymers containing 18.7% of boron are formed in 75% yield. According to DTGA data, under a helium atmosphere their mass diminishes at 900 °C only to the extent of 6%, whereas the decrease in the mass of the homopolyphenylene obtained from diethynylbenzene is 15%. These boron-containing polyphenylenes are extremely heat-resistant: they undergo only slight deformations up to the temperatures of their thermal decomposition (above 600 °C).

In order to regulate the content of the dicarbadodecaborane groups in the copolymers, the joint polycyclotrimerisation of 1,2-dicarbadodecaboranylphenylethyne (CPE) with diethynylbenzene (DEB) and phenylethyne (PE) was also carried out. For the molar proportions of the starting materials CPE:DEB:PE = 0.5:1:1, copolymers containing 11% of boron were obtained in 73% yield. Up to 27% of an insoluble polymer was formed under these conditions as a result of partial structure formation. It was noted that the mixed dicarbadodecaborane-containing polyphenylenes exhibit an enhanced thermooxidative stability. Thus the mass of the triple copolymer initially increases somewhat (up to 4%) at 350 °C, after which it remains virtually unchanged for 5 h; the mass lost by the polymer after 5 h at 550 °C exceeds only slightly 40%.[88]

It has been shown that the oligophenylenedicarbadodecaboranes of the type considered could be used as the starting materials for the synthesis of π-arenetricarbonyl complexes of transition metals.[89] The introduction of 1,2-dicarbadodecaborane groups into an oligophenylene has also been achieved as a result of the chemical modification of the oligophenylene, containing triple bonds, by decaborane in accordance with the following scheme:[90]

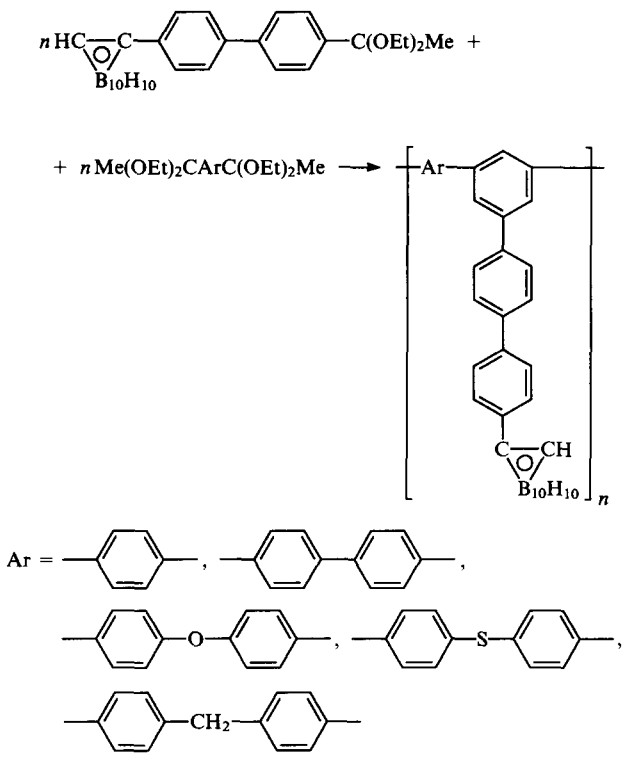


The oligophenylenedicarbadodecaborane is an amorphous pale-brown powder readily soluble in the usual organic solvents. Analysis of the polymer obtained permitted the conclusion that, under the selected chemical modification conditions, the replacement of the ethynyl groups of the oligophenylene by dicarbadodecaborane groups is almost quantitative. The absence from such an oligophenylenedicarbadodecaborane of residual ethynyl groups renders the latter (in contrast to oligophenylene) incapable of passing to an infusible and insoluble state during heating to 300 °C.

A higher thermal stability (both under an inert atmosphere and in air) is characteristic of the oligophenylenedicarbadodecaboranes than of the initial oligophenylene. According to DTGA data, the yield of the coke residue for the oligophenylenedicarbadodecaborane is 84.5% at 900 °C under a helium atmosphere, whereas for the usual oligophenylene it is 68%.

Polyphenylenes with phenyldicarbadodecaborane fragments in the chain can be obtained also by means of the trimerisation polycondensation of aromatic mono- and di-acetyl compounds in which one of the monomers is a dicarbadodecaborane-containing aromatic acetyl derivative.[91–97] In particular, when the 4′-(1,1-diethoxyethyl)biphenylyl-1,2-dicarbadodecaborane was used as the monomer, a prepolymer of the polyphenylene type was obtained.[91,92]

Different versions of the synthesis of the prepolymer were employed: at 0 and 20 °C in solution in benzene through which dry hydrogen chloride was passed; at −20 °C in solution in *o*-dichlorobenzene with dry HCl; at 100 and 150 °C in solution in *o*-dichlorobenzene or ditolylmethane in the presence of 10% toluene-*p*-sulfonic acid as the catalyst.[91,92] The final polymers were obtained by heat treatment at 450 °C.[92]



Dicarbadodecaborane-containing polyphenylenes have also been synthesised from bis(4-acetylbenzyl)- and 4-acetylbenzyldicarbadodecaboranes in which the phenylene group was separated from the dicarbadodecaborane nucleus by a methylene group.[94-96] It is noteworthy that the fraction of the enone side groups [...-R-CO-CH = C(Me)-R-...] and polyvinylene fragments in the oligomer increases (compared with their contents in the prepolymers without dicarbadodecaborane nuclei) in the polycondensation of acetyldicarbadodecaboranes or their ethyl ketals, i.e. heterounit polymers are formed in the polycyclocondensation process.[92,93]

Oligophenylenes containing diphenyl-1,2-dicarbadodecaborane groups were found to be less soluble than the prepolymers based on bis(acetylbenzyl)dicarbadodecaboranes: they dissolved fully only in the reaction solution, chloroform, and *o*-dichlorobenzene and did not dissolve in benzene, toluene and dioxane,[92] whereas the dicarbadodecaborane-containing oligophenylenes based on bis(acetylbenzyl)dicarbadodecaborane derivatives dissolve readily in toluene, cyclohexanone, dioxane, acetone, benzene, etc.[93]

The heat-treated dicarbadodecaborane-containing polyphenylene exhibits a high thermal stability. According to DTGA data, the mass of the polymers obtained from bis(acetylbenzyl)dicarbadodecaboranes increases by 18% at 400 °C as a consequence of the oxidation of the dicarbadodecaborane groups at the B-H bonds; the decrease in mass at 800 °C in air is 17%. Under the conditions of isothermal heating at 700 °C for 7-8 h, the mass of the polymers hardly changes.[93]

It has been noted that[92] the thermal stability of the polymers based on the ethyl ketal of acetylbiphenylyl-1,2-dicarbadodecaborane is higher than that of the analogous polymers based on the ethyl ketal of acetylbenzyl-1,2-dicarbadodecaborane with the same or higher boron content in the latter and for approximately the same intrinsic viscosities of the initial prepolymers. Thermomechanical tests on polymers with biphenylyl-1,2-dicarbadodecaborane groups in the macromolecules on a plastometer showed that they are not deformed up to 280 °C and for loads up to 200 kgf cm^{-2}.[92]

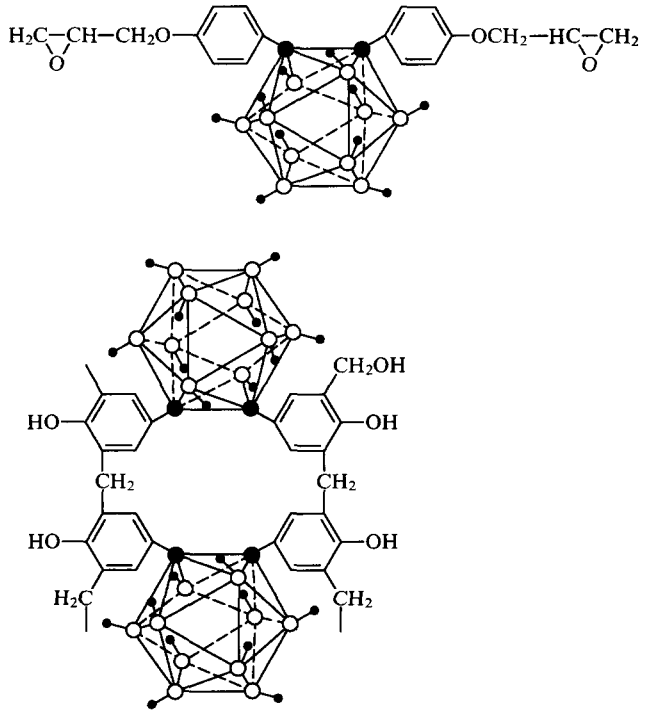
Epoxides and phenolformaldehyde oligomers based on 1,2-bis(4-hydroxyphenyl)dicarbadodecaborane have been developed.

Not only the individual 1,2-bis(4-hydroxyphenyl)dicarbadodecaborane but also mixtures of boroxyphenylenedicarbadodecaboranes [usually mono-, di-, and trisubstituted 1,2-bis-(4-hydroxyphenyl)dicarbadodecaboranes without their separation into the individual substances], obtained by the hydrolysis of (*B*-1,7-dicarbadodecaboranyl)phenyl borates and (*B*-1,7-dicarbadodecaboranyl)phenyl silicates, synthesised by the high-temperature condensation of 1,2-dicarbadodecaborane with the phenylesters of orthosilicic and orthoboric acids, may be used successfully for the synthesis of epoxide and phenol-formaldehyde phenylenedicarbadodecaborane-containing oligomers and polymer systems based on them.[98-100]

The synthesis and properties of the thermoreactive epoxyphenylenedicarbadodecaborane and 1,2-bis(4-hydroxyphenyl)-dicarbadodecaborane formaldehyde oligomers have been examined.[19,21,98-111]

Epoxide oligomers based on 1,2-bis(4-hydroxyphenyl)dicarbadodecaborane have been synthesised by a two-stage method.[101] The reaction of the 1,2-bis(4-hydroxyphenyl)-dicarbadodecaborane with epichlorohydrin was initially carried out in the presence of catalytic amounts of a tertiary amine at 50-90 °C for 6-12 h. The dichlorohydrin formed was isolated and treated in a dry inert solvent (chlorinated hydrocarbons, etc.) with solid alkali in stoichiometric proportions at a temperature not exceeding 40-50 °C. Depending on the selected 1,2-bis-(4-hydroxyphenyl)dicarbadodecaborane : epichlorohydrin molar ratio selected, oligomeric products with different molecular masses or the diglycidyl ether of 1,2-bis(4-hydroxyphenyl)-dicarbadodecaborane (see compound **13**) were obtained. For a 1 : 5 component ratio, a compound with the composition closest to that of the diglycidyl ether is formed; its melting point is 130-135 °C. The 1,2-dicarbadodecaborane-containing epoxide oligomers are readily soluble in ethanol, acetone, chloroform, tetrahydrofuran, benzene, etc.

An epoxyphenyldicarbadodecaborane oligomer with a molecular mass of 400 and a softening temperature of 30 °C was synthesised in one stage from a mixture of mono-, di-, and trihydroxyphenylenedicarbadodecaboranes[98,99] in epichlorohydrin in the presence of a 40% aqueous solution of sodium hydroxide [with boroxyphenylenedicarbadodecaboranes : epichlorohydrin : alkali molar ratios of 1 : 10 : (2-4)] at 60 °C for 2-3 h.



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The epoxyphenylenedicarbadodecaborane oligomers obtained are hardened with the aid of familiar hardening agents (acid anhydrides, amines).[99,101] The study of the hardening of oligoepoxyphenylenedicarbadodecaborane in the presence of 30 mass% of an anilinoformaldehyde oligomer (specimen 1) or 15 mass% of a polyethyleneamine (specimen 2) showed that the oligopeptide is structured most vigorously in the latter case.[97] Heating of a composition comprising the oligoepoxide and the polyethyleneamine for 1 h at 100 and 125 °C leads to ~97% hardening. The structure formation process takes place more slowly for the composition comprising the oligoepoxide and the anilinoformaldehyde oligomer. The degree of hardening of this composition in the temperature range 100–200 °C increases continously, attaining approximately 91% after heating for 8 h. According to DTGA data, in air (at a heating rate of 5 K min^{-1}) both oligoepoxide specimens, hardened at 200 °C, begin to lose mass in the temperature range 250–300 °C, the rate of degradation of specimen 1 being somewhat higher than that of specimen 2: at 350 and 600 °C, the mass of specimen 1 diminishes by 24% and 37%, while that of specimen 2 diminishes by 8% and 21% respectively. However, the overall decrease in the mass of both specimens is the same at 900 °C and amounts to 35%. On the other hand, the usual (not containing dicarbadodecaborane groups) epoxyoligomer, hardened by the anilinoformaldehyde oligomer, is fully combusted at 600 °C.[97]

Homogeneous and mixed phenolformaldehyde polymers with diphenylenedicarbadodecaborane fragments in the chain have been synthesised by the reaction of formaldehyde with 1,2-bis-(4-hydroxyphenyl)dicarbadodecaborane or with a mixture of the latter and phenol using different ratios of the starting materials.[21,100,101,104,109] The study of the polycondensation of 1,2-bis(4-hydroxyphenyl)dicarbadodecaborane with formaldehyde (the reaction was carried out in isopropyl alcohol at 93–94 °C in the presence of NaOH using an aqueous formaldehyde solution) and of the structure of the product showed that, according to IR spectroscopic data, dicarbaundecaborate derivatives are not formed in this process.[103] It has been noted that, depending on the nature of the catalyst, the process conditions, and the ratio of the initial components, oligomers of both the resol and novolac type may be obtained.[111] Oligomers of the resol type are formed in the presence of basic catalysts [for example, NaOH, NH_4OH, and $Ba(OH)_2$] whereas oligomers of the novolac type are formed in the presence of acid catalysts (for example, hydrochloric acid and toluene-*p*-sulfonic acid) for 1,2-bis(4-hydroxyphenyl)dicarbadodecaborane : formaldehyde at molar ratios ranging from 1 : 0.8 to 1 : 4.

The synthesis of mixed resols based on 1,2-bis(4-hydroxyphenyl)dicarbadodecaborane and phenols taken in proportions ranging from 1 : 3 to 1 : 21 for a 1.5 : 1 molar ratio if the formaldehyde and phenolic components has been described.[107] The polycondensation was carried out without a solvent in the presence of a 25% aqueous solution of ammonia (0.3 mol per mole of phenols) at 90 °C for 3 h. With decrease in the content of the dicarbadodecaborane-containing groups in the oligomer, the softening temperature of the latter fell from 110 to 60 °C, while its molecular mass increased from 650 to 890. In contrast to the resol obtained solely from the 1,2-bis(4-hydroxyphenyl)dicarbadodecaborane, the mixed dicarbadodecaborane-containing resols exhibit an increased fluidity. These oligomers are hardened under the conditions usual for phenolformaldehyde resols, forming resites containing only 2%–4% of the acetone-soluble fraction.

The study of the chemical transformations on heating dicarbadodecaborane-containing resols and the corresponding resites showed that, in the temperature range from 50 to 200 °C, structure formation in the dicarbadodecaborane-containing oligomer takes place via the mechanism usual for resols. At temperatures of 200–300 °C and above, the dicarbadodecaborane groups of the resites undergo appreciable chemical transformations, the extent of which depends significantly on the heating conditions (air, vacuum).[104] It has been suggested that the chemical transformations involving the dicarbadodecaborane groups of the resites are in fact responsible for their enhanced thermal stability and the high yields of the coke residue compared with the known polymers.

The greatest differences between the stabilities of the usual phenolformaldehyde and dicarbadodecaborane-containing resites are observed in thermooxidative degradation. According to DTGA data, in air the mass of the dicarbadodecaborane-containing resite begins to increase at 350 °C and above (at 900 °C the increase is 4%), whereas the usual hardened resol decomposes fully under these conditions.[104]

The mixed dicarbadodecaborane-containing resites based on 1,2-bis(4-hydroxyphenyl)dicarbadodecaborane and phenol also exhibit an increased thermal stability, the decrease in their mass on heating in air depending in a definite manner on the content of the dicarbadodecaborane groups. However, the introduction of even small amounts of dicarbadodecaborane groups into the copolymer decreases significantly the mass loss. Thus the decrease in the mass of the hardened cooligomer obtained for the 1,2-bis(4-hydroxyphenyl)dicarbadodecaborane : phenol = 1 : 21 molar ratio is 45% at 900 °C.[106]

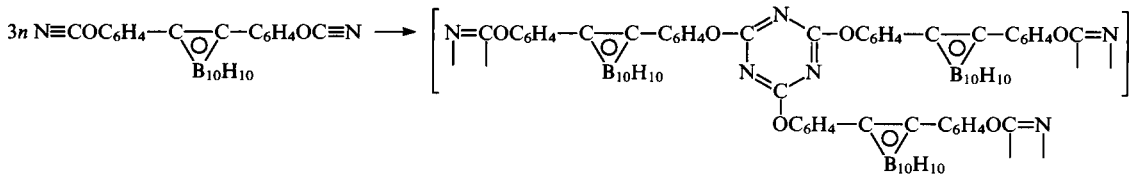
A number of studies have been devoted to the elucidation of the nature of the high thermal stability of the dicarbadodecaborane-containing resites.[105,107–110] Analysis of the structural transformations in the dicarbadodecaborane-containing resites over a wide temperature range (200–2500 °C), resorting to X-ray diffraction and various spectroscopic research methods, suggested that the oxidation of the B–H groups of the dicarbadodecaborane fragments and other processes involving their consumption, which is accompanied by the evolution of an appreciable amount of hydrogen, is most characteristic of the 1,2-bis(4-hydroxyphenyl)dicarbadodecaboraneformaldehyde resites in the temperature range 300–450 °C. This leads to an increase in the density of the network in the resites as a result of the formation of the energetically strong B–B, B–O–B, and B–C bonds.

By virtue of the presence of such a thermally stable macronetwork system, the radical species produced (large molecular formations or low-molecular-mass degradation products) are unable to emerge from the 'cage' and undergo secondary recombination processes. Nor can one rule out the possibility that the hydrogen split off from the B–H groups may interact with the radical species, inhibiting further polymer decomposition processes.[108]

The high thermal stability of the 1,2-bis(4-hydroxyphenyl)-dicarbadodecaboraneformaldehyde and epoxyphenylenedicarbadodecaborane polymers has also been used to enhance the thermal characteristics of the hardened polymer compositions based on the usual polymers of this type.[98,112] Thus the hardened compositions comprising phenolphthaleinformaldehyde and 1,2-bis(4-hydroxyphenyl)dicarbadodecaboraneformaldehyde (based on boroxyphenylene-1,7-dicarbadodecaboranes) resols are destructured to a lesser extent than the phenolphthaleinformaldehyde resite. According to DTGA data, the decrease in the mass of a hardened specimen (obtained for a 1 : 1 mass ratio of the resols) in air at 900 °C is 40%, whereas the phenolphthaleinformaldehyde resite decomposes almost completely at the same temperature. In the presence of 50 mass% of the epoxyphenylenedicarbadodecaborane oligomer, the yield of the coke residue is 60% greater than in the case of the unmodified phenolphthaleinformaldehyde resite.[98]

Modification of an epoxide oligomer [based on 1,1,3-tris-(hydroxyphenyl)propane and epichlorohydrin] by a dicarbadodecaborane-containing phenolformaldehyde oligomer [based on 1,2-bis(4-hydroxyphenyl)dicarbadodecaborane and formaldehyde] makes it possible to increase the thermal stability and the coke number of the hardened epoxyphenolformaldehyde polymer.[112] Thus, whereas for the hardened polymer obtained for the epoxide : dicarbadodecaborane-containing resol = 3.3 : 1 mass

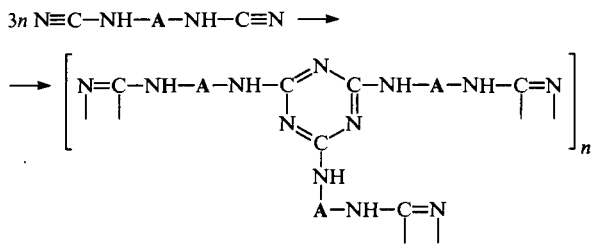
Scheme 12



ratio, the temperature of the onset of decomposition in air is about 260 °C, the yield of the coke residue on heating to 600 °C is 60%, and the decrease in mass on heating in vacuo at 350 °C for 3 h is 15%, for the corresponding hardened epoxyphenolformaldehyde polymer based on the same oligoepoxide and an anilinephenolformaldehyde oligomer the temperature of the onset of decomposition in air is about 200 °C, the yield of the coke residue on heating to 600 °C is 20%, and the decrease in mass on heating in vacuo at 350 °C for 3 h is 45%.

We shall consider yet another type of polymer with diphenyldicarbadodecaborane fragments in the chain. The diphenyldicarbadodecaborane fragments were introduced into the macromolecules by means of the thermal polycyclotrimerisation of the dicyano-esters of 1,2-bis(4-hydroxyphenyl)dicarbadodecaborane (Scheme 12).[113] Such dicarbadodecaborane-containing polymers with *s*-triazine rings in the macromolecule are obtained with a high degree of conversion (98%) of the functional groups, i.e. in the final stage of the process these polymers are regularly cross-linked dense-network systems. The temperature of the onset of the deformation of such a polymer is 375 °C when a load of 0.8 kgf cm^{-2} is applied to the specimen; according to DTGA data, the temperature of the onset of decomposition in air is 385 °C; the polymer has an amorphous structure.

Dicarbadodecaborane-containing cross-linked thermally stable and heat-resistant polymers containing melamine structures in the main chain have been synthesised by the polycyclotrimerisation of diphenyl-1,7-dicarbadodecaborane-containing biscyanamides or their mixtures with aromatic mono- and bis-cyanamides.[113,114]



A = C_6H_4—$CB_{10}H_{10}C$—C_6H_4

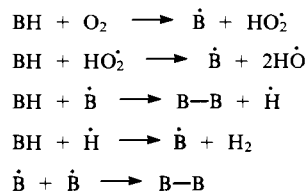
The temperature of the deformation of the polymelamine based on 4,4′-bis(4-cyanamidophenyl)dicarbadodecaborane is 490 °C; the temperature of the onset of the decrease in mass in air is 370 °C. According to X-ray diffraction data, the polymer has an amorphous structure with signs of crystallinity.

V. The mechanism of the thermal transformations of polyarylenedicarbadodecaboranes and the radical arylation of dicarbadodecaborane(12)

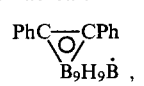
The study of the linear polyheteroarylenedicarbadodecaboranes showed (see Section III) that the formation under comparatively mild conditions (250–300 °C) of three-dimensional networks as a result of reactions involving the dicarbadodecaborane groups is most characteristic of these polymers. In the presence of oxygen, the formation of new bonds in the dicarbadodecaborane-containing polymers occurs more vigorously under these conditions compared with an inert medium or a vacuum. There is no doubt that the elucidation of the nature and mechanism of the formation of new thermally stable bonds with participation of the dicarbadodecaborane groups is of fundamental importance for the explanation of the behaviour of polyarylenedicarbadodecaboranes at elevated temperatures and of the formation of thermostable secondary products. Taking this into account, a study of the thermal transformations of 1,2-diphenyl-1,2-dicarbadodecaborane was undertaken.[115]

It was established that, when diphenyl-1,2-dicarbadodecaborane is heated in air in the temperature range 260–300 °C, the product of the reaction occurring with evolution of hydrogen contains, together with the initial compound, a substance which is a diphenyl-1,2-dicarbadodecaborane dimer according to gel-permeation chromatographic, ebullioscopic and mass-spectrometric data. Detailed analysis of this compound by various spectroscopic methods suggested that under these conditions the diphenyldicarbadodecaborane fragments in the dimer are linked by a single B–B bond, the formation of which most probably involves the boron atoms in the 9- or 12-position which are most remote from the carbon atoms in the dicarba-*closo*-dodecaborane(12) icosahedron.

The study of the conditions under which this reaction is carried out showed that, in the presence of phenols (familiar inhibitors of free-radical reactions), the yield of the dimer falls sharply, whereas heating of 1,2-diphenyl-1,2-dicarbadodecaborane in the presence of *tert*-butyl peroxide—a source of free radicals—is accompanied by the formation of the dimer under much milder conditions. The results suggested that the reaction constituting the basis of the dimerisation of 1,2-diphenyl-1,2-dicarbadodecaborane is of a radical type and, when the dicarbadodecaborane is heated in air, the reaction is initiated by oxygen.



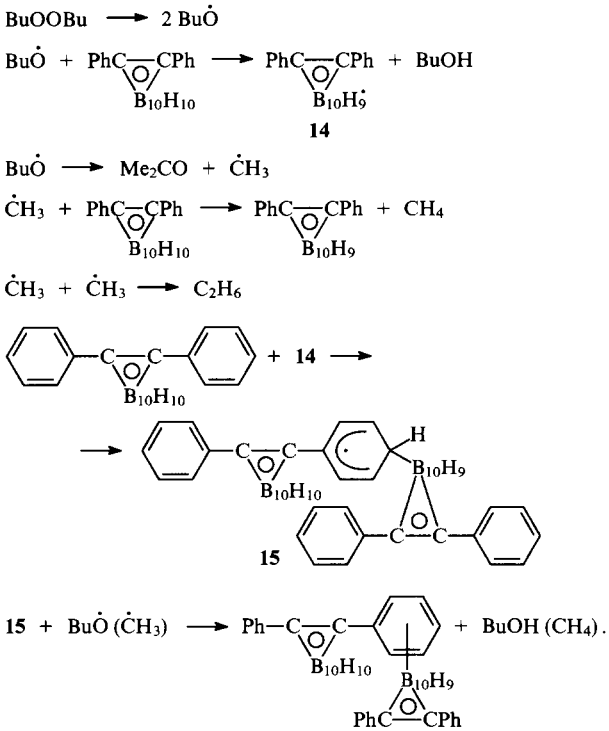
It is noteworthy that the dimer is also formed on heating in vacuo, but this requires much more severe conditions (500 °C and above). Evidently during the high-temperature heat treatment, homolytic dissociation of the B–H bond of the dicarbadodecaborane nucleus takes place with formation of the radicals



the recombination of which leads to the dimer. Such severe conditions, necessary for the formation of the dimer in vacuo, indicate that oxygen is an initiator of both the formation of the diphenyl-1,2-dicarbadodecaborane dimer and evidently of the structure formation in the dicarbadodecaborane-containing polymers.

The study of the thermal decomposition of *tert*-butyl peroxide in 1,2-diphenyl-1,2-dicarbadodecaborane at 150 °C for 5 h showed that it results in the formation of *tert*-butyl alcohol, acetone, methane, ethane, and small amounts of hydrogen together with polymeric dicarbadodecaborane-containing products with the maximum degree of polarisation (n = 10)

determined from gel-permeation chromatographic data.[116] The yield of the polymeric products is directly proportional to the amount of decomposed peroxide and amounts to 58%–70% of theoretical. The calculated yield of the products of the polymerisation of 1,2-diphenyl-1,2-dicarbadodecaborane and the total amount of the butyl alcohol and methane obtained are similar. The study of the structure of the dicarbadodecaborane-containing products by ^{13}C and ^{11}B NMR spectroscopy permitted the conclusion that dimers and oligomers (via a boron–carbon bond) are formed under these conditions. They are mixtures of isomers in terms of the boron atoms of 1,2-diphenyl-1,2-dicarbadodecaborane and the position in the aromatic ring. The reactions occurring in the thermolysis of *tert*-butyl peroxide can be represented schematically as follows:

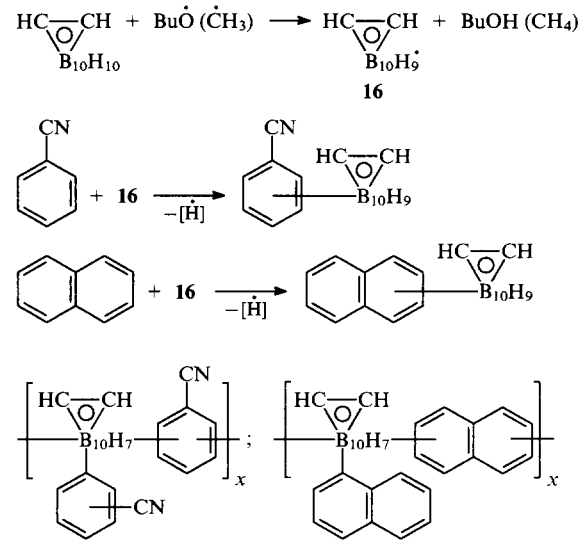


The virtually total absence of molecular hydrogen from the reaction products, the agreement between the total molar amounts of methane and butyl alcohol and the total number of B–C bonds in the products of the oligomerisation of 1,2-diphenyl-1,2-dicarbadodecaborane, and the formation of a B–C bond suggested that the mechanism of the radical reaction of 1,2-diphenyl-1,2-dicarbadodecaborane involves bimolecular aromatic homolytic substitution via the formation of an intermediate radical σ-complex between the 1,2-dicarbadodecaboranyl radical and the aromatic compound.

The boron-centred dicarbadodecaboranyl radicals were obtained as a result of the abstraction of the hydrogen atom from the B–H groups in 1,2-, 1,7-, and 1,12-dicarbadodecaboranes by the *tert*-butoxyl radicals. They were detected by the EPR method in the form of spin-adducts with 2,4,6-tri-*tert*-butyl-4-methylcyclohexa-2,5-dien-1-one.[117]

In order to confirm this mechanism of the dimerisation and oligomerisation of 1,2-diphenyl-1,2-dicarbadodecaborane in the presence of a free radical source, a study was made of the interaction of 1,2- and 1,7-dicarbadodecaboranes with aromatic compounds such as benzonitrile and naphthalene in the presence of *tert*-butyl peroxide at 200 °C.[118] It was established that the reactions occur in this case in accordance with the following scheme:





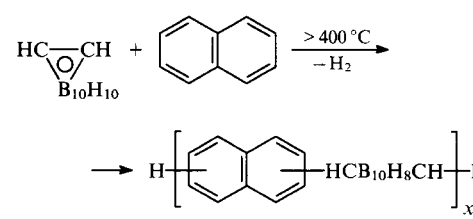
x = 5–10

Under conditions where the intermediates are not removed, only oligomeric products with x = 5–10 are formed. The products of the recombination of the dicarbadodecaboranyl radicals and the aromatic compounds were not detected.

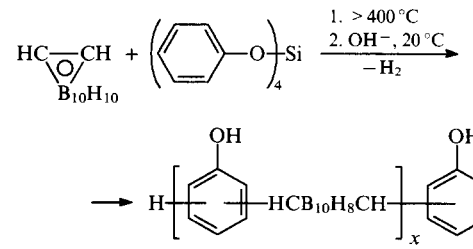
Since the products of the homolysis of the bonds at elevated temperatures can also serve as sources of free radicals, the dicarbadodecaboranes(12) were heated at 350–490 °C in the presence of aromatic compounds (naphthalene)[119] and also in the gas phase at 630–750 °C.[120] It was indeed established that under these conditions the dicarbadodecaboranes(12) undergo thermal radical condensation with the aromatic compounds in both condensed and gas phases with evolution of hydrogen.

In the condensed phase for degrees of conversion of 85%–95% [with respect to the dicarbadodecaborane(12)], oligomers soluble in aromatic hydrocarbons, ketones, and other solvents are formed (Scheme 13).

Scheme 13



x = 8–10



x = 2–3

The thermal condensation in the gas phase (at 630–750 °C) was investigated in relation to the interaction of 1,7-dicarbadodecaborane with benzene.[120] It was found that the products of this condensation for low degrees of conversion of 1,7-dicarbadodecaborane (up to 33%) are isomeric boron-substituted phenyl-1,7-dicarbadodecaboranes, namely 2-, 4-, 5-, and 9-phenyl-1,7-dicarbadodecaboranes, 2-phenyl-1,12-dicarbadodecaborane, and biphenyl. For high degrees of conversion, attained by

reintroducing the reaction solution into the reactor, the appearance of unidentified products with a higher molecular mass, tentatively disubstituted 1,7-dicarbadodecaboranes, was observed. An increase in the reaction temperature led to an increase in the yield of biphenyl, which is apparently due to the higher activation energy for this side reaction compared with the activation energy for the thermal condensation of 1,7-dicarbadodecaborane and benzene. The latter evidently proceeds, as in the condensed phase, via a stage involving the formation of an intermediate boron-centred radical. The products of the thermal condensation in the gas phase are similar to those of the condensation in the condensed phase and constitute a mixture of all possible isomers of 1,7-dicarbadodecaborane, their content in the mixture corresponding to the number of equivalent boron atoms in the 1,7-dicarbadodecaborane molecule and being almost independent of the temperature in the experimental temperature range. The carbon atoms of 1,7-dicarbadodecaborane do not participate in this reaction.[120]

The study of the kinetics of this process was undertaken in relation to the interaction of 1,7-dicarbadodecaborane with naphthalene at 350–490 °C.[119] The reaction was carried out in glass bulbs in the gas phase. The concentrations of the initial reactants were measured with the aid of gas–liquid chromatography.

The partial reaction orders with respect to each component were calculated from the equation

$$\ln W_0 = \ln k + n \ln[HCB_{10}H_{10}CH]_0 + m \ln[C_{10}H_8]_0 \ ,$$

where W_0 is the initial rate of consumption of 1,7-dicarbadodecaborane (mol litre^{-1} s^{-1}), k the reaction rate constant, n the reaction order with respect to 1,7-dicarbadodecaborane, m the reaction order with respect to naphthalene, $[HCB_{10}H_{10}CH]_0$ the initial molar concentration of 1,7-dicarbadodecaborane, and $[C_{10}H_8]_0$ the initial molar concentration of naphthalene. It was found that the reaction orders with respect to 1,7-dicarbadodecaborane and naphthalene are close to unity. The effective activation energy for the reaction in the temperature range 440–490 °C is 221 ± 6 kJ mol^{-1}, which is significantly less than the C–H bond stength in naphthalene, the latter amounting to ~419 kJ mol^{-1}.[119]

It was established that the rate of the reaction between 1,7-dicarbadodecaborane and naphthalene is described by the following equation for degrees of conversion between 0% and 30% and at temperatures in the range 440–490 °C:

$$-\frac{d[C_{10}H_8]}{d\tau} = \frac{d[HCB_{10}H_{10}CH]}{d\tau} = k[HCB_{10}H_{10}CH]_0^{0.95\pm0.04}[C_{10}H_8]_0^{1.01\pm0.03} \ ,$$

where

$$k = 6.3 \times 10^{11.0\pm1.0} \exp\left(-\frac{221 \pm 6}{RT}\right) \Big/ \text{litre mol}^{-1}\ \text{s}^{-1}.$$

Hence it was concluded that the interaction of the dicarbadodecaborane(12) with aromatic compounds at high temperatures is described by the following scheme:

$$ArH \xrightarrow{k_0} Ar^{\cdot}$$

$$Ar^{\cdot} + BH \xrightarrow{k_1} ArH + \dot{B}$$

$$\dot{B} + ArH \underset{k_3}{\overset{k_2}{\rightleftharpoons}} ArH\dot{B}$$

$$ArH\dot{B} + BH \xrightarrow{k_4} ArH_2B + \dot{B}$$

$$ArH_2B \xrightarrow{k_5} ArB + H_2$$

$$ArH\dot{B} + \dot{B} \xrightarrow{k_6} ArB + BH$$

where ArH is the aromatic compound and BH is the dicarbadodecaborane(12).

In principle, this scheme is analogous to the mechanism of the reaction involving chain radical addition to alkenes known as the Kharasch reaction.[119] In conformity with this scheme, the rate of reaction of the dicarbadodecaborane(12) is then equal to the rate of reaction of the aromatic compound:

$$-\frac{d[BH]}{d\tau} = -\frac{d[ArH]}{d\tau} = k_4[ArHB^{\cdot}][BH] \ ,$$

and subject to the conditions $k_3 \gg k_4[BH]$, we obtain

$$-\frac{d[BH]}{d\tau} = -\frac{d[ArH]}{d\tau} = k_4\left(\frac{k_2}{k_3}\right)^{1/2}\left(\frac{k_0}{k_6}\right)^{1/2}[ArH][BH] \ .$$

Since the reactants in this reaction are polyfunctional, it is possible to employ the initial concentrations instead of the current concentrations for low degrees of conversion. In this scheme, the bimolecular abstraction reaction is an aromatic homolytic substitution reaction.[119]

The proposed reaction scheme and the experimental data yield an overall reaction order of 2, which is due to the appreciable acceleration of the reaction under the influence of the radical fragments formed. It is to be expected that the factor determining the rate of the molecular chain propagation in the reaction investigated is the stability (thermodynamic stability) of the σ-radical complex at high temperatures.

This is confirmed by the data obtained in the condensation of monosubstituted benzene derivatives, which leads, as can be seen from Table 6, to the formation of two isomers (*ortho*- and *para*-) in terms of the position of the dicarbadodecaboranyl group in the aromatic ring, each of which consists of four isomers in terms of the position in which the aryl group is substituted in the 1,7-dicarbadodecaborane nucleus.

Table 6 shows that the nature of the substituent influences the ratio of the isomers involving the 2- and 9-positions in the 1,7-dicarbadodecaborane. Since the 1,7-dicarbadodecaboranyl group exhibits different inductive effects in the 2- and 9-positions[122] (positive in the 9-positive and negative in the 2-position), it is to be expected that the presence of an electron-donating substituent in the benzene ring increases the stability of the radical complex with the 1,7-dicarbadodecaboranyl radical involving the 2-position, whilst the presence of an electron-accepting substituent increases the stability of the complex involving the 9-position, increasing thereby the rate of formation, i.e. the content, of a particular isomer in the reaction products.

Table 6. The compositions of the *B*-aryl-1,7-dicarbadodecaboranes obtained from PhX and 1,7-dicarbadodecaborane by thermal condensation at 440 °C and for the molar ratio arene:1,7-dicarbadodecaborane = 1:15.

Substituent X	Content of *para*-isomers (%)			Content of *ortho*-isomers (%)			*para*:*ortho*
	2-	4-, 5-	9-	2-	4-, 5-	9-	
H	21.5	6.5	15.0	–	–	–	–
Me	20.1	62.8	17.1	24.9	59.0	16.1	1.62
Ph	19.6	62.4	18.0	20.7	60.3	19.0	1.73
$(Me)_3Si$	20.1	62.5	17.4	22.0	63.0	15.0	2.02
MeO	22.3	61.9	15.8	24.4	63.5	12.1	1.41
PhO	16.9	67.6	15.5	19.2	65.2	15.6	1.65
Cl	17.8	62.0	20.2	24.6	47.2	28.2	2.34
CF_3	15.3	61.4	23.3	20.2	58.0	21.8	1.46

Note. The totals for isomers of the *B*-aryl-1,7-dicarbadodecaborane with the aryl group in the 4- and 5-positions in the dicarbadodecaborane nucleus are given.

Oligophenylene-, oligonaphthalene-, and oligoanthracenedicarbadodecaboranes, obtained by the high-temperature polycondensation of 1,2-dicarbadodecaborane with the corresponding aromatic compound under pressure at 400–460 °C, are coloured powders, the colours of which range from pale-yellow (benzene) to dark-brown (anthracene). For a degree of reaction of 95%, the oligomers are readily soluble in acetone, benzene, and chloroform. It was found that the Mark–Kuhn–Houwink equation for oligophenylenedicarbadodecaborane is

$$[\eta] = 4.622 \times 10^{-4} M^{0.59\pm0.09}.$$

(The reduced viscosity was determined in toluene). The average length of the Kuhn segment for this oligomer, which is 12.0 Å, makes it possible to assign the structure to the flexible-chain type.[123]

Thermal condensation of dicarbadodecaborane(12) with ferrocene is also possible. In order to investigate the mechanism of this reaction, a study was made of the process kinetics at 440 °C. It was found from the dependences of the initial rates of consumption of ferrocene on the initial concentration in the absence of dicarbadodecaboranes(12) that the rate of consumption of ferrocene under these conditions is described by the relation

$$-\frac{d[(C_5H_5)_2Fe]}{d\tau} = k[(C_5H_5)_2Fe]^{2.48\pm0.17},$$

where $k = (1.2 \pm 0.5) \times 10^3\ s^{-1}$.

The study of the dependence of the initial rates of consumption of ferrocene and the dicarbadodecaborane(12) on the initial concentration of the dicarbadodecaboranes(12) showed that variation of the concentration of the latter hardly affects the rate of consumption of ferrocene. Thus the rate of consumption of ferrocene in the course of the reaction with dicarbadodecaboranes(12) is also described by the relation presented above.

The rate of consumption of dicarbadodecarboranes(12) is proportional to their concentration in accordance with the relation

$$\frac{d[C_2B_{10}H_{12}]}{d\tau} \sim [C_2B_{10}H_{12}]^{1.76\pm0.12}.$$

The data obtained permitted the conclusion that the condensation of ferrocene with dicarbadodecaborane(12) differs fundamentally from the reaction of dicarbadodecaborane(12) with aromatic compounds[119] apparently mainly as a consequence of the high rate of the thermal degradation of ferrocene.

One can assume with a high degree of justification that the condensation of ferrocene with dicarbadodecaboranes(12) is achieved exclusively as a result of the presence of the radical products of the degradation of ferrocene, which is in its turn a heterogeneous autocatalytic process. The rate of the radical degradation of the radical products is then higher than the rate of their diffusion into the bulk of the gas phase, which is the reason for the strong dependence of the rate of consumption of dicarbadodecaboranes(12) on their concentration.

The presence of cyclopentadiene and its dimer among the products of the degradation of ferrocene in the presence of dicarbadodecaborane(12) at temperatures in excess of 350 °C shows that the primary products are cyclopentadienyl radicals.

$$(C_5H_5)_2Fe \xrightarrow{>350\ ^\circ C} 2\,C_5H_5^{\bullet} + Fe$$

$$C_5H_5^{\bullet} + 1,2\text{-},1,7\text{-}C_2B_{10}H_{12} \longrightarrow C_5H_6 + 1,2\text{-},1,7\text{-}C_2B_{10}H_{11}$$

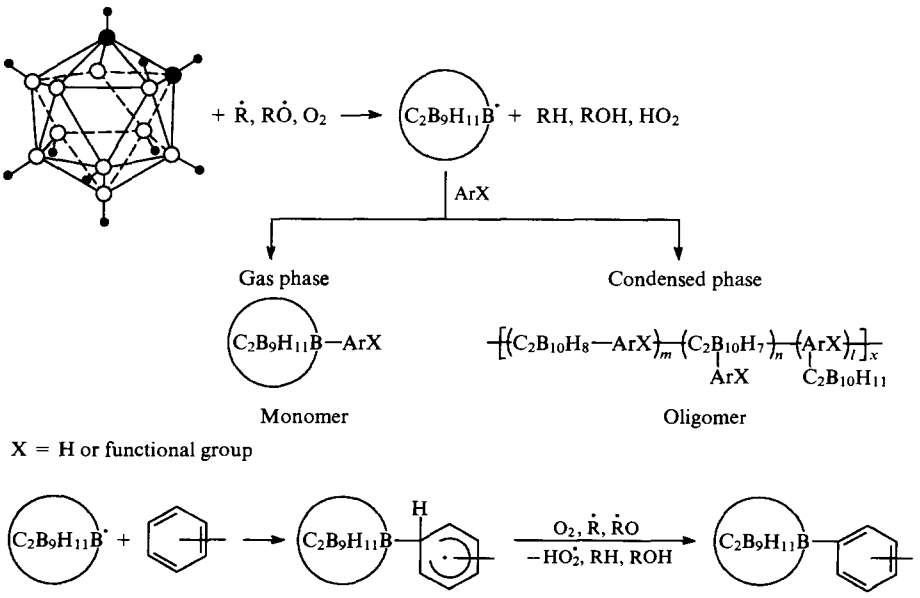
$$2\,C_5H_6 \longrightarrow \text{cyclopentadiene dimer.}$$

The formation of the unstable and reactive 1,2- and 1,7-dicarbadodecaboranyl radicals apparently constitutes a sufficient condition for the formation of the products of the condensation of *B*-ferrocenyl-1,2- and *B*-ferrocenyl-1,7-dicarbadodecaboranes in the course of their further transformations as a result of reactions analogous to homolytic aromatic substitution reactions.

The reaction involving the direct thermal arylation of dicarbadodecaboranes(12) differs from the arylation reaction examined at the beginning as regards the mechanism of the homolytic radical aromatic substitution in the presence of a free-radical source evidently only in the mechanism of the formation of the boron-centred radicals. In a general form, the radical arylation of dicarbadodecaboranes(12) may be represented by Scheme 14.

The results of the investigation presented above are important for the understanding and practical solution of the problem of the preparation of polymers based on dicarbadodecaboranes(12) and having a high thermal stability. Firstly, the transformations in such polymers at elevated temperatures, leading to the formation of dense network three-dimensional systems and giving rise to materials with a long useful life, become comprehensible. Secondly, dicarbadodecaboranes(12) can be and should be regarded as inhibitors of the thermal and thermooxidative degradation, since the radical products of the degradation of the organic fragments of the polymers interact with the

Scheme 14



dicarbadodecaborane groups and are converted into an inactive form. The dicarbadodecaborane groups are capable of forming new stable bonds of the B–C type with the boron-centred radicals (Scheme 14); nor can one rule out the formation of B–B bonds by a recombination reaction. Thus one can represent the dicarbadodecaborane-containing polymer matrix at elevated temperatures as a system involving a definite dynamic equilibrium in which the thermal destruction of the chemical bonds is compensated by the formation of new ones. A necessary consequence of these results is also that the dicarbadodecaborane groups must be introduced into polymer systems in combination with aromatic compounds in order to ensure the conditions for the transformations examined above. Thirdly, an important factor is undoubtedly the fact that the observed direct arylation of dicarbadodecaboranes(12) permits a new and much simpler solution of the problem of the synthesis of dicarbadodecaborane-containing monomers and reactive oligomers. For this purpose, it is essential to introduce the corresponding aromatic compounds into the thermal condensation reaction.

The example involving tetraphenoxysilane, presented in Scheme 13, the product of the interaction of which with 1,2-dicarbadodecaborane affords a reactive monomer with the more stable 1,7-dicarbadodecaborane groups, capable of being employed as such, constitutes an adequate illustration of the process in the condensed phase. On the other hand, the products of its hydrolysis are dicarbadodecaborane-containing phenols, which serve as starting materials for the synthesis of polymers of practical importance, in particular those of the phenolformaldehyde and epoxide types.[98] For the gas-phase arylation of dicarbadodecaboranes(12) in a flow system, it is sufficient to employ the corresponding benzene derivatives.

VI. Conclusion

Since the end of the 1960s, an extensive series of studies have been carried out on the development of new polymers with arylenedicarbadodecaborane fragments in the chain. Novel methods have been developed for the synthesis of various bifunctional dicarbadodecaborane-containing aromatic monomers and processes involving the formation from the latter of new high-molecular-mass dicarbadodecaborane-containing polymers have been investigated. A detailed study has been made of the mechanisms of the chemical reactions of polyarylenedicarbadodecaboranes, which makes it possible to understand the causes of their unusual thermal behaviour and to find new promising methods of synthesis of dicarbadodecaborane-containing monomers and polymers.

Naturally, dicarbadodecaborane-containing polymers are not produced on a large scale and in the foreseeable future will not be produced on such a scale, which, incidentally, applies also to many other interesting polyheteroarylenes with specific properties. Dicarbadodecaborane-containing polymers are special-purpose polymers used primarily in those fields where improved thermal characteristics are required for the polymeric materials.[17,19–25,124–133]

Thus the employment of dicarbadodecaborane-containing phenolformaldehyde polymers as a base for adhesive compositions proved to be promising[125,132] because hardened dicarbadodecaborane-containing resols are distinguished by a high thermal stability. Dicarbadodecaborane-containing resites hardly undergo any change in mass during ageing for 1000 h at 350 °C, whereas the usual phenolformaldehyde polymers are fully destructured under these conditions.

The combination of effective thermal properties of the dicarbadodecaborane-containing resites with the improved adhesion characteristics which are in general specific to phenolformaldehyde polymers made it possible to obtain adhesive compositions with a long useful life at 350–500 °C. The strength characteristics of certain adhesives hardly change after prolonged ageing at 500 °C. Thus when steel components are glued together by means of the adhesive based on the dicarbadodecaborane-containing phenolformaldehyde polymer, the breaking stress is 120 kgf cm^{-2} when the glued junction is subjected to shear before ageing at 20 °C and 500 °C, while after ageing for 500 h at 20 and 500 °C the breaking stresses are 116 and 118 kgf cm^{-2} respectively.

The use of the dicarbadodecaborane-containing epoxide polymers in thermostable adhesive compositions also proved successful.[19,22,23,25,125,130,132] The employment of epoxydicarbadodecaborane oligomers in compositions with furan polymers, as activators of the graphitisation process, in the technology for the preparation of carbon materials has also had a positive effect.[131]

The application of dicarbadodecaborane-containing polyphenylenes, synthesised by the polycyclocondensation of dicarbadodecaborane-containing aromatic acetyl compounds and their ketals, as thermostable binders for glass plastics with a working temperature of 400 °C and in the manufacture of thermostable constructional materials has been described.[97,126–128]

It has been suggested that dicarbadodecaborane-containing polymers of various classes be used to obtain thermostable antifriction self-lubricating coking plastics ensuring the operation of dry friction units at extreme temperatures of 350–500 °C and above: polyamides, polyarylates, polyimides, and polyoxadiazoles, capable of being converted during the preparation of the material into a high-strength coke which consists of a three-dimensionally structured polymer system, without change in the initial mass and shape of the article.[124,129,133] For example, heat-treated materials derived from dicarbadodecaborane-containing polyarylates [obtained from the acid chloride of 1,2-bis(4-carboxyphenyl)dicarbadodecaborane and 1,9-bis(4-hydroxyphenyl)fluorene or 1,2-bis(4-hydroxyphenyl)dicarbadodecaborane] and graphite has the following physicomechanical characteristics: hardness of 18–20 kgf mm^{-2}, coefficient of friction 0.05–0.09, intensity of linear wear $(2.5–5) \times 10^{-9}$, and limiting working temperature 500 °C. The use of the polyoxadiazole based on 1,2-bis(4-carboxyphenyl)dicarbadodecaborane or the polyimide based on 1,7-bis(3,4-dicarboxyphenyl)dicarba-dodecaborane and bis(4-aminophenyl) ether as dicarbadodecaborane-containing polymers in compositions makes it possible to obtain materials with a limiting working temperature of 600 °C whilst retaining effective physicomechanical characteristics.

By virtue of their specific behaviour at elevated temperatures, dicarbadodecaborane-containing polymers can also be used as stabilisers in the thermal and thermooxidative degradation of other polymers,[11,21,25,82,83,134,135] in the preparation of thermostable thermoprotective materials, and for other purposes.

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Technological polymorphism of disperse amorphous silicas: inelastic neutron scattering and computer modelling

E F Sheka, V D Khavryuchenko, I V Markichev

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Abstract. The review gives a systematic account of the results of detailed studies of the vibrational spectra of a series of industrial amorphous highly disperse silicas (aerosil, silica gel, aerogel) with the aid of inelastic neutron scattering. The observed phenomenon of technological polymorphism and the results of the quantum-chemical modelling of the structures and vibrational spectra of the corresponding polymorphic modifications are discussed. The bibliography includes 113 references.

I. Introduction

Silicas are substances whose structures are based on silicon dioxide.[1] This class of compounds combines both natural substances (ranging from quartz and cristobalite to semiprecious stones) and artificial substances (ranging from quartz glass to aerogel). The family of amorphous highly disperse silicas, incorporating aerosils, aerosilogels, silica gels, porous glasses, silochromes, and aerogels, occupies a special place among them.[2,3]

It is difficult to overestimate the importance of highly disperse silicas for chemistry and chemical engineering. They are used in large amounts in the chemical industry as adsorbents, fillers, and loosening agents[4] and also in medicine as medicinal drugs, intensifiers of biological activity of substances and medicinal drugs, chemisorbents, preservatives for live vaccines, etc. The uniqueness of silicas is due to their high surface activity, the nature of which is being vigorously investigated.[5,6]

Numerous studies have been devoted to the surface activity of disperse silicas, most of them having been carried out by empirical chemical methods. It was not until the end of the 1960s that spectrometric methods — vibrational IR and Raman spectroscopy[7–13] and NMR spectroscopy[14] – began to be used for the investigation of silicas. However, both due to experimental complexities and the difficulties in the interpretation of the data, the results proved in many respects to be qualitative, which hindered the employment of optical vibrational spectroscopy for the investigation of the structures and compositions of these substances.

In contrast to the optical vibrational spectroscopy, considerable progress on these lines has been achieved in recent years in neutron vibrational spectroscopy[15,16] because of the possibility of the reliable isolation of the parts of the spectrum corresponding to definite structural fragments of the system, including also the surface. This last advance should be noted particularly, since it is well known that inelastic thermal neutron scattering (INS) constitutes in the general case a bulk-phase research technique owing to the considerable mean free path of neutrons in the medium (of the order of 10^{-2} m).[17] However, if the specific surface increases, as happens in the case of highly disperse substances, or if the surface of the specimen is coated by hydrogen-containing substances [the nuclei of the lightest hydrogen isotope (protium), referred to below simply as hydrogen, have an exceptionally high neutron scattering cross-section and the amplitude of their displacements during vibrations is also high], then the contribution of the scattering by the surface vibrations increases significantly. The situation is favourable not only for hydrogen-containing adsorbents but also for the vibrations of the support as a result of the 'riding effect'.[18,19] Disperse silicas satisfy both conditions examined above, so that the application to them of INS spectroscopy proved extremely successful. As a result of a special series of experiments,[20–29] it has been possible to determine both the vibrational spectra of the bulk (or core) of a series of representatives of these substances and the vibrational spectra of the surface regions. The data obtained for a set of different industrial silicas proved fundamentally significant. It was shown that different vibrational spectra of the cores and surface regions corresponding to the silicas investigated are so different that it became necessary to assign these substances to fundamentally different structural formations.[30–32] Thus a phenomenon, called technological polymorphism, has been observed spectroscopically.[30] It served as the basis of a new algorithmic approach to the computational modelling of the substances investigated.[30–32] The modelling, carried out at the level of modern quantum-chemical methods,[33–35] made it possible to construct models of

E F Sheka, I V Markichev Laboratory for the Spectroscopy of Adsorption and Catalytic Processes, Department of General Physics, Russian Friendship Among Peoples University, ul. Ordzhonikidze 3, 117302 Moscow, Russian Federation.
Fax (7-095) 954 03 36 Tel. (7-095) 952 11 86 (E F Sheka)
V D Khavryuchenko Institute of Surface Chemistry, National Academy of Sciences of Ukraine, prosp. Nauki 31, 252028 Kiev, Ukraine.
Currently at the I M Frank Neutron Physics Laboratory of the Joint Institute for Nuclear Research, 141980 Dubna, Russian Federation.

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the structures which explain the behaviour of the vibrational spectra of different types of silicas and to establish an unambiguous relation between this phenomenon and the differences between the chemical technologies employed for the preparation of the products. The validity of the proposed approach was demonstrated by the successful comparison of the calculated and experimental vibrational spectra measured with the aid of INS.

The aim of the present review is to give a systematic account of the results obtained and the methods for their treatment in order to discover and develop an approach to the study of a specific phenomenon — technological polymorphism. This phenomenon, first thoroughly investigated for disperse silicas, proved to be one of the distinctive features of nanomaterials of virtually any class [36] and its understanding is one of the decisive factors for the creation of the basic materials for the immediate future.

II. General characteristics of disperse silicas

1. Structural properties and IR absorption

Disperse amorphous silicas are obtained in the condensation and polymerisation accompanying the hydrolysis of silicon tetrahalides, their organic orthoesters, and silicic acid salts. [1] The polymerisation leads to the formation of siloxane (SiOSi) chains and nonplanar rings with different numbers of atoms. The spatial disposition of these chains and rings gives rise to the bulk structure (core) of the silica. The same chains and rings make up its surface. The valence bonds involving the surface silicon atoms are then saturated only on the inner side of the surface. On the outer side there is a 'valency excess', which is saturated by hydroxy-groups in the presence of water molecules. The active surface centres produced readily adsorb water, as a result of which a characteristic shell consisting of hydroxy-groups and adsorbed water arises around the siloxane core. This view of the structure of amorphous disperse silicas has been described in the well known monograph by Iler. [1] During the years which have elapsed since its publication, this view has not undergone significant changes despite the solution of many of the specific problems (see the latest monographs [4,5]). Fig. 1 illustrates a structural scheme for disperse silica, which was implicitly adopted for products of any origin as recently as three years ago. The siloxane chain represents the surface layer of the atoms of the base, the fragments of its inward branching simulating the development of bulk-phase structure. The unsaturated bonds of the surface silicon atoms are blocked by hydroxy-groups, but both the number of groups per silicon atom and their distribution on the surface have not been in general clearly determined. The outer layer of the fragment is occupied by the molecules of adsorbed water, the positions of which relative to the surface groups are illustrated to a large extent arbitrarily. In essence, the model clearly presents the interpretation of the atomic structure of the bulk phase and the surface of disperse silica which has arisen on the basis of the study of their IR absorption spectra.

Attempts to investigate the vibrational spectra of disperse silicas by optical spectroscopic methods (IR absorption and total internal distorted IR reflection, Raman scattering) have been undertaken repeatedly. [7-13] However, owing to the intense absorption by the siloxane matrix, [37] the studies have been concentrated mainly in the spectral range 3000–4000 cm^{-1}, which contains the stretching vibrational frequency of the hydroxy-groups and water. The results obtained yield a contradictory picture even when combined with deuterium–hydrogen exchange data [11,13] and remain to a large extent qualitative, which can be seen from the generalised picture presented in Table 1. It follows from the table that it is virtually impossible to establish the differences between, for example, aerosil, silica gel, and aerogel on the basis of data obtained in the range 3000–4000 cm^{-1}. As regards the most structure-sensitive regions in the ranges 0–400 cm^{-1} and 500–1000 cm^{-1}, the first is fully obscured in the IR spectra by the absorption due to the siloxane core, while the second has been little investigated (for the same reason). [37-39] The available information about this spectral range is derived mainly from the analysis of compound frequencies.

The main conclusions reached on the basis of the study of the IR absorption reduced to the following:

1. The similarity of the behaviour of different disperse silicas in a series of basic reactions [1-5] suggests the similarity of the structures of their surfaces and for this reason investigations are mainly carried out on different specimens of aerosil as the chemically purest silica.

2. As a result of the concentration of studies mainly in the spectral range 3000–4000 cm^{-1}, the principal objects of study are the hydroxyl coating and the adsorbed water.

3. The surface of aerosil is uniformly coated by silanol groups with a density of ~0.046 of a group on 1 $Å^2$, which corresponds to an average distance between them of 0.7 Å. [5] The existence of silanediol groups is not disputed, but according to the data of different workers their proportion varies from 4% to 40%. [5,14] Silanetriol groups have not been detected on the surface of aerosil under the usual conditions. [40]

4. The adsorbate–support system in the case of the water–silica system consists of two partners: the silanol group and the water molecule. The problem reduces to the type of interaction between the partners. Some workers support the view that the interaction between water and silica is of the coordinative type, [6] whilst others suggest that the water molecule is bound to a hydroxyl centre via a hydrogen bond. Among the recent studies devoted to this question, special mention must be made of the studies by Lygin and coworkers, [14,41,42] who attempted to account for the mechanism of the adsorption of water on the basis of the investigation of the dynamics of the deuterium–hydrogen exchange involving the hydroxy-groups by monitoring the intensities of the absorption bands due to the OH and OD

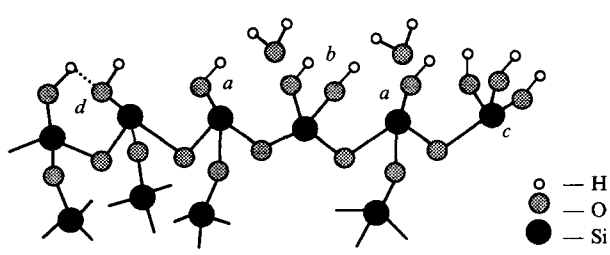


Figure 1. Schematic representation of the structure of amorphous silica: (*a*) silanol groups; (*b*) a silanediol group; (*c*) a silanetriol group; (*d*) hydrogen-bonded groups.

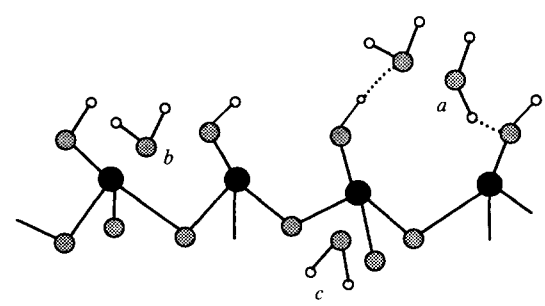


Figure 2. Schematic representation of the positions of the adsorbed water molecules on the surface of amorphous silica: [6] (*a*) hydrogen-bonded water; (*b*) water coordinated in the *cis*-position; (*c*) water coordinated in the *trans*-position.

Table 1. The absorption band frequencies for the vibrations of the free hydroxy-groups of silicas treated at high temperatures.[13]

Specimen	T/°C	Frequency/cm^{-1}		Interpretation
		OH	OD	
Porous glass	550	4540	–	Compound stretching vibrations of the free hydroxy-groups in SiOH and the SiO groups
	750	4500	–	Compound stretching and deformation vibrations of the free hydroxy-groups in SiOH
Aerogel	700	4520	3363	Compound stretching and out-of-plane deformation vibrations of the free hydroxy-groups in SiOH and SiOD
Porous glass	750	3850	2840	Compound deformation vibration of the free hydroxy-groups in SiOH and SiOD and compound stretching vibrations in SiO_4
	550	3749	2761	Stretching vibrations of the free hydroxy-groups in SiOH and SiOD
	600	3740	2760	–
Silica gel	400	3749	2761	–
	940	3748	–	–
	500	3740	–	–
Aerosil	940	3750	–	–
	500	3748	–	–
Aerogel	700	3750	2740	–
Aerosil	450	3743	–	–
	400	3737	2755	–
	400	3747	2760	–
Silica gel	400	3500	–	Stretching vibrations of the hydroxy-groups in $Si(OH)_2$
Porous glass	400	2000	–	Combination and overtone vibrations of the silica core
		1870	–	
Aerogel	600	1635	–	–
Silica gel	400	950	–	Deformation vibrations in SiOH or the stretching vibrations of the OH group relative to Si
	400	870	–	Deformation vibrations in SiOH
Aerogel	700	770	603	Out-of-plane deformation vibrations in SiOH

groups (at 3749 and 2761 cm^{-1} respectively). Two conclusions were reached on the basis of these investigations: (1) water is adsorbed on hydroxy-groups and (2) on the surface of aerosil there are sections with significantly different rates of adsorption of water, i.e. there are hydroxy-groups with significantly different structures. Similar conclusions have been reached[43] from calculations by the method of molecular dynamics. The possible positions of the water adsorbed on silica are illustrated in Fig. 2.

Overall, studies of the IR absorption failed to provide answers to the following principal problems of the chemistry of disperse silicas:

to what extent are the structures of the cores of different industrial forms of amorphous disperse silicas identical;

how are their surfaces formed and what is the distribution of the hydroxy-groups on the latter;

what are the conditions for the existence of silanol, silanediol, and silanetriol groups on the surface;

what are the mechanisms of the adsorption of different substances, primarily water, on the surfaces of these products.

This situation made it necessary to seek new ways for discriminating between substances. Inelastic neutron scattering is an effective spectroscopic method. This made it possible to transfer the study of the vibrational spectrum to the range 0–1500 cm^{-1}, which contains the most structure-sensitive deformation and torsional vibrations of the hydroxy-groups, water, and the siloxane cores, and to raise the question of the measurement of the vibrational spectra of individual structural components of each silica specimen.

2. Application of inelastic neutron scattering spectroscopy to the study of vibrational spectra

INS spectroscopy is a comparatively new method for the study of surfaces. Initially studies with the aid of elastic (diffraction) and inelastic (vibrational spectroscopy) neutron scattering[17,44] were directed to the study of the bulk-phase characteristics, because, owing to the high penetrating capacity of the neutron, the contribution of the surface atoms to the scattering spectrum of the specimen was small. However, as stated in the Introduction,

the situation became more favourable for highly disperse specimens, which has been confirmed in relation to disperse silicas. In the study of the INS by these specimens, the principal advantages of neutron spectroscopy were fully manifested: sensitivity to the nuclei of hydrogen atoms and to the hydrogen–deuterium isotope substitution, the absence of selection rules in energy transfer, the involvement of a broad spectrum of vibrational states in the scattering process, etc.

One of the first productive studies of the vibrations of water adsorbed on a silica surface was carried out in 1981.[45] The preceding studies in the period 1964–1975[46–48] devoted to this problem were carried out at room temperature, which limited the possibility of studying low-frequency vibrational modes. Two specimens of silicas (silica gel) were investigated[45] at 15 K: Gasil 200 (calculated pore diameter 21 Å, specific surface 850 $m^2 g^{-1}$) and Spherisorb S20W (89 Å and 232 $m^2 g^{-1}$ respectively). The main result of this investigation was the demonstration that the spectrum of the vibrations of water within the silica gel pores differs from the vibrational spectrum of ordinary ice (Fig. 3) and that the spectral maximum, located at 80 meV (640 cm^{-1}) undergoes a bathochromic shift on passing from silica gel with a small pore diameter to one with a large pore diameter. Thus it is seen from Fig. 3 that, for the maximum moisture content in the specimen, the principal peak of the spectrum virtually coincides with the principal band in the spectrum of H_2O ice, the position of which is indicated by a vertical straight line. When the specimen is dried, the position of this peak in the silica gel spectrum shifts towards lower frequencies. A similar effect has been observed also on passing to a specimen with a smaller pore size. In the discussion of the causes of this shift, a model involving the adsorption of water on neighbouring surface hydroxy-groups was proposed, but this model was merely qualitative.

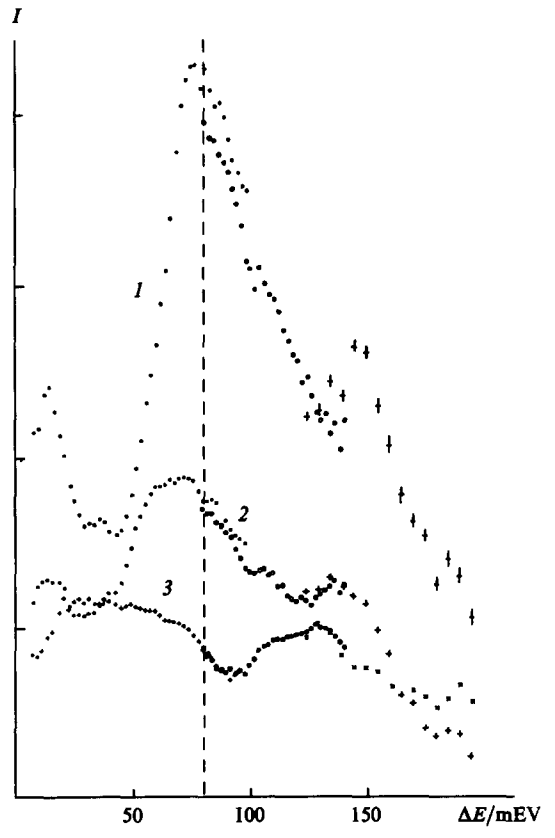


Figure 3. INS spectra of the silica gel Gasil 200 ($T = 15$ K) for different moisture contents in the specimen.[45] Moisture content (%): (*1*) 13; (*2*) 4; (*3*) specimen dried at 150 °C.

It was also established that the properties of water in the region of contact with the surface differ significantly from its properties in the bulk phase. Thus the density,[49] diffusion coefficient,[50] and viscosity of water[51,52] change in the vicinity of the silica surface. A diffraction study[52–55] showed that the water in the pores has the structure of ice in the cubic modification *Ic*; under these conditions, ordinary ice consists of hexagonal crystals *Ih*. This effect can be explained by the change in the structure of water near the silica surface, but the explanations remain qualitative particularly bearing in mind the remark made by Li et al.[56] that the structures of the surfaces of the silicas themselves are different. On the basis of model calculations and experiments at 15 K on a Vycor glass specimen (a boron-containing glass) with an average pore diameter of 30 Å and a specific surface of 180 $m^2 g^{-1}$, it was shown in the same study that there is no distinct interface in the form of layers of different density in the silica–water system. It was postulated that in fact the ice structure in the layers subject to a marked influence of the surface is similar to the structure of liquid water, where a large number of hydrogen bonds have been broken. Comparison of the vibrational spectra of water adsorbed on glasses with the spectra of ordinary ice,[57] which proved to be fairly similar (Fig. 4), led to the conclusion that the water in the Vycor glass pores is present in two forms: as the bulk-phase water and as the water adsorbed on the walls of the pores. This conclusion has been confirmed by the considerable similarity between the difference spectrum of the 'air-dry specimen – ice' and the spectrum of a 'dried specimen' (Fig. 5). On the basis of this similarity, the hypothesis that quasi-free water is present in the pores was put forward.[56] However, the paper presents only qualitative considerations concerning the contribution of the ice spectrum to the spectrum of the glass specimen with a 100% moisture content.

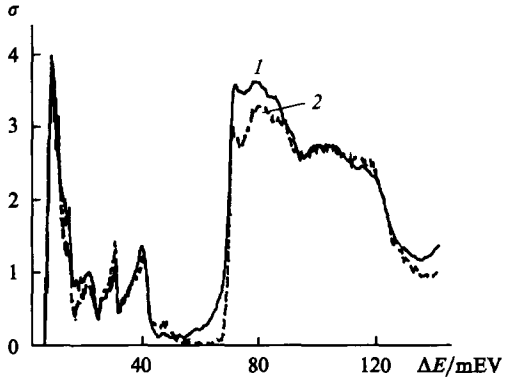


Figure 4. INS spectra of ice: (*1*) ice in the porous Vycor glass;[56] (*2*) hexagonal ice.[57]

Among the latest studies on the vibrational spectroscopy of surfaces using INS, mention should be made of investigations of silicas the surfaces of which were modified by various organic compounds,[58] the surface vibrations of hydrogen adsorbed on nickel[59] and molybdenum,[60] the vibrations of water and ammonia adsorbed on manganese and zirconium oxides,[61] and the vibrational spectra of quartz glass[62] and natural silica minerals such as zeolites[63] and opal.[64] A large series of studies has been devoted to the vibrational spectra of different modifications of ice.[65–76] A series of studies[77–81] devoted to fractal excitations in aerogel should be considered separately.

It is seen from the above survey that INS makes it possible to raise the question of the study of the surfaces of disperse silicas. However, the inadequate number of systematic experimental spectroscopic studies and failure to consider the problem of the differentiation of the surface components of the vibrations from the overall spectrum have led to failure to obtain virtually any important results at this point.

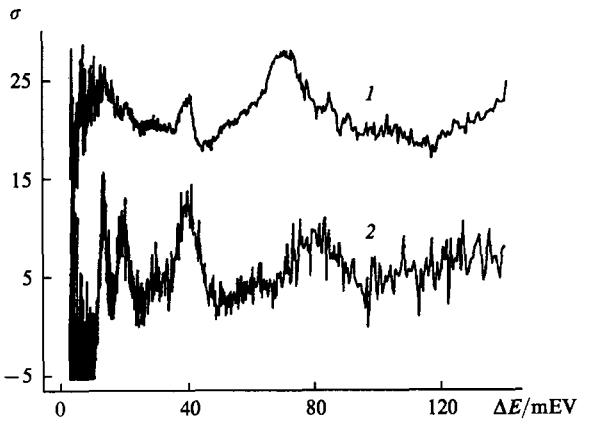


Figure 5. INS spectra of water adsorbed on the walls of the pores in the porous Vycor glass:[56] (*1*) residual moisture content in the dried specimen 10%; (*2*) 'specimen with 100% moisture content – hexagonal ice' difference spectrum.

The problem of discriminating between different silicas has been to a large extent solved in a series of investigations[20-29] undertaken with the aim of systematic study of the vibrational spectra of specimens of different disperse silicas prepared in a definite manner. They included a detailed consideration of the additive model of the composition of a disperse silica and a refinement of the concepts of the core and of the hydroxyl and water shells. A differential-correlation method for the determination of the spectra of the system from the experimentally measured spectra on the basis of the postulate that the spectra of independent systems are not correlated has been proposed and justified. The principal stages of this investigation, which led to a new type of formation of polymorphic modifications — technological polymorphism — are presented below. The results of computational modelling designed to understand this phenomenon at the atomic level will be presented in the succeeding Sections.

III. Techniques for the measurement and treatment of inelastic neutron scattering spectra

1. Primary treatment of the spectra

INS vibrational spectroscopy is based on the fact that, having entered the test specimen, a thermal energy neutron can transfer part of its energy in the excitation of a vibrational mode in the substance or can absorb this excitation, acquiring the corresponding energy and undergoing inelastic scattering thereby. The change in the energy of the neutron can be detected by various procedures.[17,44] The scattering of the next neutron takes place independently of the previous one with excitation – absorption of the same or a different vibrational mode, as a result of which it is possible to obtain the vibrational spectrum of the test specimen by measuring the neutron scattering intensity during the scanning of the energy transferred or acquired by the neutron.

In the experimental method for the determination of the energy lost by the neutron during time of flight, which is the principal procedure for the measurement of the INS in a high-flux IBR-2 reactor,[82] the INS spectrum can be described (see, for example, Bokhenkov et al.[83]) by the function

$$N(t_0) = \Delta t_0 \iiint dE_0\, dE\, dt\, F(E_0,E,t_0,t)\sigma(E_0,E,\phi,T) \ , \qquad (1)$$

where $N(t_0)$ is the number of neutrons which have arrived in the analyser during the time interval Δt_0 at time t_0, $\sigma(E_0, E, \phi, T)$ describes the scattering law for the nuclei (E_0 and E are the energies of the incident and scattered neutrons, ϕ is the scattering angle, and T is the temperature), and $F(E_0, E, t_0, t)$ is the instrument function, which includes the energy distribution of the incident and scattered neutrons and the time synchronisation condition. The neutron scattering cross-section σ is described by the following sum in the general case:

$$\sigma(\omega,t) = \sigma^{(1)}(\omega,T) + \sigma^{(\mathrm{mph})}(\omega,T) + \sigma^{(\mathrm{mpl})}(\omega,T) \ , \qquad (2)$$

where the superscripts (1) (mph), and (mpl) correspond to single-phonon, multiphonon, and multiple scattering.

The single-phonon incoherent scattering cross-section has the form

$$\sigma^{(1)}(\omega,\phi,T) = \sum_i \frac{d^2\sigma_i^{\mathrm{inc}}}{d\omega\, d\Omega} \qquad (3)$$

$$= \frac{k}{k_0}\frac{\hbar|Q|^2}{2M\omega}\sum_i (b_i^{\mathrm{inc}})^2 \frac{\exp(-2W_i)}{1-\exp(-\hbar\omega/kT)} G_i(\omega) \ ,$$

$$G_i(\omega) = \frac{1}{M_i}\sum_j \int dq |A_j^i(q)|^2 \delta[\omega - \omega_j(q)] \ . \qquad (4)$$

Here $G_i(\omega)$ is the density of the vibrational states of the substance weighted quadratically in terms of the amplitudes of the displacements of the ith nucleus,[83,84] k_0 and k are the wave vectors of the incident and scattered neutrons, Q is their difference, b_i^{inc} is the amplitude of the incoherent scattering by the ith nucleus (the cross-sections for scattering by the nuclei forming part of the composition of the silicas are presented in Table 2), M_i is the mass of the ith nucleus, W_i is the Debye – Waller factor, A_j^i is the amplitude of the displacement of the ith nucleus corresponding to the jth vibrational mode, and $\hbar\omega = E_0 - E$ is the transmitted energy. The quantity

$$G(\omega) = \sum_i (b_i^{\mathrm{inc}})^2 G_i^{\mathrm{inc}}(\omega) \ , \qquad (5)$$

is referred to as the doubly amplitude-weighted density of states (AWDS). This quantity can in fact be obtained from the experimental spectrum (1) by solving the converse problem subject to the condition that the scattering spectrum is determined by single-phonon processes. However, deconvolution problems are in general not soluble, so that in experimental practice involving INS a somewhat approximate function $\tilde{G}(\omega)$ serves as an analogue of the exact function $G(\omega)$. It is defined[82] as

$$\tilde{G}_T(\omega) = \frac{N_T[t(\omega)]}{\phi[t(\omega),E(\omega)]K(\omega,T)} \ . \qquad (6)$$

Table 2. Overall neutron scattering cross-sections.[17]

Atom/substance	Overall scattering cross-section σ°/barn[a]
H	81.5
D	7.6
O	4.24
Si	2.2
OH	85.74
OD	11.84
H_2O	167.24
D_2O	19.44
SiO_2	10.68

[a] σ° is determined by the sum of the cross-sections of the nuclear coherent and incoherent scattering by the nth type nucleus.

Here $\phi[t(\omega),E(\omega)]$ is the transformed apparatus function of the spectrometer, while the function $K(\omega, T)$ has the form

$$K(\omega,T) = \frac{k}{k_0}\frac{\hbar|Q|^2}{2\omega}\frac{\exp(-2W_i)}{1-\exp(-\hbar\omega/kT)}, \quad (7)$$

and can be readily calculated, provided that the angular configuration of the experiment is known.

The spectra $N(t)$ presented below were obtained on a KDSOG-1M time-of-flight spectrometer with inverse geometry in the IBR-2 high-flux reactor.[82] All the spectra were normalised with respect to the same number of scattering nuclei (per 100 g of the substance) and the same time of measurement. This makes it possible to carry out a quantitative comparative analysis of the spectra obtained. The low temperature served as a sufficient basis for the hypothesis that single-phonon scattering processes play a dominant role in the $N(t)$ spectra,[84] which made it possible to determine the required AWDS spectra in conformity with Eqn (6).

2. The set of disperse silicas

The series of studies discussed were carried out for three industrial highly disperse silica products: type A380 aerosil (specific surface 380 $m^2\ g^{-1}$), the silica gels SG100 and SG20 (average pore diameters 100 and 20 Å respectively), and the aerogel AG200 (density 200 kg m^{-3}). In conformity with the principal model according to which disperse silicas of any origin are three-component systems consisting of a silica core and hydroxyl and hydrate shells,[1] specimens differing in the partial contributions of these components were prepared. Each of the silicas investigated was represented by an isotypical set of specimens.

An air-dry specimen is the final product of the corresponding technological chain. It was stored in the open air at room temperature and the corresponding humidity. The spectrum of the air-dry specimen will be henceforth designated by $\mathcal{S}p^{(1)}$. The dried specimen was obtained by drying the air-dry specimen in air at a temperature specific to each specimen. The spectrum of the dried specimen will be designated by $\mathcal{S}p^{(2)}$.

A deuteriated specimen was obtained by a deuterium exchange procedure involving the successive drying of the specimen in a closed vessel with subsequent cooling in heavy water vapour; the drying–cooling cycle was repeated several times. The spectrum of the deuteriated specimen will be designated henceforth by $\mathcal{S}p^{(3)}$.

The set of spectra $\{\mathcal{S}p^{(j)}\}$ constitutes the basis for the determination of the spectra of the individual components of the silicas using the differential-correlation method for the resolution of the initial spectra.[85]

3. The construction of the basis for the spectrum of a complex system. Criterion of a zero linear correlation coefficient

Any method for the resolution of the spectrum of a complex system into the spectra of its components is based on an additive model, according to which the overall spectrum of the system $\mathcal{S}p^{(j)}$ can be represented by the sum of spectra:

$$\mathcal{S}p^{(j)} = \sum_{i=1}^{m} k_i^{(j)} Sp_i\ . \quad (8)$$

Here $k_i^{(j)}$ are the weighting factors of the spectra, the product $k_i^{(j)}Sp_i$ represents the partial spectrum of the ith component in the overall compound spectrum $\mathcal{S}p^{(j)}$, and j are the numbers of the independent spectra of the test system referring to its modifications differing in the partial contributions of the components. The spectra Sp_i are referred to as the basis spectra.

Two limiting cases are known for which the resolution of the compound spectrum $\mathcal{S}p^{(j)}$ has been achieved. In the first, which may be called the case of the complete set of basis spectra, all the basis spectra Sp_i are known and the order n of the system of the initial Eqns (8) is unity. The solution of the problem involves the finding of the coefficients $k_i^{(j)}$. It is usually believed that the best solution is that which corresponds to the condition for a minimum in the discrepancy functional[86]

$$\chi^{(j)} = \sum_{r}^{N}\left[\mathcal{S}p^{(j)}(r) - \sum_{i=1}^{m} k_i^{(j)} Sp_i(r)\right]^2\ , \quad (9)$$

where the summation is carried out with respect to N points in the spectrum. The method based on this criterion is well known as the method of least squares. Both the experimentally measured spectra and model functions of the exponential, Gaussian, Lorentzian, etc. types can be used as the spectra Sp_i.[86] The parameters of the resolution to be determined are the weighting factors $k_i^{(j)}$ and the parameters of the model functions.

In the second case, or in the case of a complete set of weighting factors, all the coefficients $k_i^{(j)}$ are known, the order of the system of initial equations is $n = m$, and the basis spectra Sp_i are to be determined. Eqns (8) reduce to a system of linear algebraic equations. The main problem in its solution is that of determinedness.[87,88] The interpretation of the AWDS spectra of disperse silicas, the problem of the resolution of the overall spectrum into those of the core and the hydroxyl and water components arose naturally. From the mathematical standpoint, it involved the resolution of the compound spectrum when neither the basis spectra nor the corresponding weighting factors were fully known. A differential-correlation method was proposed for the solution of this problem.[85] It involves the construction of a physically significant basis Sp_i for the system, which is based on the equation

$$Sp_i = \sum_{j=1}^{n} æ_i^{(j)} \mathcal{S}p^{(j)}\ ,\ i = 1,\ 2,\ \ldots,\ m, \quad (10)$$

on the assumption that there is no linear correlation between the basis spectra Sp_i. This requirement was formulated as the criterion of a zero correlation coefficient of the basis spectra (the ZCC criterion), which is an analogue of the condition for the orthogonality of n-dimensional vectors. In other words, if the components of the complex system can be regarded as independent, then their basis spectra are also not correlated. Using the expression for the second moment of the standard deviations of two physical quantities,[86] it is possible to obtain a mathematical expression for this criterion in the form

$$\rho = \frac{\sum_{r}^{N}\left[Sp_i(r) - \overline{Sp_i}\right]\left[Sp_k(r) - \overline{Sp_k}\right]}{\left\{\sum_{r}^{N}\left[Sp_i(r) - \overline{Sp_i}\right]^2 \sum_{r}^{N}\left[Sp_k(r) - \overline{Sp_k}\right]^2\right\}^{1/2}}\ , \quad (11)$$

where

$$\overline{Sp_i} = \frac{1}{N}\sum_{r}^{N} Sp_i(r)\,, \quad (12)$$

represents the average spectral line, and N denotes the number of points in the spectrum. The condition involving the equality $\rho = 0$ implies that the numerator in Eqn (11) is zero, which is represented conventionally as follows:

$$C(Sp_i, Sp_k) = 0\ . \quad (13)$$

It is easy to show that Eqn (13) is valid not only for the pair of spectra Sp_i and Sp_k but also for their linear combinations of the type

$$C\left(Sp_i, \sum_{s\neq 1}^{m} k_s\, Sp_s\right) = 0\,,$$

or

$$C(Sp_i + Sp_l, \sum_{s\neq i,l}^{m} k_s\, Sp_s) = 0. \quad (14)$$

The practical employment of the ZCC criterion begins with finding the simplest linear combination (10) in order to express the left-hand component in Eqn (14). In the limit, it is a simple difference $D\mathcal{S}p^{(ij')} = \mathcal{S}p^{(j)} - \mathcal{S}p^{(j')}$. This difference spectrum should correctly reproduce either the form of the Sp_i spectrum or the sum of the spectra $Sp_i + Sp_l$, i.e. it should define them to within a constant multiplier. The right-hand component in Eqn (14) can be represented as the residual spectrum

$$R\mathcal{S}p^{(iij')} = \mathcal{S}p^{(j)} - a^{(iij')}D\mathcal{S}p^{(ij')},$$

where $a^{(iij')}$ is a parameter ensuring the absence of correlation between the spectra $R\mathcal{S}p^{(iij')}$ and $D\mathcal{S}p^{(ij')}$ in the form of Eqn (14).

By solving Eqns (14) for $a^{(iij')}$, we find the required value of this parameter:

$$a_0^{(iij')} = \frac{\sum_r^N D\tilde{\mathcal{S}}p^{(ij')}(r)\tilde{\mathcal{S}}p^{(j)}(r)}{\sum_r^N \left[D\tilde{\mathcal{S}}p^{(ij')}(r)\right]^2}, \qquad (15)$$

where

$$D\tilde{\mathcal{S}}p^{(ij')} = D\mathcal{S}p^{(ij')} - \overline{D\mathcal{S}p}^{(ij')},$$

while

$$\tilde{\mathcal{S}}p^{(j')} = \mathcal{S}p^{(j)} - \overline{\mathcal{S}p}^{(j')}.$$

The bar above the expression denotes the average spectral lines [Eqn (11)]. The spectrum $a_0^{(iij')}D\mathcal{S}p^{(ij')}$ represents either the basis spectrum Sp_i or the sum of the basis spectra $Sp_i + Sp_l$. On the other hand, the residual spectrum

$$R_0\mathcal{S}p^{(iij')} = \mathcal{S}p^{(j)} - a_0^{(iij')}D\mathcal{S}p^{(ij')}$$

describes the residual combination of basis spectra entering into $\mathcal{S}p^{(j)}$ after the subtraction of the spectrum $a_0^{(iij')}D\mathcal{S}p^{(ij')}$ from the latter. By repeating this procedure and scanning with respect to the indices j and j', it is possible to determine the entire set of basis spectra $\{Sp_i\}$. This method has been used successfully to obtain the basis spectra of aerosil, silica gel, and aerogel.[25-27]

IV. Vibrational spectra of disperse silicas

1. Aerosil

a. Specimens and initial spectra

An air-dry specimen of the aerosil A380 is a powder consisting of small spherical particles with a specific surface of 380 $m^2\ g^{-1}$. According to low angle X-ray measurements, the average particle size is 150 Å.[19] After the specimen had been heated in air for 6 h at 750 °C, dried A380 was obtained. In its turn, the dried specimen was subjected to isotopic substitution of hydrogen atoms in the hydroxyl and water shells by deuterium atoms in the following sequence: three heating steps in air (750 °C, 4 h) with subsequent cooling in heavy water vapour to room temperature. This resulted in the formation of a deuteriated A380 specimen.

The set of these three specimens comprised the aerosil A380 family. The time-of-flight INS spectra of the specimens of this family together with the AWDS spectra obtained in accordance with Eqn (6) are presented in Fig. 6. In addition to the spectra of the three specimens indicated above, the figure presents the $N(t)$ and AWDS spectra of the glass obtained by sintering the aerosil. In a certain sense, these are reference spectra representing the spectrum of the bulk-phase vibrations of close-packed silica (see below).

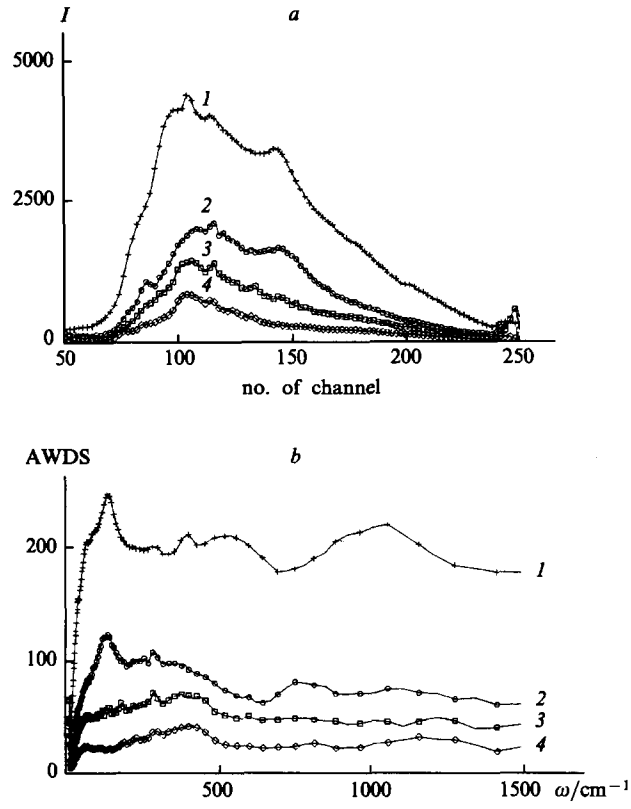


Figure 6. Experimental vibrational spectra of the A380 aerosil family ($T = 10$ K):[20] (*a*) time-of-flight INS spectra; (*b*) AWDS spectra; (*1*) air-dry specimen; (*2*) dried specimen; (*3*) deuteriated specimen; (*4*) aerosil glass.

b. Basis spectra of components of aerosil

Formulation of the problem of the resolution of the initial spectra. The spectra of the aerosil components constitutes a set of three basis spectra $\{Sp_i\}$, where the indices $i = 1, 2, 3$ correspond to the spectra of the water shell, the OH shell, and the silica core. Whereas the physical significance of the basis spectrum Sp_3 is fairly clear, a more detailed consideration is needed for the first two spectra. Apart from the vibrations of water and the hydroxy-groups, they include the vibrations of groups of atoms with which these differentiated systems interact. Thus one should include in the vibrational spectrum of the hydrate shell the vibrations of the silicon–oxygen centre (with the corresponding composition) linked to it. The number of such centres, interacting with water, is known[1,5] to be much smaller than the total number of hydroxy-groups on the surface even under the conditions of the complete saturation of the surface by adsorbed water. The remaining three groups form the hydroxyl shell. The vibrations of these groups constitute the basis of the vibrational spectrum of the hydroxyl shell. However, in addition to this, the vibrations of the surface silicon atoms and of the oxygen of the silica core make an appreciable contribution to the given vibrational spectrum. The above two types of vibrations affect the hydrogen atoms of the hydroxy-groups participating in the corresponding vibrational motions as a consequence of the familiar 'riding effect'.[18,19]

The experimental AWDS spectra of the initial and modified aerosils normalised with respect to 100 g of the mass of the specimen give rise to the set $\{\mathcal{S}p^{(j)}(\omega)\}$, in which the quantities $j = 1, 2, 3$ correspond to the spectra of the air-dry, dried, and deuteriated specimens. If the partial spectra of the air-dry specimen are designated as the basis spectra, then Eqns (8) assume the form (overleaf):

$$\mathcal{S}p^{(1)} = Sp_1^{(1)} + Sp_2^{(2)} + Sp_3^{(3)} ,$$
$$\mathcal{S}p^{(2)} = \alpha_1 Sp_1^{(1)} + \alpha_2 Sp_2^{(2)} + \alpha_3 Sp_3^{(3)} , \quad (16)$$
$$\mathcal{S}p^{(3)} = \beta_1 Sp_1^{(1)} + \beta_2 Sp_2^{(2)} + \beta_3 Sp_3^{(3)} .$$

Before proceeding to the construction of this basis, it is necessary to derive the relations between the coefficients of Eqn (16), the knowledge of which makes it possible to optimise the construction of the difference spectra. We shall consider this procedure in relation to aerosil. The parameters α_3 and β_3 are determined from the equality

$$Sp_3^{(1)} = \alpha_3 Sp_3^{(1)} = \beta_3 Sp_3^{(1)} ,$$

which follows from the identity of the spectra of the silica core in all the specimens. Thus

$$\alpha_3 = 1, \quad \text{and} \quad \beta_3 = 1 . \quad (17a)$$

It is known from literature data [1] that, when aerosil is dried at 750 °C, the adsorbed water and some of the hydroxy-groups are fully removed from the surface and the following two relations are established thereby:

$$\alpha_1 = 0, \quad \text{and} \quad \alpha_2 < 1 . \quad (17b)$$

The weighted contributions of the partial spectra of water and the hydroxyl shell to the spectrum of the deuteriated specimen $\mathcal{S}p^{(3)}$ must be much less than unity because, as a consequence of the strong suppression of the scattering by hydrogen nuclei, the intensity of the scattering by this specimen is much lower than the intensity of the scattering by the air-dry specimen, which follows from Fig. 6. Thus

$$\beta_1 \ll 1, \quad \text{and} \quad \beta_2 \ll 1 . \quad (17c)$$

It is also known [1] that the percentage content of the atoms substituted as a result of deuterium exchange in the water and hydroxyl shells is fairly accurately the same, so that

$$\beta_1 = \beta_2 = \beta . \quad (17d)$$

Thus the following conditions are imposed on the coefficients of Eqn (16):

$$\begin{aligned} &\alpha_3 = 1, \quad 0 < \beta_1 < 1 \\ &\beta_3 = 1, \quad 0 < \beta_2 < 1 \\ &\alpha_1 = 0, \quad \beta_1 = \beta_2 = \beta \\ &\alpha_2 < 1. \end{aligned} \quad (18)$$

In conformity with Eqns (18), the system of basic Eqns (16) is transformed into

$$\mathcal{S}p^{(1)} = Sp_1^{(1)} + Sp_2^{(1)} + Sp_3^{(1)}$$
$$\mathcal{S}p^{(2)} = 0 + \alpha_2 Sp_2^{(1)} + Sp_3^{(1)} \quad (19)$$
$$\mathcal{S}p^{(3)} = \beta Sp_1^{(1)} + \beta Sp_2^{(1)} + Sp_3^{(1)} .$$

Construction of the basis. When the differential-correlation method for the resolution of the spectrum of multicomponent systems is used, there is a possibility of a set of different versions determined by the selection of the initial difference spectrum in Eqns (14). It has been shown that [25-27] the same final result is then achieved with an adequate accuracy. We shall consider as an example one such version. We construct the initial difference spectrum in the form

$$D\mathcal{S}p^{(13)} = \mathcal{S}p^{(1)} - \mathcal{S}p^{(3)} . \quad (20)$$

It is a linear combination of the basis spectra Sp_1 and Sp_2 and, in conformity with Eqns (19), it assumes the form

$$D\mathcal{S}p^{(13)} = (1-\beta)[Sp_1^{(1)} - Sp_2^{(1)}] . \quad (21)$$

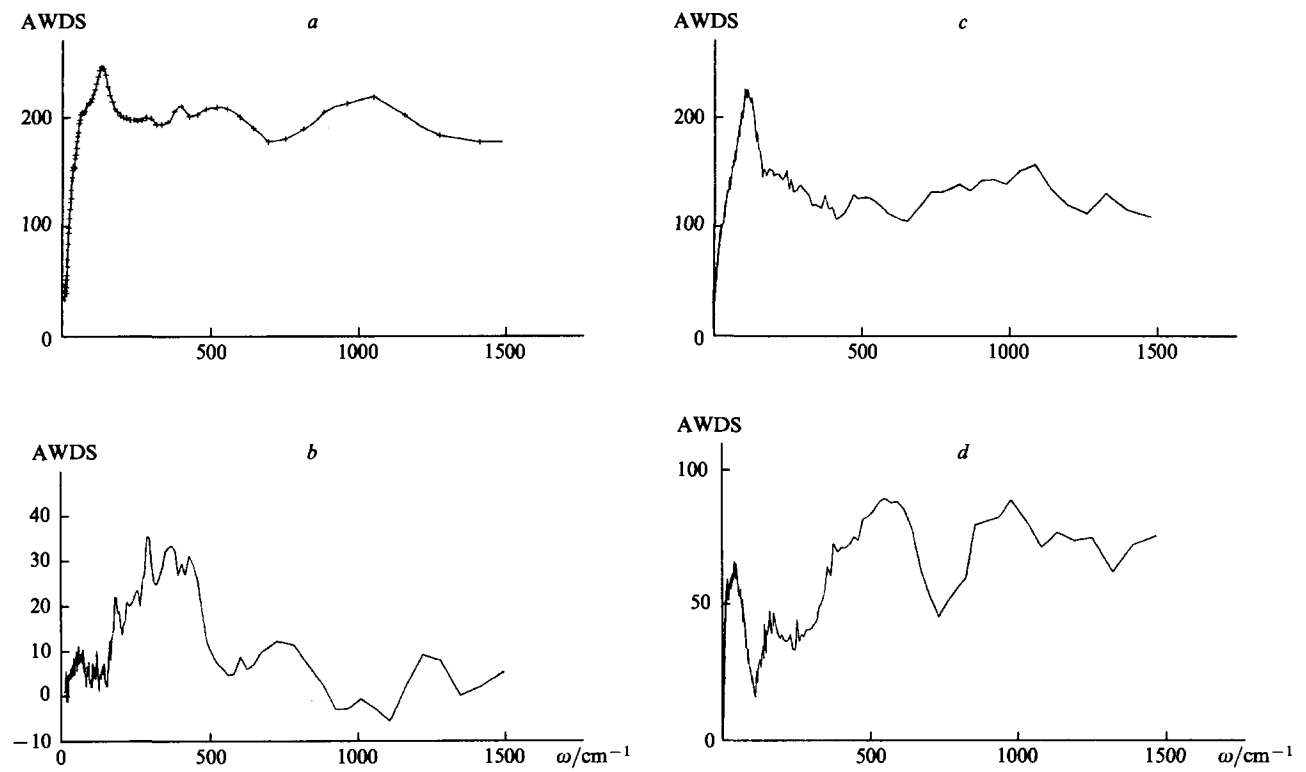


Figure 7. Overall AWDS spectrum of an air-dry specimen (*a*) and the basis spectra of the components of the aerosil A380: (*b*) core; (*c*) hydroxyl shell; (*d*) adsorbed water ($T = 10$ K).[25]

We construct the residual spectrum

$$R\mathcal{S}p^{(113)} = \mathcal{S}p^{(1)} - a^{(113)}D\mathcal{S}p^{(13)}, \quad (22)$$

and impose the requirement that it is not correlated with the spectrum $D\mathcal{S}p^{(13)}$,i.e. that condition (14) holds in the form

$$C(R\mathcal{S}p^{(113)}, D\mathcal{S}p^{(13)}) = 0 . \quad (23)$$

Ultimately we obtain the spectra

$$a_0^{(113)}D\mathcal{S}p^{(13)} = Sp_1^{(1)} + Sp_2^{(1)} , \quad (24)$$
$$R_0\mathcal{S}p^{(113)} = Sp_3^{(1)} .$$

The corresponding coefficient $a_0^{(113)}$ is calculated by Eqn (15).

We now consider the difference spectrum

$$D\mathcal{S}p^{(21)} = \mathcal{S}p^{(2)} - Sp_3^{(1)} . \quad (25)$$

According to Eqns (19), it is given by $\alpha_2 Sp_2^{(1)}$, i.e. it represents the partial spectrum of the hydroxyl shell in the spectrum of the dried A380. Using the difference spectra $a_0^{(113)}D\mathcal{S}p^{(13)}$ and $D\mathcal{S}p^{(21)}$ obtained, we construct the residual spectrum

$$RD\mathcal{S}p = a_0^{(113)}D\mathcal{S}p^{(13)} - a^{(21)}D\mathcal{S}p^{(21)}, \quad (26)$$

and impose the requirement that the ZCC conditions hold between this spectrum and the spectrum $D\mathcal{S}p^{(21)}$ in the form

$$C(RD\mathcal{S}p, D\mathcal{S}p^{(21)}) = 0 . \quad (27)$$

Having determined $a_0^{(21)}$ in conformity with Eqn (15), we obtain

$$a_0^{(21)}D\mathcal{S}p^{(21)} = Sp_2^{(1)}, \quad \text{and} \quad R_0D\mathcal{S}p = Sp_1^{(1)} . \quad (28)$$

Thus the basis of Eqns (19) has been constructed. Fig. 7 presents the AWDS spectra of an air-dry aerosil specimen together with the spectra of its three components.[25] It has been established[24] that the initial spectra of air-dry aerosils with different specific surfaces (and particle sizes) agree satisfactorily, so that the basis spectra constructed refer to the entire class of aerosils.

2. Silica gels

a. Specimens and initial spectra

The series of studies under discussion dealt with the vibrational spectra of two families of silica gels originating from industrial specimens of type KSM-G (lumpy, finely porous, granulated silica) manufactured by the Mendeleev Chemical Factory and characterised by different pore sizes, namely 20 and 100 Å (SG20 and SG100 respectively). The family of each silica gel included three specimens:[26] $j = 1$ — air-dry initial industrial specimen stored at room temperature and under the usual conditions of humidity; $j = 2$ — dry specimen obtained from the initial specimen by drying in air for 72 h at 135 °C; $j = 3$ — deuteriated specimen obtained from the initial specimen as a result of three drying cycles at 135 °C with subsequent maintenance for 24 h in heavy water vapour at room temperature.

An additional study was made of the spectrum of rapidly frozen water, which is necessary for the comparative analysis of the spectrum of the aqueous component.

The experimental INS spectra of specimens belonging to the SG20 and SG100 families and the corresponding AWDS spectra obtained in conformity with Eqn (6) have been described in detail.[20]

b. Basis spectra of components of silica gels

The procedure used to obtain the basis spectra of silica gels is similar to that described above for aerosil with the sole difference that, as a consequence of somewhat different relations between the coefficients of Eqn (16), the basic system of equations assumes the form[26]

$$\begin{aligned} \mathcal{S}p^{(1)} &= Sp_1^{(1)} + Sp_2^{(1)} + Sp_3^{(1)} , \\ \mathcal{S}p^{(2)} &= \alpha_1 Sp_1^{(1)} + Sp_2^{(1)} + Sp_3^{(1)} , \\ \mathcal{S}p^{(3)} &= \beta Sp_1^{(1)} + \beta Sp_2^{(1)} + Sp_3^{(1)} . \end{aligned} \quad (29)$$

Figs 8 and 9 present the spectra of air-dry specimens together with the basis spectra of their components. Two features of the spectra obtained are striking. First, the basis spectra of the test silica gel specimens are significantly different. This factor, i.e. the

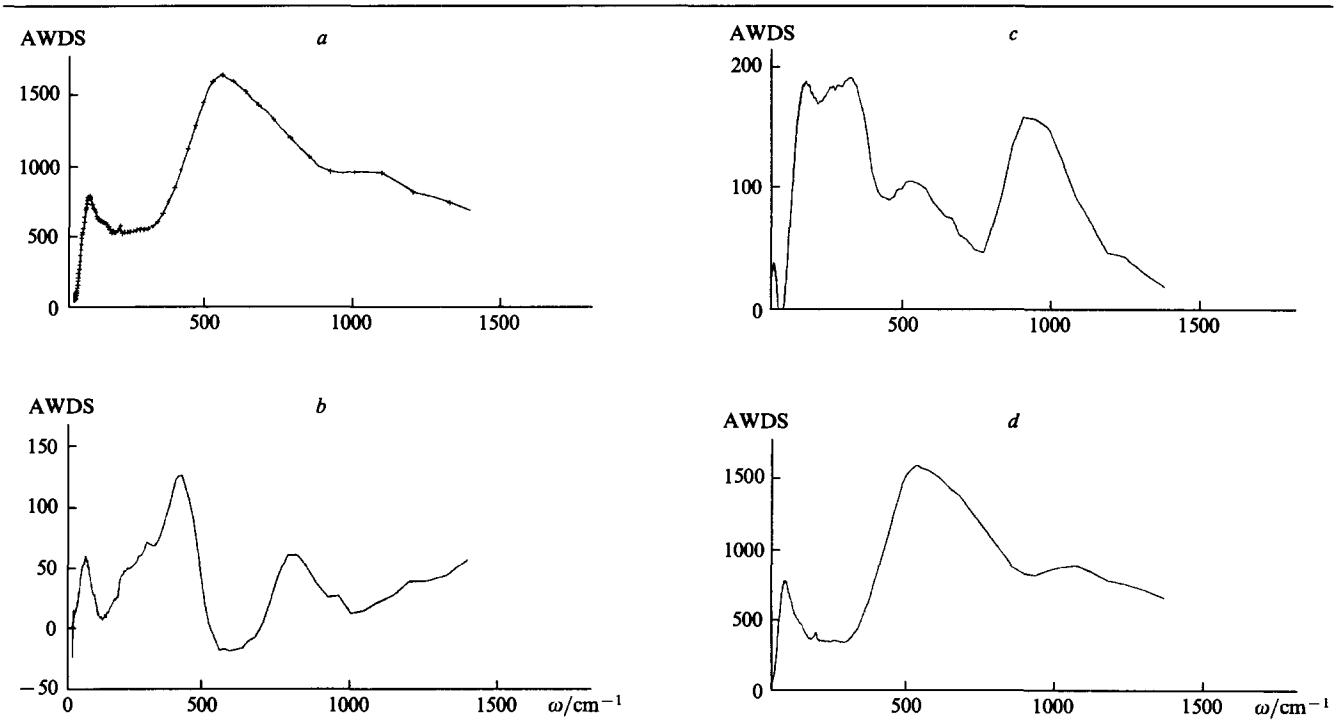


Figure 8. Overall AWDS spectrum of an air-dry specimen (*a*) and the basis spectra of the components of the silica gel SG20: (*b*) core; (*c*) hydroxyl shell; (*d*) aqueous component ($T = 10$ K).[26]

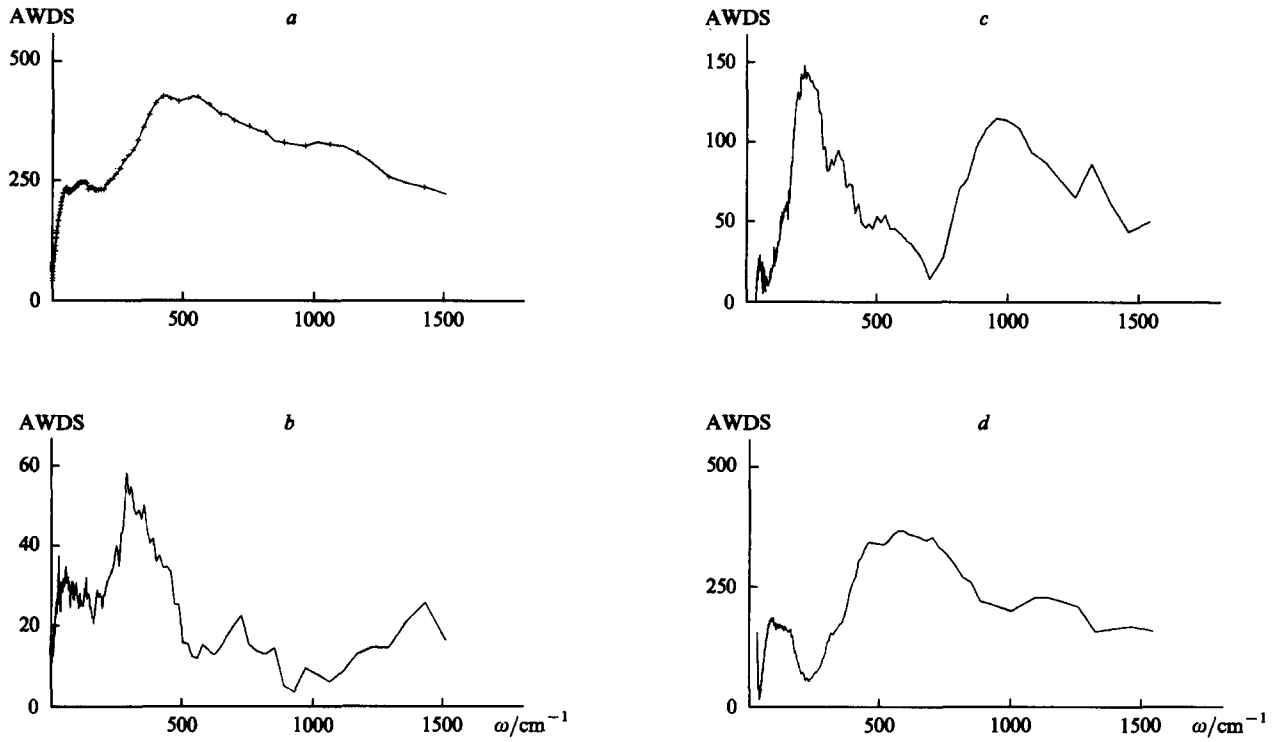


Figure 9. Overall AWDS spectrum of an air-dry specimen (*a*) and the basis spectra of the components of the silica gel SG100: (*b*) core; (*c*) hydroxyl shell; (*d*) aqueous component ($T = 10$ K).[26]

poor reproducibility of the absorption spectra of silica gels, has also been noted in the study of their IR absorption.[8,11,12] As will be shown below, this difference is not associated with the difference between the values of the numerical parameter describing the pore sizes and is determined by the exceptional lability of the structure of the silica gels, as a consequence of which it is virtually impossible in principle to achieve the reproducibility of the spectra on passing from one silica gel specimen to another.

The second feature concerns the basis spectra of the water shells. In contrast to aerosil with its globular structure, in the porous structures of silica gels water may be not only adsorbed but may be also retained in a quasi-free form. Therefore, in characterising the aqueous component of this substance, it is more correct to speak of the retained water. Fig. 10 presents the AWDS basis spectra of the aqueous components of the silica gels SG20 and SG100 together with the spectra of the rapidly frozen water. Despite the clear-cut difference between the spectra of the aqueous components of both specimens, the similarity of both spectra of the rapidly frozen water is striking. Such an evident similarity, which has been observed also by other investigators[45,56] (Figs 3 and 4), confirms the earlier conclusion[56] that the silica gel pores contain water of two types: water adsorbed on the inner surfaces of the pores and quasi-free water.

In conformity with this view, it has been postulated[26] that the basis spectra *1* and *2* in Fig. 10*a* consist of the spectra of the adsorbed and quasi-free water. The observed difference between the spectra of water in the silica gels SG20 and SG100 can then be explained qualitatively. The finely porous silica gel SG20 contains more water [about 16 mass% (it is known that the smaller the pore, the greater the amount of water retained in it as a consequence of the greater surface tension)][1] and its main bulk comprises quasi-free water. This is the reason why the AWDS spectrum of the water component of SG20 is in this case so similar to the spectrum of rapidly frozen water. Owing to the large pore size, silica gel SG100 retains less water (~5 mass%) and its AWDS spectrum therefore manifests the spectrum of the adsorbed water, which is almost completely masked in the first case. [A similar conclusion has been reached by Li et al.[56] (Figs 4 and 5).]

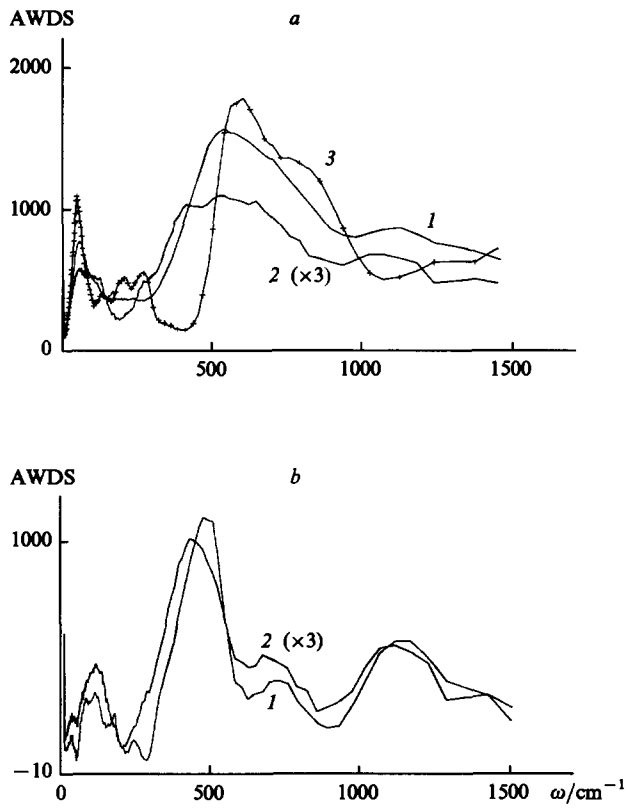


Figure 10. AWDS basis spectra of the aqueous components of silica gels ($T = 10$ K):[26] (*a*) overall spectra; (*b*) spectra of adsorbed water; (*1*) silica gel SG20; (*2*) silica gel SG100; (*3*) rapidly frozen water.

The spectra of water of both types have been obtained separately by means of qualitative analysis using the differential-correlation method for the resolution of the spectra of a complex system. It was postulated that the quasi-free and adsorbed water are separated in space. As in the case of aerosil, the adsorbed water is understood as complex structural formations incorporating water molecules interacting with the adsorption centres. It has also been postulated that the internal coordinate systems of the adsorbed and quasi-free water are independent, so that their vibrational spectra should not be correlated if one disregards the false correlation induced by the random coincidence of the frequencies of the vibrational modes.

The procedure used to resolve the initial basis spectra of the aqueous components were as follows.[26] In conformity with Eqns (16), it is possible to set up the following system of equations:

$$\begin{aligned} \mathcal{S}p^{(1)}(\omega) &= Sp_1 + Sp_2 \ , \\ \mathcal{S}p^{(2)}(\omega) &= \alpha_1 Sp_1 + \alpha_2 Sp_2 \ , \\ \mathcal{S}p^{(3)}(\omega) &= \beta Sp_1 \ , \end{aligned} \tag{30}$$

where superscript j denotes the number of the initial spectrum: $j = 1$ corresponds to the AWDS basis spectrum $Sp_1^{(1)}$ of the water shell of the silica gel SG20 (curve *1*, Fig. 10*a*), $j = 2$ corresponds to the AWDS basis spectrum $Sp_1^{(1)}$ of the silica gel SG100 (curve *2*, Fig. 10*a*), and $j = 3$ corresponds to the AWDS spectrum of 1 g of the rapidly frozen water (curve *3*, Fig. 10*a*).

The quantities Sp_1 and Sp_2 in Eqns (30) denote the basis spectra of the quasi-free and adsorbed water, which are assumed to be the same for both silica gels. On the basis of studies[55,56] in which it is claimed that the INS spectra of free ice and the ice within the pores are virtually maintained [remain the same?], it was postulated that the vibrational spectrum of free water $\mathcal{S}p^{(3)}$ determines the form of the basis spectrum Sp_1.

If one constructs two difference spectra

$$\begin{aligned} D\mathcal{S}p^{(13)} &= \mathcal{S}p^{(1)} - a^{(13)}\mathcal{S}p^{(3)} \ , \\ D\mathcal{S}p^{(23)} &= \mathcal{S}p^{(2)} - a^{(23)}\mathcal{S}p^{(3)} \ , \end{aligned} \tag{31}$$

and imposes the requirement that the ZCC criterion holds in the form

$$\begin{aligned} C(D\mathcal{S}p^{(13)}, \mathcal{S}p^{(3)}) &= 0, \\ C(D\mathcal{S}p^{(23)}, \mathcal{S}p^{(3)}) &= 0, \end{aligned} \tag{32}$$

then, by solving these equations it is possible to determine the coefficients $a_0^{(13)}$ and $a_0^{(23)}$ in accordance with Eqn (15) and to obtain the spectra $D_0\mathcal{S}p^{(13)} = Sp_2(1)$ and $D_0\mathcal{S}p^{(23)} = Sp_2(2)$. These spectra are presented in Fig. 10*b*. They proved to be virtually identical. The percentage contents of free (η_{fr}) and adsorbed (η_{ad}) water in the test silica gel specimens corresponding to the coefficients $a_0^{(13)}$ and $a_0^{(23)}$ are presented in the equations for the ZCC criterion [Eqns (32)].[26]

Specimen	η_{fr}	η_{ad}
Silica gel SG20	14.0	3.7
Silica gel SG100	1.8	1.3

However, the identity of the AWDS spectra of the adsorbed water in the two silica gels is surprising against the background of the large difference between their two other basis spectra. This finding is apparently based on the competition between two processes: the formation of a 'drop' of the quasi-free water and adsorption. Evidently, among the set of silicon–hydroxyl centres of three types, forming the hydroxyl shell of silica gel and ensuring the adsorption of water, only one centre may prove capable of competition (otherwise, the water would not have collected into drops). Naturally, this centre is the same in each silica gel, which is in fact the reason for the identity of the AWDS spectra of the water adsorbed on it. As will be shown below, this explanation received a well-founded confirmation in the quantum-chemical modelling of the model structures of silica gels.

3. Aerogel

a. Specimens and initial spectra

The test specimen of the aerogel AG200[27] consisted of a monolithic lump of a solid substance with a mass density of 200 kg m^{-3}. The specimen, stored in air, was initially air-dry; it was dried in air at 100 °C for seven days, which resulted in a dried specimen. The latter was in its turn subjected to the H → D isotope exchange. The specimen was maintained at 100 °C under atmospheric conditions for 12 h and was then placed in a desiccator, where it was kept for 12 h in heavy water vapour. The cycle was repeated with the specimen maintained for 6 h at each stage, which resulted in a deuteriated specimen. The time-of-flight INS spectra of the family of the above aerogel specimens and the corresponding AWDS spectra, obtained in conformity with Eqn (6), have been described in detail.[27]

b. Basis spectra of the components of the aerogel

In contrast to aerosil and silica gels, the chemistry of the surface of the aerogel has been studied to a much lesser extent. The initial inferences concerning the structure of the aerogel surface were made on the basis of the analysis of the chemical-technological process involving its preparation. According to the scheme employed in this process,[3] the principal component of the aerogel cores is a siloxane chain and the main contribution to the hydrogen-containing surface region comes from the hydroxy-groups, the number of which increases with increase in the length of the polymer chain.

In the isolated chains, each silicon atom of the siloxane core is linked to two hydroxy-groups. Consequently, the polymer structure formed consists of a chain of silanediol groups. On the other hand, if the chains are cross-linked in pairs, giving rise to a strip, then the silicon atoms of the strip each carry only one hydroxy-group. It has been suggested that this type of cross-linking process actually occurs in gel formation.[3]

The presence of silanol or silanediol groups on the surface of the silica core usually leads to the adsorption of water under atmospheric conditions. The existence of adsorbed water on the surface of the aerogel has been confirmed by the mass-spectrometric study of the products desorbed from its surface on heating to 100–150 °C.[3] This is also indicated by the analysis of the measured INS spectra.[27] Thus, when the specimen is dried under conditions corresponding to the preferential desorption of water, its vibrational spectrum undergoes a significant change in form and its integral intensity diminishes almost by a factor of two. Comparison of the AWDS spectra within the family of the AG200 specimens shows that the maintenance of the initial AG200 specimen in heavy water vapour reduces the intensity of the spectrum almost by a factor of three. This shows that the surface region of the air-dry aerogel contains an appreciable number of hydrogen atoms, because isotope exchange is concentrated mainly in this region. The marked smearing of the structure of the spectrum on raising the temperature may be regarded as another confirmation of the presence of water in the surface region of the aerogel.[27] Such smearing is similar to that observed in the spectra of air-dry aerosil and silica gel specimens,[22] which has been attributed to the facilitation of the diffusion of water on the surface with increase in temperature.

Thus the surface region of the air-dry aerogel contains hydroxy-groups and adsorbed water. By analogy with other disperse silicas, the aerogel becomes as a result of this a three-component system consisting of a silica core and hydroxyl and aqueous components.

The ratios of the coefficients in Eqn 16, describing three experimental spectra of aerogel specimens, proved similar to the ratios for silica gels, so that Eqns (29) serve as a basis also for the aerogel. By repeating the procedure described above for silica gel, it is possible to obtain a set of basis spectra of the aerogel, which

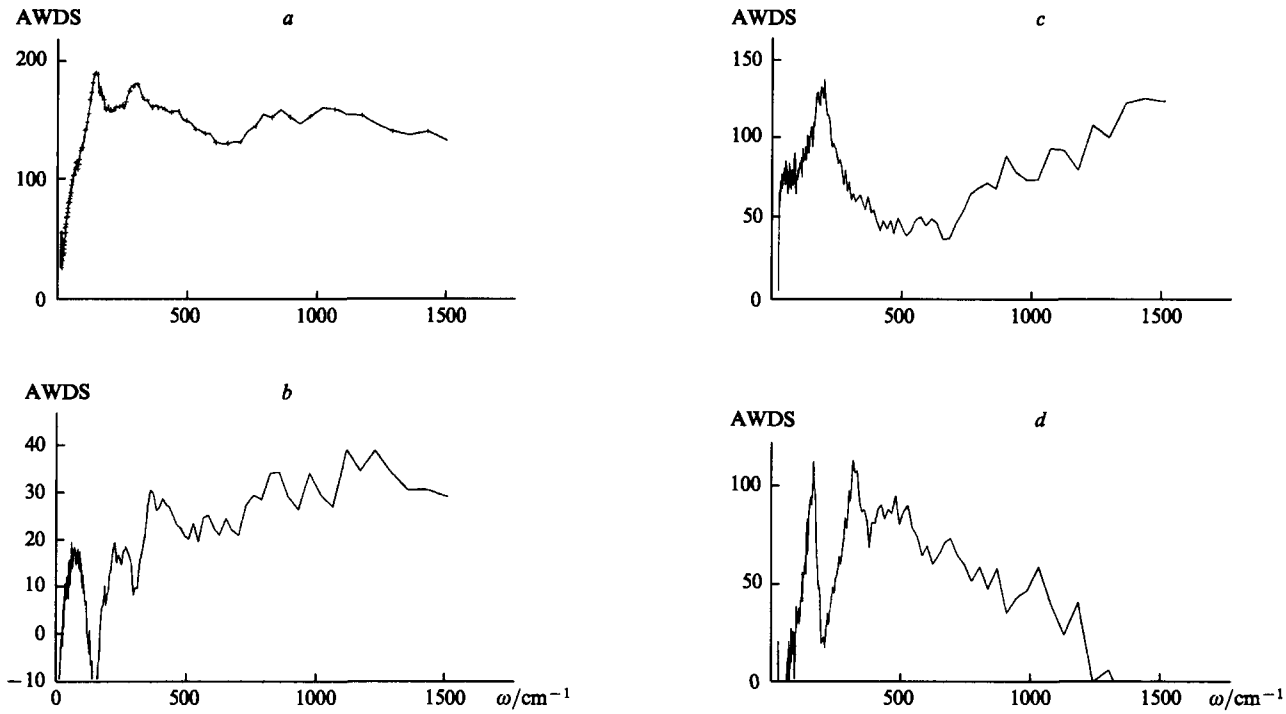


Figure 11. Overall AWDS spectrum of an air-dry specimen (*a*) and the basis spectra of the components of the aerogel AG200: (*b*) core; (*c*) hydroxyl shell; (*d*) adsorbed water ($T = 10$ K).[27]

are presented in Fig. 11 together with the spectra of the air-dry specimen. The clearly expressed 'quasi-molecular' structure of the spectra presented can be seen. As regards the vibrational spectrum of the core, its structure is more characteristic of polymers than a close-packed amorphous solid (see, for example, Gribov[89]). This agrees with the chain model of the aerogel core, which is a consequence of specific polymerisation and condensation processes in the preparation of disperse silica.[90] The narrow band form of the spectra of adsorbed water indicates, on the one hand, the absence of a collective interaction between the molecules, and, on the other, the same type of orientation of the adsorbed water molecules. The latter indicates in its turn a definite uniformity of the adsorption centres and that they are fairly widely scattered.

V. Comparative analysis of the vibrational spectra of disperse silicas and their components

1. Vibrational spectra of silica cores

The basis vibrational spectra of the cores of the test silicas are presented in Fig. 12. In addition, the figure shows (curve *2* in Fig. 12*a*) the vibrational spectrum of the glass obtained by sintering the aerosil A380. It is seen that the spectra of the cores of all the substances have a similar form and resemble the spectrum of the glass, which corresponds to the bulk-phase vibrations of close-packed silica (each consists of four bands located in the same spectral regions). At the same time, considerable differences are observed both between the spectra of disperse silicas and between the latter and the spectrum of the glass. This concerns the distribution of the intensities in each spectrum and of the absolute intensities of each of them. The vibrational spectrum of the aerosil core is closest to that of the spectrum of the glass, while the vibrational spectrum of the aerogel is most different. It is a remarkable fact that the spectra of the cores of the two silica gels investigated (SG100 and SG20) with different average core sizes (100 and 20 Å) differ significantly from one another.

Analysis of the differences observed in the form of the spectra can be conveniently begun with a brief description of the spectrum of the glass. Four bands in the regions 0–200 cm^{-1} (*I*), 200–500 cm^{-1} (*II*), 500–950 cm^{-1} (*III*), and 950–1300 cm^{-1} (*IV*) clearly stand out in this spectrum. According to the analysis of the vibrational spectrum of the free SiO_4^- ion[6] and the α-quartz crystal,[91] the deformation vibrations associated with the variation of the O–Si–O angle make the main contribution to region *II*. In regions *III* and *IV*, this role is assumed by the symmetrical and asymmetric stretching vibrations of the Si–O bond. Calculation of the vibrational spectra of a series of large model clusters has shown that this assignment can be extended also to amorphous structures. According to the calculation, region *I* of the vibrational spectrum of the core is made up of the vibrational modes of the translational motion of the atoms and the deformation vibrations associated with changes in the Si–O–Si angles. The assignment of the frequencies in regions *II*–*IV* agrees with that quoted above.

The aerosil glass and aerosil. As already stated, the spectra of this pair of substances (Fig. 12*a*) are closest to one another. A similar conclusion was reached on the basis of IR absorption spectra.[39] This finding undoubtedly indicates that the structure of the aerosil core is close-packed. The AWDS spectra of the glass show that the intensity of the bands in the ranges 0–220 cm^{-1} and 560–1500 cm^{-1} appreciably exceeds that of the aerosil spectrum. A detailed analysis of the difference spectrum suggested[25] that this difference is caused by the presence in the glass, in contrast to the 'absolutely dry' (by definition) aerosil core, of small amounts of adsorbed water. For a quantitative explanation of the observed difference, 0.3 mass%–0.5 mass% of water is sufficient. The possibility of the existence of such amounts of water in the glass has been confirmed by several pieces of chemical evidence.[6]

Silica gels. Regions *I*–*IV* again stand out clearly in the basis spectra of the silica gel cores (Figs 12*b* and 12*c*). However, a significant rearrangement of the spectra and an increase in their

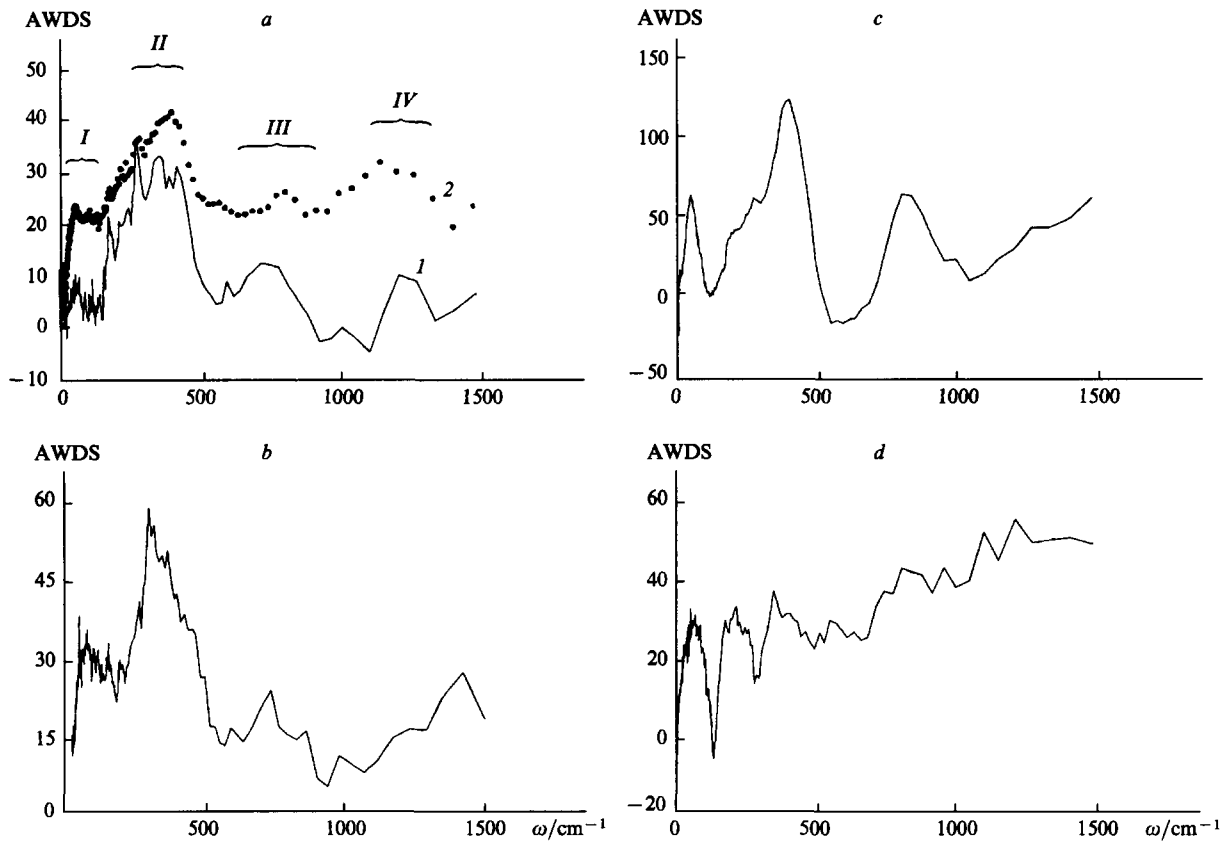


Figure 12. Basis vibrational spectra of the cores of disperse silicas (T = 10 K):[28] (*a*) aerosil A380 (curve *1*) and glass (curve *2*); (*b*) silica gel SG100; (*c*) silica gel SG20; (*d*) aerogel AG200.

intensity compared with the spectrum of aerosils are striking. The main characteristic feature of these spectra is, as stated above, the fact that they differ for different silica gels. This is manifested to the greatest extent in regions *I* and *II* corresponding to deformation vibrations. These changes can be understood if one postulates that a fairly broad distribution of the Si–O–Si and O–Si–O angles exists in the silica gels and that, on passing from one specimen to another, the distribution changes. The changes in the region of the deformation vibrations are accompanied by appreciable changes also in regions *III* and *IV* of the Si–O bond stretching vibrations. The combination of these findings permits the conclusion that the structures of the silica gels investigated differ from one another and that they all differ appreciably from the close-packed structure.

Aerogel. The principal characteristic feature of the basis vibration spectrum of the aerogel core (Fig. 12*d*) is its narrow band 'quasi-molecular' structure, as a result of which it resembles the vibrational spectra of polymers.[89] On the other hand, the narrow-band structure of the basis spectrum in regions *I* and *II* indicates narrow distributions of the deformation modes in the region where the angles in the silicon–oxygen tetrahedra vary, which indicates, in its turn, a quasi-regular structure of the test substance. Consequently, the aerogel core constitutes a new type of structure in addition to the aerosil and silica gel structures.

Comparative analysis of the basis vibrational spectra of the cores of the test silicas permitted the conclusion that there is a qualitative difference between the structures of these substances, which indicates the presence of several polymorphic modifications of disperse amorphous silica. The difference between the core structures entails also a difference between the structures of the surface regions of the test materials.

2. Vibrational spectra of the hydroxyl components

The basis vibrational spectra of the hydroxyl components of the set of disperse silicas under discussion are presented in Fig. 13. Despite the appreciable differences between the spectra, it is possible to distinguish in all of them two vibrational regions characteristic of and common to all of them: 0–380 cm^{-1} (*I*) and 700–1100 cm^{-1} (*II*). The differences between the spectra may be characterised in terms of the differences between the structures in these regions and also in terms of the intensity of the continuous spectrum of the support and the absolute intensity.

The torsional vibrations of the OH group relative to the Si–OH bond (region *I*) and the deformation vibrations of this bond (region *II*) make a significant contribution to the vibrational modes corresponding to the differentiated regions *I* and *II*. The third structural element of the basis spectra of the hydroxyl components is the vibrations of the set of atoms of the silica core affecting the hydroxy-groups (the 'riding effect').[18,19] This effect consists of the following features. The hydrogen atoms linked to the oxygen atoms of the hydroxy-group participate also in other vibrational modes, describing, for example, the deformation of the Si–O–Si and O–Si–O angles, the stretching and deformation vibrations of the Si–O bond, etc. Owing to the anomalously high sensitivity of neutron scattering to hydrogen atoms, there is a response to the set of core vibrations, so that the frequencies due to the corresponding support arise in the AWDS spectra of the hydroxyl components, the range of which coincides with the range of the bulk-phase vibrations of the base illustrated in Fig. 12.

The narrow-band structure of the vibrational spectra of the hydroxyl components of aerosil and aerogel in region *I* indicates a certain uniformity of the orientations of the OH groups relative to the silicon atoms to which they are bound. From this one may conclude that the hydroxy-groups on the surfaces of both

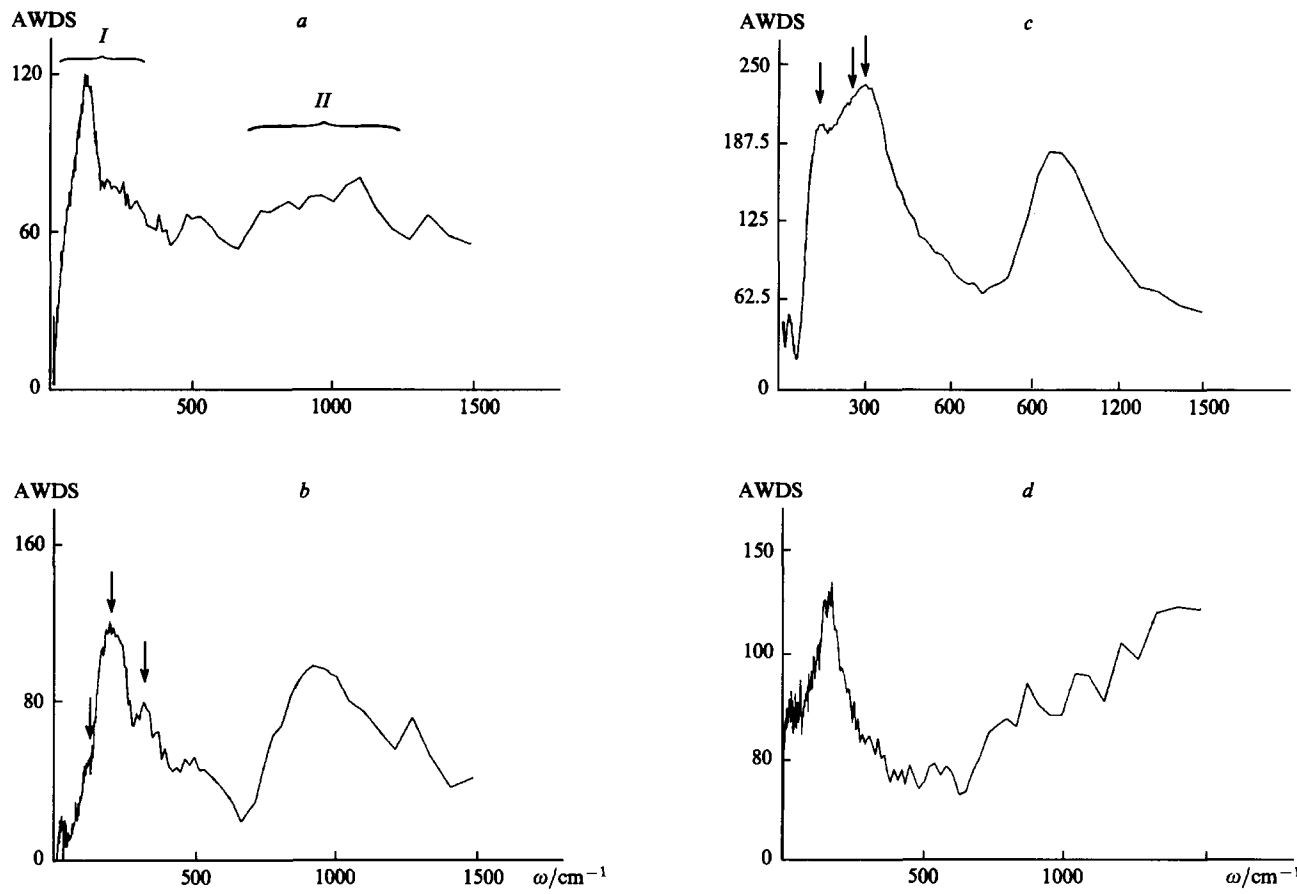


Figure 13. Basis vibrational spectra of the hydroxyl components of disperse silicas (T = 10 K): [28] (*a*) aerosil A380; (*b*) silica gel SG100; (*c*) silica gel SG20; (*d*) aerogel AG200.

substances are predominantly of the same type. This agrees with the results of studies on the structure of the hydroxyl coating on aerosil,[5] which established that 80%–85% of the surface hydroxy-groups are of the silanol type. The closeness in frequency of the first peaks in the aerosil and aerogel spectra and the similarity of their shapes suggests that silanol groups play the main role on the aerogel surface.

In contrast to the spectra of the hydroxyl components of aerosil and aerogel, the vibrational spectra of these components in different silica gels have a complex structure in region *I* and an intense and distinct peak in region *II*. The spectra of different silica gels also differ significantly from one another. The line intensities in the spectrum of the hydroxyl vibrations in the silica gel SG20 are twice as high as in the spectrum of the silica gel SG100. The principal structural differences are concentrated in region *I*: a redistribution of the intensities between the three characteristic peaks at frequencies of 80, 230, and 380 cm^{-1}, designated by arrows in Figs 13*b*, and 13*c*, is observed. The position of the first peak coincides with the positions of the peaks in the vibrational spectra of aerosil and aerogel.

The observed characteristics of the vibrational spectra of the hydroxyl components of silica gels have been explained qualitatively on the basis of the analysis of the possible structure of the hydroxyl shell on silicas.[28] The hydroxyl components may be made up of silicon–hydroxyl groups of three types: silanol $(OH)_1$, silanediol $(OH)_2$, and silanetriol $(OH)_3$. They all exhibit deformation vibrations of the Si–OH bond with similar frequencies,[5] so that the vibrational spectrum of the hydroxyl component of any composition should contain a band in the region of 1000 cm^{-1}, which can in fact be observed in the spectra in Fig. 13. We may note that the band in the spectra of silica gels is much more distinct than in the spectra of aerosil and aerogel.

The vibrational spectrum of the hydroxyl component of aerosil is in essence the vibrational spectrum of silanol groups. The difference between this spectrum and the vibrational spectra of the hydroxyl components of silica gels can be interpreted as evidence that the silanol groups, even if they are present in the hydroxyl component of the silica gel (which is indicated by the presence in the silica gel spectra of a peak with a maximum at 80 cm^{-1}), they are not the main element. It has been concluded that silanediol and silanetriol groups should participate in the formation of the hydroxyl components of silica gels. The possible presence of these groups in the loose structure of silica gel had already been reported.[40]

Thus the hydroxyl component of silica gel is a set of different silicon–oxygen groups, the weighting factors of which depend on the structure of the silica core. The difference between the structures of the silica cores of both silica gels determine also the different structures of the hydroxyl components.

3. Vibrational spectra of the adsorbed water

Fig. 14 presents the basis vibrational spectra of the aqueous components of aerosil, aerogel, and silica gel.[26]

The results of quantum-chemical calculations on the interaction of water with an isolated silanol centre have shown[92,93] that the nature of the vibrational modes changes significantly when the number of water molecules attached to the centre is altered.[93] In the case of a single molecule, the vibrational spectra of the water molecule coordinated to the silicon atom and the molecule bound to the centre by a hydrogen bond are strikingly characteristic. When the number of attached molecules reaches six, the overall spectrum acquires features typical for both characteristic spectra indicated above. However, in conformity with the analysis of the vibrational modes, the adsorption

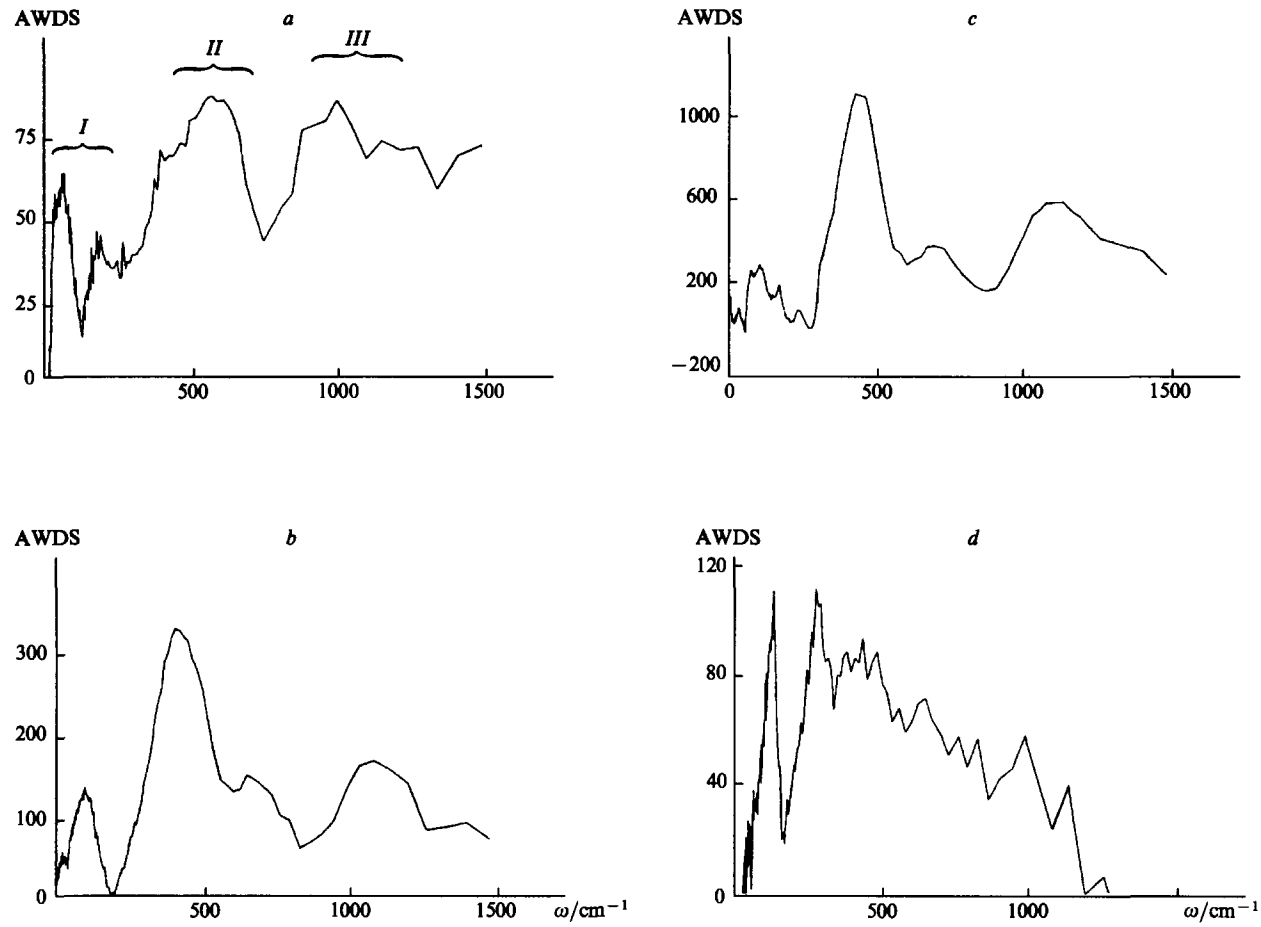


Figure 14. Basis vibrational spectra of water adsorbed on disperse silicas ($T = 10$ K):[28] (*a*) aerosil A380; (*b*) silica gel SG100; (*c*) silica gel SG20; (*d*) aerogel AG200.

complex vibrates under these conditions as a single whole in which the structurally differentiated coordinated and hydrogen-bonded molecules are not dynamically distinguishable. The details of this analysis can be found in the communication of Khavryuchenko and Sheka.[93] The characteristic nature of the vibrational spectra of single water molecules will be used below for a qualitative description of the characteristic features of the spectra illustrated in Fig. 14.

Three spectral ranges may be distinguished in these spectra. The low-frequency range 0–350 cm^{-1} (*I*) contains the stretching vibrational frequencies of the Si...OH_2 groups, the torsional vibrational frequencies of these groups, and the deformation vibrational frequencies of the hydrogen bonds of the interacting water molecules. The middle frequency range 350–850 cm^{-1} (*II*) is characterised by an intense structural peak and is mainly due to the deformation vibrations of the hydrogen bonds. This peak is the principal structural element in the spectrum of rapidly frozen water (Fig. 10*a*). The high-frequency region of the spectrum (850–1200 cm^{-1}) contains two peaks, which are associated with the deformation vibrations of the water molecule coordinated to the silicon atom and with the deformation vibrations of the Si–OH bond forming part of the adsorption centre.

The adsorbed water in the silicas investigated has been subjected to structural-dynamic analysis based on the above assignment of the vibrational modes.[28] The spectrum of the water adsorbed on aerosil shows that the adsorption of water on its surface is of a collective type, i.e. the water molecules form a 'quasi-drop' on the silanol centre during the adsorption process.[24,28,93] This hypothesis has been confirmed by calculations of the equilibrium configurations of the water molecules on large clusters, modelling the aerosil structure (see Section VII).

The spectrum of the water adsorbed on silica gel (Figs. 14*b* and 14*c*) differs significantly from the spectrum of water adsorbed on aerosil. This shows that the nature of the centres responsible for the adsorption of water on these silicas is different, which agrees with the conclusion reached in the previous section. Analysis of the spectrum of the water adsorbed on silica gel from the standpoint of the assignment of the frequency ranges *I*–*III*[28] led to the following conclusions. As in the case of aerosil, the adsorption of water on silica gel takes place collectively because the double peak in region *II* predominates in the vibrational spectrum. The form of this peak is similar to that of the analogous peak in the spectrum of rapidly frozen water (Fig. 10*a*), but the former is displaced towards lower frequencies and the ratio of the intensities of its components is different. This may be a consequence of the binding of the water 'drop' to the adsorption centre. Comparison of the spectra of water adsorbed on aerosil and silica gel shows that such binding of the drop is weaker in the case of silica gel than in the case of aerosil. The 900 cm^{-1} peak is absent from the spectrum of water adsorbed on silica gel, which indicates the virtually complete absence of coordinated water on the surface. The considerable width of the peak in region *I* indicates, as in the case of aerosil, the collective nature of the adsorption of water. The surprising coincidence of the spectra of adsorbed water for both silica gels noted above can be naturally explained by the above analysis and also the analysis of the structure of the hydroxyl shells of silica gels. Since these shells consist of a set of three silicon–hydroxyl groups, the water

molecule interacts with each independently, so that a competition of the groups in relation to the adsorption of water arises. The 'strongest' group, corresponding to the highest energy of the bonds between the water molecules and the centre, wins under these conditions. Since this group is one of the three indicated above, it should be the same both for the silica gel SG100 and the silica gel SG20. Thus the spectra of the adsorbed water should be identical for both silica gels and the difference between them reduces merely to the difference between the absolute intensities, which is associated with the fraction of the adsorption centres on the surfaces of silica gels differentiated in this way.

The AWDS spectrum of the water adsorbed on aerogel (Fig. 14*d*) differs markedly from the spectra presented above. In the first place, one should conclude that there is no distinct intense peak in region *II* of this spectrum, which indicates a significantly smaller number of hydrogen bonds between the water molecules on the aerogel surface. It has therefore been postulated[28] that the layer of adsorbed water is formed not by drops, as in the case of aerosil and silica gel, but predominantly by isolated molecules. This conclusion has also been confirmed by the distinctly structured nature of the vibrational spectrum of the low-frequency region *I*. The positions of the peak maxima in this region are nevertheless close to the positions of the peak maxima in the aerosil spectrum (Fig. 14*a*). This shows that the main water adsorption centre in aerogel is also a silanol group, which is in full agreement with the conclusions reached in the preceding section. The conclusion reached has been confirmed also by the presence of a maximum at 900 cm^{-1}. It is less pronounced than the maximum in the spectrum of water in aerosil but is observed quite reliably. According to Markichev et al.,[28] the change in the ratio of the intensities at the maxima in the spectra of water in aerosil and aerogel reflects the fundamentally different character of the adsorption in these substances: collective in the case of aerosil and individual in the case of aerogel. The latter conclusion is quite natural if we recall that water is adsorbed on the free outer surfaces of small aerosil particles. The steric hindrance to the formation of a drop is determined solely by the density of the silanol groups on the surface. It has been established experimentally that this density is such that it corresponds to an average distance between the silanol centres of ~ 7 Å.[6] This is sufficient for the formation of a quasi-drop, consisting of several water molecules, on an isolated silanol centre. In contrast to this, the active surface of aerogel is internal,[3] so that the role of steric hindrance to the formation of a quasi-drop is enhanced.

The above comparative analysis of the basis spectra of the components of the disperse silicas investigated made it possible to establish, despite its qualitative nature, that aerosils, silica gels, and aerogels should be regarded as fundamentally different structural formations. Here it is important to note that these differences extend to both bulk-phase, core structures and to the structures of the surface regions on these substances. Since the substances differ solely by the technology used in their preparation, the observed structural variability constitutes the phenomenon of technological polymorphism in an amorphous disperse silica.

VI. Technological polymorphism and classification of disperse amorphous silicas

The establishment of the existence of technological polymorphism in amorphous disperse silicas is important both intrinsically and as a basis for a new approach to the formulation of the problem of the computational modelling of these substances. In the development of this approach, it proved convenient to classify the observed modifications, formulating for each of them a set of distinctive features.[32] This was achieved by employing the principal crystal-chemical criteria proposed by Liebau.[94]

1. Fundamentals of the crystal chemistry of silicates

In his fundamental study, Liebau showed[94] that silicates are characterised by an extremely pronounced variability of their chemical and structural properties of a much greater extent than any other group of chemical compounds (with the exception of organic carbon compounds). At the same time, analysis of about 1000 compounds established that all the silicates can be divided into a small number of classes and subclasses in conformity with the classification based on the following fairly simple crystal-chemical principles:

1. Since the Si–O bond is the strongest in all the silicates investigated, the principal fragment determining the structure of the silicate is the polyhedron (SiO_n) and the type of structure is determined by the ways in which the polyhedra are linked to one another.

2. The coordination number of silicon (CN) in compounds having the general formula $M_xSi_yA_z$ and Si–A–M bonds tends to increase (CN > 4). This tendency is stronger the higher the electronegativity of the nearest neighbours — the A atoms. Oxygen has an intermediate electronegativity and may be incorporated in both the tetrahedra (SiO_4) and the octahedra (SiO_6), the tetrahedra being preferred.

3. The tetrahedra (SiO_4) are linked to one another usually via the vertices and not via their edges and faces.

4. One oxygen atom can participate in not more than two tetrahedra (SiO_4).

5. For each silicate anion, the difference between the number of junctions Δs between different tetrahedra (SiO_4) [where s is the number of junctions, i.e. the number of oxygen atoms in the tetrahedron (SiO_4) incorporated in other tetrahedra (SiO_4)] tends to decrease.

6. The bond lengths and bond angles tend to deviate from the average values $(Si-O)_{av} = 1.62$ Å, $(O-Si-O)_{av} = 107.47°$, and $(Si-O-Si)_{av} = 140°$ as little as possible. These six rules are not laws, exceptions to them being known,[94] but nevertheless their infringement is in most cases energetically unfavourable and therefore improbable.

A series of parameters have been introduced in order to describe the way in which the tetrahedra (SiO_4) are linked to one another in silicates. Without listing all the parameters, we shall consider the most important of these for further consideration, namely the dimensionality and multiplicity. The dimensionality of tetrahedral silicate structures D characterises the type of packing in the initial structural units and assumes the values $D = 0-3$. Thus isolated tetrahedra (SiO_4) as well as isolated cyclic and acyclic fragments have the dimensionality $D = 0$: $D = 1$ for isolated chains, $D = 2$ for isolated layers, and $D = 3$ for skeletal structures.[94] The multiplicity M characterises the formation of multiple tetrahedral structures with the same dimensionality as the initial structural units [isolated tetrahedra (SiO_4), isolated chains, isolated rings, and isolated layers].

The general nomenclature for silicates, presented in Table 3, has been introduced in conformity with the values of these parameters. Silicates with isolated tetrahedra (one, two, and three) belong to the class of oligosilicates. Silicates whose anions consist of rings comprising the tetrahedra (SiO_4) are referred to as cyclosilicates. Depending on whether they contain isolated, double, or triple rings, the prefixes mono-, di-, etc. are added to their names. Structures containing silicate chains are called polysilicates. They can be further subdivided into monopolysilicates with isolated chains, dipolysilicates with double chains or strips, etc. Phyllosilicates are made up of layers of tetrahedra (SiO_4); they can also be subdivided into mono- and diphyllosilicates. Silicates with a three-dimensional framework consisting of the tetrahedra (SiO_4) are called tectosilicates.

Further subdivision of silicates into subclasses is determined by the operation of the general parsimony principle, which presupposes that, for a specified composition, the system tends to have the minimum possible number of geometrically and chemically different groups.[94]

Table 3. The chemical nomenclature for silicates.[94]

Class	Dimensionality	Multiplicity (M)		
		1	2	3
Oligosilicates	0	Monosilicates	Disilicates	Trisilicates
Cyclosilicates	0	Monocyclosilicates	Dicyclosilicates	Tricyclosilicates
Polysilicates	1	Monopolysilicates	Dipolysilicates	Tripolysilicates
Phyllosilicates	2	Monophyllosilicates	Diphyllosilicates	Triphyllosilicates
Tectosilicates	3	Tectosilicates		

2. Classification of disperse silicas in conformity with the crystal chemistry of silicates

The principal crystal-chemical rules presented above contain nothing specific to crystal structures and it was therefore natural to suppose that they hold also in the case of amorphous structures.[32]

Crystalline silicates with mixed dimensionality and multiplicity are unknown in nature. This is apparently to be expected also for the amorphous state, so that amorphous structures can also be classified in accordance with Table 3. A specific feature of the test substances is the establishment of a classification mode for each of them, which is possible in the analysis of the technological procedure used in their preparation.[32]

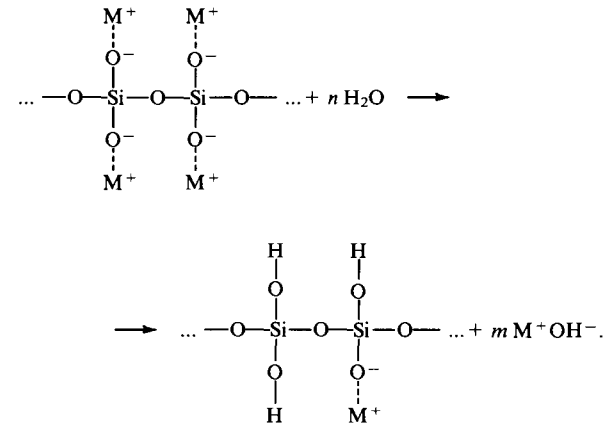
Disperse silicas are obtained under the conditions of the simultaneous occurrence and competition of two processes: the hydrolysis of the initial product, which leads to the formation of silicon–oxygen tetrahedra containing between one and four hydroxy-groups, and the subsequent polycondensation of these fragments.[1-3] Polycondensation results in the formation of the nucleus of the future structure of the final product: particles of aerosil, a silica gel sol, and an element of the capillary structure of aerogel. The technological procedures differ in the initial products subjected to hydrolysis, the medium in which these processes are carried out, and external conditions (temperature, pressure, etc.).

Aerosil. Silicon tetrachloride is used to obtain aerosil. It is hydrolysed in an oxygen–hydrogen flame at atmospheric pressure and a temperature of about 2000 K. The hydrolysis, which proceeds in accordance with the reaction

$$SiCl_4 + 4H_2O = 4HCl + Si(OH)_4 ,$$

results in the formation of orthosilicic acid, the product of the polycondensation of which is in fact aerosil. The solid nuclei formed in the plasma are carried away from this zone and enter a cold zone, forming larger agglomerates, which are virtually ideal spherical particles of amorphous silica. The process involving polycondensation, the formation of nuclei, and their agglomeration is in many respects similar to the formation of small metal particles.[95]

Silica gel. Silica gel is usually obtained from aqueous solutions of alkali metal silicates in the presence of an acid.[2] The silicates employed are known to contain even in the initial state chains of the tetrahedra (SiO_4), which serve as the nuclei of the future solid-state structure. The essential feature of the process may be represented by considering the following simplified scheme:



The metal silicate hydrolyses in aqueous solution, which leads to the formation of chains of the tetrahedra (SiO_4) of differing length in which each silicon atom is linked to two hydroxyls. Such chains are known to cyclise at high concentrations to form rings with different numbers of silicon atoms. The hydroxide anion is capable of rupturing the Si–O–Si linkage connecting neighbouring tetrahedra, so that a dynamic equilibrium is established after a time in solution between the ring formation and disruption processes. In order to shift the equilibrium towards polycondensation, an acid is added to the solution, whereupon the ring disruption process virtually ceases and rings are actively formed in the medium and merge with one another. The primary hydrolytic process does not usually go to completion, so that negative oxygen ions are retained in the rings, holding solvated metal ions in their vicinity. It has been established[2] that the presence of such solvated ions plays a decisive role in the stabilisation of the gel.

Aerogel. The technological industrial process for the preparation of this product is based on the acid- or alkali-catalysed hydrolysis of tetraethyl orthosilicate (TEOS):[90]

$$Si(OEt)_4 + nH_2O \longrightarrow (RO)_3SiOH + m\,EtOH ,$$

R = H, Et.

The 'initial silanol' obtained as a result of this reaction can have a complex composition depending on the nature of the group R. The hydrolysis is accompanied by the condensation of the 'silanols', completed by the formation of a silicate polymer:

$$(RO)_3SiOH + OH^- \longrightarrow (RO)_3SiO^- + H_2O ,$$

$$(RO)_3SiO^- + (RO)_3SiOH \longrightarrow (RO)_3SiOSi(RO)_3 + OH^- .$$

The growth of the polymer chain is controlled by the concentration of water and TEOS and by the pH of the solution. The acid-catalysed processes lead to the formation of short chains as a rule. If the catalyst is an alkali, longer chains are obtained. The combination and cross-linking of the chains results in the formation of the gel.

Analysis of the technological processes for the preparation of various disperse silicates has shown that the structural fragments making up the structure of the future product are different in all three cases.[32] Thus the 'principle of close packing' of the tetrahedra (SiO_4) in the bulk phase operates in the formation of the aerosil particles. According to Liebau's classification,[94] the dimensionality of the structure obtained is three and, by analogy with tectosilicates, aerosil was assigned to the class of amorphous tectosilicas.

The principal structural unit in silica gels comprises ring structures of arbitrary composition, the dimensionality of which is $D = 0$, as a result of which they were assigned to the class of amorphous cyclosilicas, analogous to cyclosilicates.

The principal structural element of the aerogel framework comprises chains. In this case, the dimensionality of its structure is unity and it was therefore classified as an amorphous polysilica analogous to polysilicates.

Thus amorphous tecto-, cyclo-, and poly-modifications are the technological polymorphic forms of disperse silicas. This idea served as the basis of an algorithm, which was used in the construction of model structures of amorphous silicas.

VII. Computational modelling of the initial structures of amorphous silicas

The concept underlying the computational modelling of polyatomic systems, which has made it possible to achieve the closest approach to the description of the properties of real nanomaterials, has been actively developed during the last few years.[15,31,36] This concept is based on a joint spectral experiment including computational and real experiments linked by feedback. The modelling process is regarded as a problem the successful solution of which is determined by the optimum selection of four of its main components, namely: (a) the quantum-chemical method for calculations relating to polyatomic clusters of nanometer size; (b) the procedure for calculations on the available powerful high-speed computers; (c) a structure-sensitive experimental method for testing the validity of the results obtained; (d) an adequate experimental object ensuring the establishment of a feedback between the calculations and the real experiment.

The need to operate with clusters of nanometer size leads to a conclusion in favour of one of the quantum-chemical semiempirical methods. Significant progress in this field has been achieved in recent years both by virtue of the stimulating studies of Dewar's school[96] and as a result of the development of new computational methods or new versions of those already existing. Zaets's program packs on computational chemistry, based on the MNDO, MNDO/H, AM1 (*sp* basis set) (CLUSTER-Z1 program pack),[97] and NDDO (*spd* basis set) (CLUSTER-Z2 program pack)[98] methods, should be included among the latter. These program packs have been executed in a form, which ensures a high accuracy of the computation for polyatomic systems combined with a comparatively small expenditure of computing time. When installed on the personal computers of the PC AT 486/Pentium and SUN SPARCstation class, they made it possible to perform calculations in a short time for a wide variety of polyatomic clusters of nanometer size, in particular systems such as silica, silicon nitride, nickel, aluminium, etc. (for a brief review of the results, see Sheka et al.[36]).

However, the calculated data obtained do not as yet solve the problem of modelling, since the question of the correspondence of these data to reality arises. The nanometer clusters used as the model have no molecular analogues, so that the principal characteristic of the molecular system — the energy and other integral characteristics — become merely descriptive quantities and cannot be subjected to an experimental test. Only vibrational spectra, which are largely determined by a short-range interaction, are the actual the property of the system for which the cluster approximation is sufficiently accurate. From the standpoint of the numerical experiment, the modelling of the surface does not differ from the modelling of the core structure. However, the need for a feedback in relation to the real experiment at the level of the investigation of the vibrational spectra requires that the investigator select an object which is as close as possible to the clusters being modelled. This is why in the course of the numerical modelling of the adsorption properties of the surfaces of nickel,[19,99,100] silica,[32-35] and silicon nitride[101] the vibrational spectra of the corresponding modifications of these substances having nanometer size were employed as the experimental parameter.

When the problem of the computational modelling of a large cluster is formulated, the qualitatively new problem of the selection of the procedure for the modelling of the initial structure arises. It is well known[102] that in most cases chemical interactions are of the short-range type, so that structural elements separated by distances exceeding the chemical bond length hardly affect one another. As a result of this, there arises the risk that the site and direction of the development of the structure 'will not be guessed correctly'. The situation is frequently aggravated by the fact that nonrigid structures, to which those of silica belong in particular, are characterised by a large set of close minima on the total electronic energy surface. One of the ways of solving this problem involves algorithmic modelling, the essential feature of which consists in the construction of the initial structure of the cluster with the aid of a definite algorithm based on 'evidence of the origin' of the corresponding product containing a set of distinctive features characteristic only of the latter.[103] This approach has been used in the modelling of the structures of disperse silicas.[32-35]

1. Computational modelling of aerosil

The computational modelling of the structure and adsorption properties of aerosil[33] consisted of the following stages:

1. the construction of the initial structures of polyatomic clusters of nanometer size;
2. computational modelling by means of semiempirical quantum-chemical methods of the structures constructed;
3. computational modelling of the adsorption properties of the clusters investigated in relation to water molecules;
4. calculation of the doubly amplitude-weighted density of the vibrational states of the cluster and of inelastic neutron scattering spectra with subsequent comparison of the calculated and experimental spectra.

a. Initial structural models

On proceeding to the construction of the initial clusters, it is useful to introduce the concept of small, medium, and large clusters having brought them into correspondence with the principal ideas concerning crystal-chemical fragments and the types of their packing in conformity with the assignment of the test structure to a particular structural class. The main structural fragment of silicates and silicas is the silicon – oxygen tetrahedron (SiO_4). This tetrahedron is in fact usually considered in the computational modelling of silica systems (see, for example, Refs 6, 92, 104, and 105). However, in the light of the multivariability of the structures of disperse silicas, such a model cluster is inadequate for the description of their properties. Therefore, in the computational modelling of this family of substances, special definitions were formulated and introduced: the concept of a small cluster as a structural model of a peripheral (surface) functional group was introduced; the concept of a cluster of medium size as a structure describing the packing of small clusters in accordance with the classification of the structure and reproducing correctly the short-range distribution of atoms; the concept of a large cluster as a structure in the ideal version designed to reflect the correct bulk-phase structure of the substance and the distribution of functional groups on its surface.

Since aerosil is an amorphous tectosilica, the clusters modelling the structure of its core must be of the skeletal close-packed type. The close-packed crystal structures of silica are known to contain rings of siloxane chains with a small number of members: four-membered in quartz[106] and six-membered in cristobalite[107] and tridymite.[108]

The structural models of individual small rings are presented in Fig. 15. They were obtained as a result of total optimisation by the AM1 method with the aid of the quantum-chemical programs of the CLUSTER-Z1 pack.[33] These and all subsequent calculations were performed on personal computers of the type PC AT 386/387-33 and 486-66. The clusters are presented in a projection 'from above'.

We may note that, although the silicon atoms are located in one plane only in the Si3c cluster, in the remaining clusters the

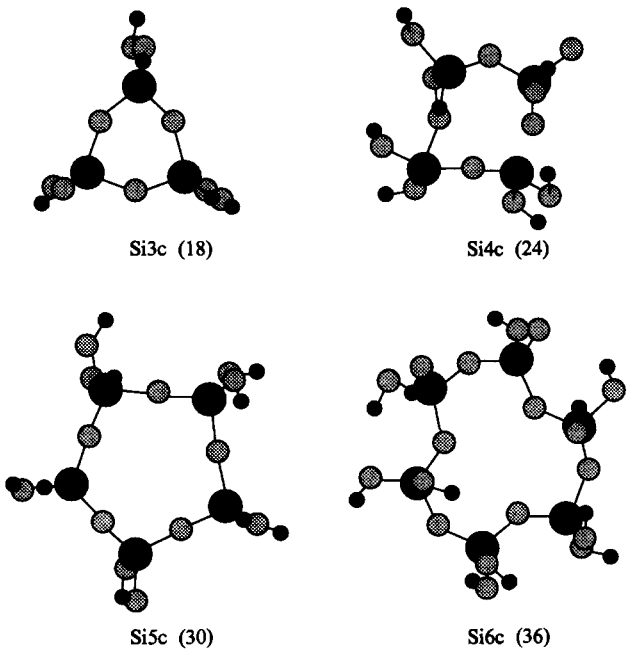


Figure 15. Small rings of silicon–oxygen tetrahedra Si*n*c (calculation by the AM1 method);[33] *n* is the number of silicon atoms in the ring (c) (here and in Fig. 16 the numbers of atoms in the cluster are indicated in brackets).

silicon rings are also close to planarity. In contrast to these, large rings with more than six carbon atoms have a distinctly nonplanar structure. The structure made up of large rings is inevitably looser. Thus polyhedra the faces of which consist of small rings served as a model of the bulk-phase structure of aerosil. In constructing model 'structures', preference was given to nonplanar six-membered rings ('hexagons') because the nuclei of the aerosil particles are formed at a high temperature where the β-cristobalite crystal structure is more stable.[33] The choice of the 'hexagon' motif made it possible to propose a fairly simple algorithm for the successive growth in the size of the model cluster, which can be represented by the formula

$$\mathrm{Si6c} + 4n\,\mathrm{Si} + 6m\,\mathrm{Si},$$

where $n = 1, 2, 3$ and $m = 1, 2, 3\ldots$ for $n > 3$. This algorithm corresponds to a development of the cluster structure such that the addition of the first four silicon atoms to the basic Si6c six-membered ring is accompanied by the formation of an adamantane-like skeleton containing three 'hexagons' (Fig. 16*a*). The addition of each succeeding group of four silicon atoms leads to the formation of three new 'edges', from which new 'faces' of the cluster being formed are produced, so that the Si10 cluster is converted into a Si14 cluster and the latter into a Si18 cluster, etc. Under these conditions, the cluster grows in width and its development in depth, starting with $n = 3$, requires the addition of six silicon atoms. The set of Si10, Si18, and Si24 clusters obtained as a result of the application of this algorithm is presented in Fig. 16.

b. Analysis of the model structures of aerosil

Whereas the first member of this series can be assigned to clusters of medium size, the last two clusters belong to the class of large ones. Analysis of their structure shows that the selected algorithm for the growth in the size of the cluster not only reproduces the bulk-phase structure of the substance but also makes it possible to discover the trend in the distribution of the functional groups on its surface. In the test system, these are silanol $(OH)_1$ and silanediol $(OH)_2$ groups. With increase in the size of the cluster, the silanediol groups, which are the only ones present in the isolated rings (Fig. 15), are gradually substituted by silanol groups

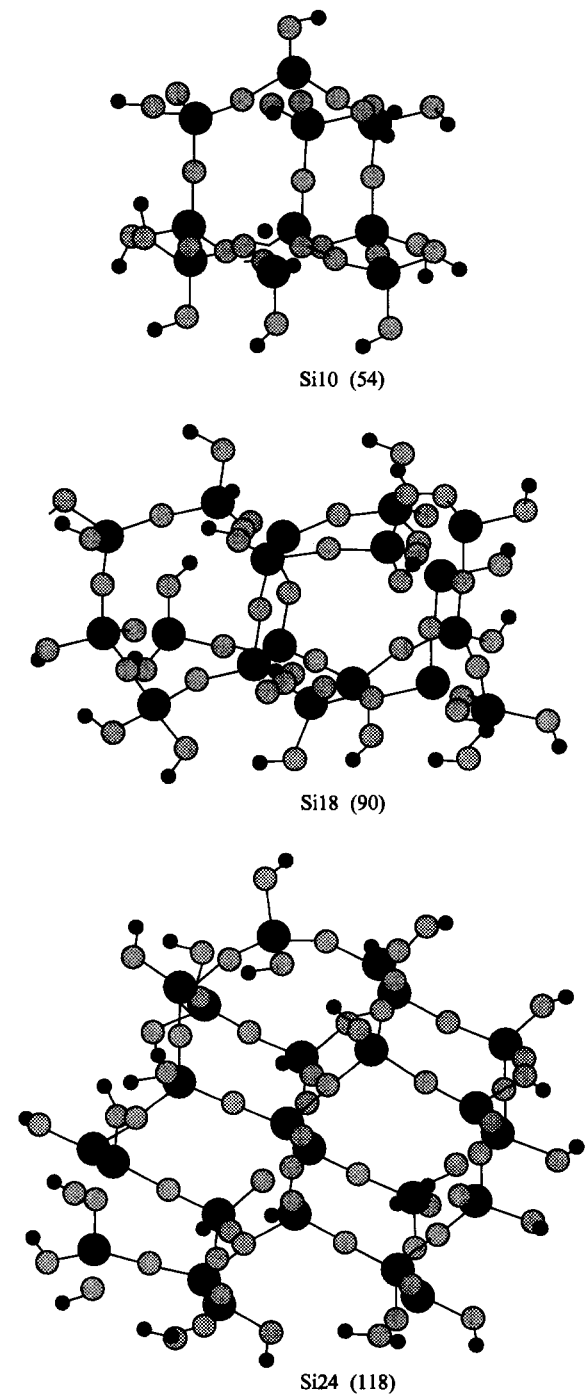


Figure 16. Clusters with a close-packed structure (calculation by the AM1) method.[33]

and are displaced to the periphery. Fig. 16 shows that cyclic close-packed structures contain no silanetriol groups. These groups arise only when a kind of branching of the structure takes place.[33]

Table 4 presents the numerical characteristics of the clusters demonstrating the dynamics of the variation in the numbers of silanol and silanediol groups in the clusters of the close-packed structure. The table shows that there are no $(OH)_1$ groups in the isolated cyclic clusters. These groups appear only in the compactly bound structure of the Si10 cluster. The ratio of the numbers of the $(OH)_1$ and $(OH)_2$ groups still indicates the predominance of the silanediol groups under these conditions. It is known from experimental results that the hydroxyl shell of the aerosil particles may contain not more than 20% of

Table 4. Quantitative characteristics of the model clusters of aerosil.[33]

Cluster	Number of atoms			Number of groups		Linear size/Å	
	Total	Si	O	$(OH)_1$	$(OH)_2$	min.	max.
Rings							
Si3c	18	3	3	–	3	3.57	6.62
Si4c	24	4	4	–	4	3.62	8.11
Si5c	30	5	5	–	5	3.65	9.00
Si6c	36	6	6	–	6	3.62	8.72
Si8c	48	8	8	–	8	5.60	11.34
Si10c	60	10	10	–	10	5.18	13.07
Si14c	84	14	14	–	14	5.18	15.71
Bulk-phase structures							
Si10	54	10	12	4	6	8.57	11.16
Si14	72	14	18	8	6	9.00	14.30
Si18	90	18	24	10	7	10.52	15.41
Si24	118	24	36	15	7	10.52	16.02

silanediol groups.[5] Thus it is evident that neither the free rings themselves nor the compact structures made up of a small number of rings can serve as an acceptable model of the structure of an aerosil particle. With increase in the size of the cluster, the ratio of the hydroxy-groups changes in favour of silanols (see the Si14 cluster and so on) and tends to increase. This increase is slow, but estimates have shown that, when the selected algorithm for the increase in the size of the cluster is used, the ratio of the numbers of the $(OH)_1$ and $(OH)_2$ groups may reach 5 – 6 in favour of the former when the size of the cluster increases to dimensions comparable with 100 – 200 Å. It is then evident from the analysis of model structures that the silanediol groups exist mainly at the apices of the terminal edges, i.e. on the irregularities of the structure of a real particle. The tendency in the variation of the structure of the hydroxyl shell of the clusters thus discovered means that the specific content of the hydroxy-groups on the surface of aerosil should vary in opposition to the variation of its specific surface (radius), which has in fact been observed experimentally.[109]

The proposed algorithm for the growth of the cluster is undoubtedly not the only one possible — it merely corresponds to the most probable structures of the close-packed amorphous silica, reflecting fully the quaternary coordination of the silicon atoms in the dense structure formed by the 'hexagons'. The irregularity of the structure over the macroscopic distances characteristic of the amorphous state is apparently due to the fact that four-, five-, and six-membered rings adjoin one another among close-packed atoms. However, the considerations presented above concerning the tendency towards the distribution of the functional groups in a real particle remain valid for rings of all sizes.

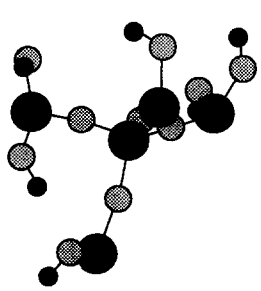


Figure 17. A fragment of the Si18 cluster (calculation by the AM1 method) demonstrating the alternating distribution of the surface Si atoms with the hydroxy-groups and tetrahedral Si atoms coordinated only to the siloxane oxygen atoms.[33]

Taking into account the foregoing, the Si18 cluster may be regarded as the real model of the surface of an aerosil particle. This applies not only to the distribution of the hydroxy-groups but also to the formation of the experimentally established[5] alternating structure comprising silicon atoms in which a silicon atom attached to a hydroxy-group adjoins another surface silicon atom involved in tetrahedral coordination with only four siloxane oxygen atoms (Fig. 17).

On the basis of the results obtained, the following models of the small, medium, and large clusters of the model structures of aerosil may be proposed.

The principal functional group on the surface of aerosil is an isolated silanol group. As a result of this, the simplest model of a small cluster may be a silicon – oxygen tetrahedron based on three silicon atoms and containing one OH group. The interaction of this cluster with water has been considered as the basic model.[15,92,100,110] The results agree satisfactorily with experimental vibrational spectra of water adsorbed on the surfaces of aerosil particles.

A similar small cluster with a silanediol group may serve as the simplest model of isolated silanediol groups on the surface of aerosil. These groups are located on structural irregularities and their contribution to the aqueous and hydroxyl components of aerosil is comparatively small. As shown above, silanetriol groups are foreign to the close-packed aerosil structure and as external formations are naturally unstable; their presence on the surfaces of aerosil particles is hardly possible.

The model Si10 cluster is an example of a cluster of medium size reproducing the packing of small clusters. The Si18 and Si24 model clusters are large clusters which not only model the bulk-phase packing in the core of an aerosil particle but also describe the distribution of the hydroxy-groups on its surface. Apparently a further increase in the size of the cluster is hardly useful because it is unlikely that qualitatively new information would be obtained in view of the small radius of action of the chemical interaction forces.

The structures presented have been used to calculate the vibrational spectra of the core and the hydroxyl component of aerosil and also the spectra of the water adsorbed on them.

c. Vibrational spectra of the core and the hydroxyl component

Fig. 18 presents the experimental AWDS basis spectrum of the aerosil core and two calculated spectra. The latter were obtained with the aid of the COSPECO program pack for computational vibrational spectroscopy.[111] The field strength data were obtained in a quantum-chemical calculation in terms of the AM1 approximation (with the CLUSTER-Z1 program pack). The first spectrum refers to the Si18 cluster (Fig. 18, curve *2*). It has already been stated above that this cluster is a realistic model of a

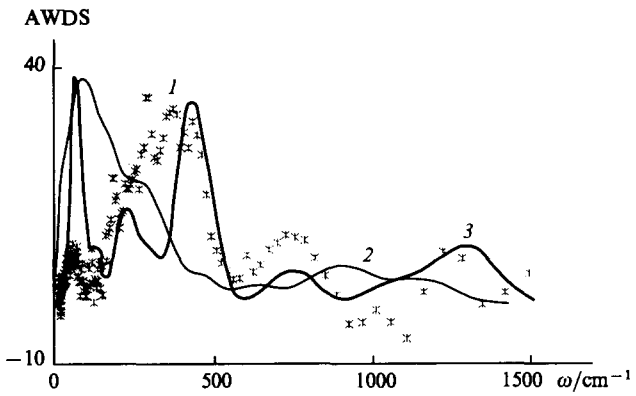


Figure 18. Vibrational spectrum of the aerosil core: (*1*) experimental curve ($T = 10$ K);[25] (*2*) calculation for the Si18 cluster; (*3*) calculation for the Si10ch siloxane chain under cyclic boundary conditions.[103]

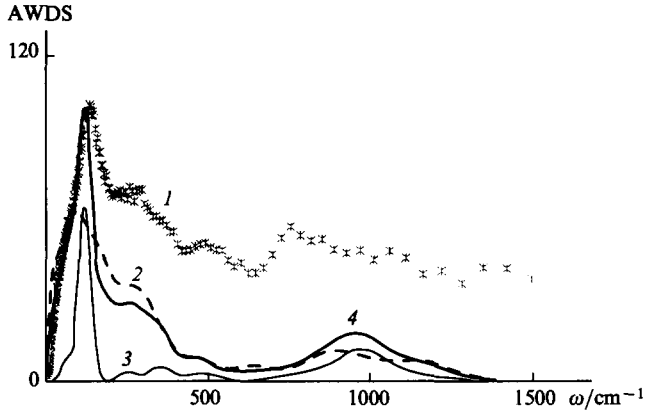


Figure 19. Vibrational spectrum of the hydroxyl coating on aerosil: (*1*) experimental curve ($T = 10$ K);[25] (*2*) calculation for the hydroxyl coating on the Si18 cluster; (*3*) calculation of the surface vibrations of the Si18 cluster; (*4*) the sum of curves *2* and *3*.[103]

large cluster. At the same time, the calculated spectrum differed so much from the experimental one that this appeared discouraging at first sight. Analysis of the causes of the observed discrepancy revealed a completely new problem. The point is that the vast majority of the silicon atoms of this cluster are found to be surface atoms after careful examination, so that their kinematic behaviour differs significantly from the behaviour of the inner atoms while the force constants are fully retained for each selected pair of atoms. In order to eliminate this effect within the framework of the clusters considered, it was necessary to increase their size almost by an order of magnitude, which rendered any computational study unrealistic. However, another approach to the solution of this problem is also possible. In considering the structures of the close-packed Si18 and Si24 clusters, one may note that they consist of a set of Si–O–Si chains inclined to the basis plane† of the clusters. Each three neighbouring chains in sections parallel to this plane form a typical close-packed hexagonal structure. Thus the chain may be regarded as a translationally equivalent structural unit with the aid of which the bulk-phase structure of aerosil may be constructed. Fig. 18 presents the results of the calculation of the vibrational spectrum corresponding to a chain containing ten silicon atoms for cyclic boundary conditions (curve *3*). The force constants in this chain were taken from the Si18 cluster. Evidently, the calculated and experimental spectra agree well. The band at 80 cm^{-1} is an exception. It is due to the out-of-phase translational motion of the silicon–oxygen tetrahedra. With increase in the length of the chain, it splits into an increasing number of components and its maximum diminishes, so that for several hundred silicon atoms it will undoubtedly assume a form consistent with experiment. The complete agreement between the positions of the maxima of all the bands in the calculated and experimental spectra is striking.

Fig. 19 presents the experimental and calculated AWDS spectra of the hydroxyl coating of aerosil. Curve *2* corresponds to the spectrum presented above for the Si18 cluster, which represents the vibrational spectrum of the surface atoms. Curve *3* represents the vibrational spectrum of the atoms bound to the ten $(OH)_1$ groups contained in the Si18 cluster. As stated in Section IV, the hydroxyl component of the AWDS spectrum of aerosil should consist of the vibrational spectra of the hydroxy-groups and the surface core atoms sensitised by these hydroxy-groups as a result of the 'riding effect'. The real AWDS spectrum represents a combination of these spectra with the correct ratio of the hydroxy-groups and surface silicon atoms. Curve *4* in Fig. 19 corresponds to the sum of the spectra *2* and *3* in proportions of 1:1. Evidently, this spectrum agrees very well with the experimental one.

† The introduction of the term basis plane is in this case arbitrary. It implies the section which reveals the hexagon ornament of the structure.

d. Compositional structure and vibrational spectrum of adsorbed water

The reliability of the results of the modelling of the structure of an aerosil particle made it possible to consider in greater detail the problem of the adsorption of water.[93] As stated above, the Si10 cluster belongs to the class of medium-size clusters, which makes it possible to reproduce the real structural correspondence between an isolated functional group and the core of the substance. Fig. 20 presents the optimised structure of this cluster (for further details, see Khavryuchenko and Sheka[93]), interacting with six water molecules (MNDO/H approximation, CLUSTER-Z1 program pack).[97]

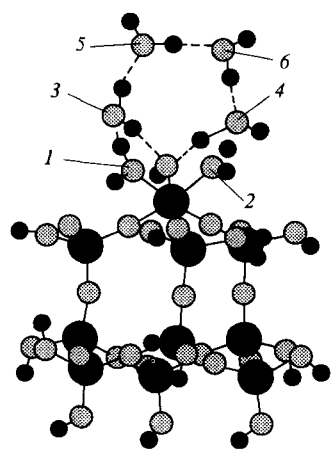


Figure 20. The Si10w6 (72) cluster with six water molecules (calculation by the MNDO/H method).[103]

Water molecules are adsorbed collectively on the aerosil surface, which confirms the conclusion reached as a result of a qualitative analysis of the experimental spectrum of the water adsorbed on aerosil (see Section V). The first two molecules are coordinated to the silicon atom of a silanol group, whereupon its coordination number becomes six. The remaining water molecules are hydrogen-bonded. Fig. 21 presents the

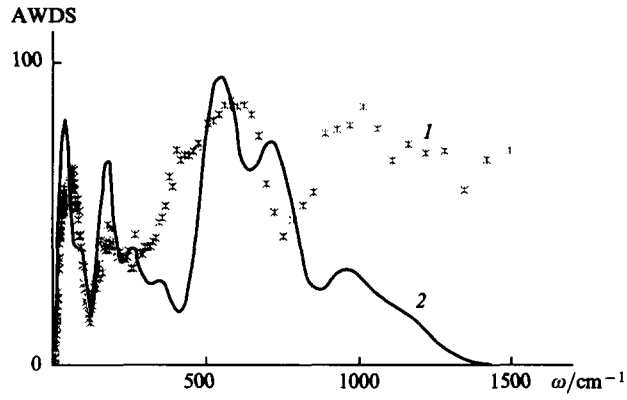


Figure 21. Vibrational spectrum of the water adsorbed on aerosil:[103] (*1*) experimental curve ($T = 10$ K);[25] (*2*) calculation for the Si10w6 cluster.[103]

experimental and calculated AWDS spectra. As in the preceding spectra, the calculated spectra were slightly corrected as regards frequency.

Evidently, the principal features of the calculated and measured spectra agree. The higher intensity of the experimental spectrum compared with the calculated one in the high-frequency region may be associated with the contribution of two and more multiphonon states in the experimental spectrum. The unduly low intensity in the low-frequency region is associated with the fact that the composition of the water adsorption complexes on the surface of aerosil is nonuniform:[93] apart from the centres containing six molecules, there are centres in which the number of molecules ranges from one to five. The problem of obtaining complete agreement between the calculated and experimental spectra thus includes the problem of the determination of the number of these centres.

The satisfactory agreement obtained between the calculated and experimental basis spectra of the aerosil components on the whole indicates the legitimacy of the models presented, describing the close-packed structure of amorphous silica.

2. Computational modelling of silica gels

Silica gel is known to be characterised by a considerable variability of its properties.[2] This applies both to the poor reproducibility of the product already in the stage involving its preparation and to the variation of its properties and their sensitivity to external conditions. One may claim that the principal property of silica gel is the 'flow' of its structure, so that each silica gel specimen does not represent the same and fixed structural state of amorphous silica but constitutes an 'instantaneous photograph' in a chain of structural transformations. In view of the foregoing, the problem of the modelling of the silica gel structure is by no means simple, since it is not known which particular 'instantaneous photograph' of the real structure is to be reproduced. Proceeding to the modelling of the structural clusters of silica gel, Khavryuchenko and Sheka[34] did not have as their aim the reproduction of a particular structural configuration. Their aim was to find answers to the following principal questions which are associated nowadays with the silica gel structure,[28] namely: how are the silica gel pores formed; on what factors does their size depend; why do the vibrational spectra of the core and hydroxyl shell of silica gel depend on the pore size; what does the experimentally observed adsorbed and quasi-free water in the pores represent; why does the vibrational spectrum of the adsorbed water not depend on the pore size.

The structure of silica gel (cyclosilica) is based on rings of silicon–oxygen tetrahedra of different size. It has been noted that the loose structure characteristic of silica gel is made up of rings of fairly large size. The structural models of several such large rings were first constructed and optimised within the framework of the MM2 program[112] and were then additionally optimised by the AM1 method with the aid of the CLUSTER-Z1 program pack.[97] It was found that, with increase in its size, the structure of the ring increasingly deviates from planarity. At the same time, an appreciable tendency towards the 'cellular subdivision' of the ring with formation of smaller rings is observed.

It is natural to suppose that the silica structure is produced as a result of rings of different size being joined together. It is noteworthy that the rings must be sufficiently large, since the condensation of rings with four, five, and six silicon atoms leads to the formation of close-packed structures of the type of aerosil or quartz glass.[33] There is no doubt that these small rings also participate in the formation of the silica gel structure, but they are most likely to play merely a binding role.

Large rings are as a rule highly distorted and nonplanar, so that on combination of, say, two such rings, they may 'fold up'. Bearing in mind that the gel is formed in the presence of solvating alkali metal ions, it is logical to suppose that the main role of the ion is to stabilise such a structure. Fig. 22 presents one of the possible structures formed by two rings containing seven and eight silicon atoms and having two common siloxane bonds. Evidently, these rings represent the 'folds of a half-open blister'. The presence of a solvated ion within this structure probably prevents its folding up and promotes the extension of the rings. On this basis, it has been postulated that silica gel consists of a solid framework having the structure of an open network similar to the pattern on a poorly inflated football with an irregular shape.[34] In contrast to the cells on the usual football or the regular fullerene structures of the C_{60} and C_{70} types, the cells in this framework do not consist of ideal hexagons and pentagons but are nonplanar rings of silicon–oxygen tetrahedra of different size. The retention of the form of the framework during synthesis is ensured by the solvated ions (one or several), after the removal of which pores of different size remain.

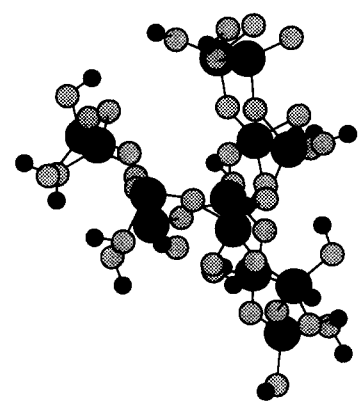


Figure 22. The Si13dc(75) cluster consisting of two rings (Si7c and Si8c) (initial model).[34]

It is important to note that the formation of the rings, contact between them, and the formation of the framework bounding the pore are undoubtedly statistical processes. They are naturally subject to the influence of external conditions. Thus certain rings may be opened in some cases. Their number is determined, in particular, by the concentration of acid. This probably explains the difficulty of reproducing the silica gel structures, mentioned above. The aggregation of such elementary frameworks in accordance with the close-packing principle, applied to spherical or quasi-spherical particles, leads in its turn to the formation of a globular mesostructure, which has in fact been observed experimentally.[2]

In conformity with the foregoing, the hierarchy of clusters describing the silica gel structure is as follows. The small structures modelling the peripheral functional groups (in the given case hydroxy-groups) are closed and open cyclic structures comprising eight and more silicon atoms as well as the sites of contact between two rings. The clusters of medium size, reproducing the packing of small clusters and the short-range distribution of atoms, are model macrocyclic structures, which may differ in the type of junctions incorporating one, two, and more silicon atoms. The large clusters, representing the distribution of atoms over long distances and the distribution of functional groups, may be considered to comprise a fragment of the surface of the framework consisting of 2–3 junctions.

The proposed model of the silica gel structure does not conflict with the known macroscopic properties of this substance. Furthermore, it makes it possible to explain qualitatively a number of microscopic properties which have not been accounted for hitherto, including vibrational spectra. It is seen from the models presented that the silica gel core consists of an open network comprising chains of siloxane bonds. The large width of the size distribution of the rings in this structure and its lability are evident, as a result of which there is a possibility of the variability of the distribution of the Si–O–Si and O–Si–O bond angles from specimen to specimen, with which the principal changes in the observed spectra of the core are associated (Fig. 8).[26]

The hydroxyl components of silica gels represent a set of three silicon-hydroxyl groups, namely the silanediol groups of the closed rings, the silanetriol groups at the ends of the opened rings, and the silanol groups at the points of contact between the rings. Thus their vibrational spectra are compound. They depend on the number of silicon-hydroxyl groups of different types. On the other hand, it is evident that the ratios of the numbers of these groups are statistically distributed over a fairly wide range of values and may be different even for different fractions of the products of the same technological cycle. It has been postulated[34] that the difference between the observed vibrational spectra of the hydroxyl components of the silica gels SG100 and SG20, presented in Fig. 9, is in fact associated with this factor.

As regards the vibrational spectrum of the adsorbed water (Fig. 13*b*), its constancy under conditions such that the adsorption centres are heterogeneous and compete with one another reflects the fact that the same centre wins this competition in each specimen. Since such a centre is one of the three possible silicon-hydroxyl groups, it is common to all the specimens. Calculations, which are being continued, will make it possible to discover which particular silicon-hydroxyl groups determine the adsorption of water in silica gel. In contrast to aerosil, in the structures of silica gels both identical and different silicon-hydroxyl groups adjoin one another, so that the simplest small clusters, representing isolated groups in aerosil, cannot be regarded as suitable structural models. This is why the rings themselves or fairly extended fragments of these rings as well as their junctions should be considered as small clusters in the case of silica gel.

3. Computational modelling of aerogel

The simplest model of the structure of aerogel (a polysilica) is a chain of silicon–oxygen tetrahedra.[32] Each silicon atom in this chain is linked to two oxygen atoms of the siloxane chain and to two hydroxy-groups. Thus the principal functional group of the hydroxyl component of aerogel, consisting of isolated chains, should be a silanediol group. However, comparative analysis of the basis vibrational spectra of the hydroxyl components of different disperse silicas (see Section V) established that the main element of the hydroxyl component of aerogel is a silanol group. It is natural to postulate that aerogel is not a monopolysilica made up of single chains but is a dipolysilica or a more complex one (see Liebau's classification[94]), the structural fragments of which are double or more complex strips. In view of the large number of capillary cavities in the macrospecimen, it is difficult to suppose that it consists of multichain strips, since its density should then be fairly high. It is most likely that the number of chains in the strips hardly exceeds 2–3. One of the possible structures of this kind is presented in Fig. 23. The structure is nonplanar. Attention should be drawn to the quasi-regular structure of the cells in the middle section of the chain. The principal size parameter of the model cluster is the length of the strip and therefore the boundary between a cluster of medium size and a large cluster is fairly arbitrary. The point of junction of several strips, one of the possible models of which is illustrated in Fig. 24, constitutes a special site within the structure.

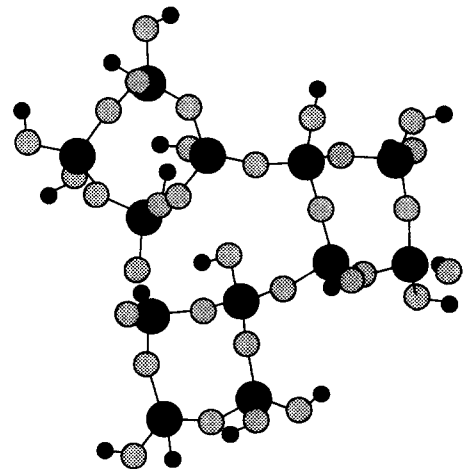


Figure 24. Cluster involving the junction of the Si12b(63) strips (initial model).[35]

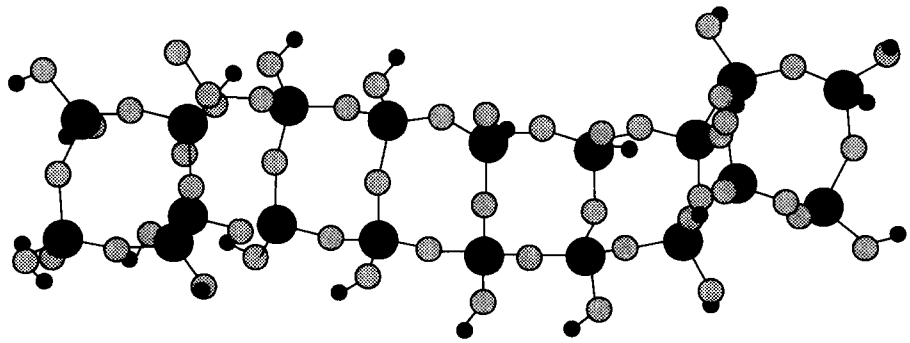


Figure 23. The Si20b(96) strip cluster (initial model).[35]

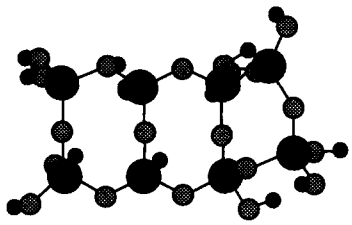


Figure 25. A small cluster of the structure of aerogel Si8b(42) (initial model).[35]

The main functional groups on the periphery of the strip are silanols. Nevertheless, it is evident from the analysis of the model of the aerogel structure that the cluster containing an isolated silanol group and constituting a satisfactory model of the silanol groups of aerosil cannot model the functional groups of aerogel. The reason for this is the fact that, in contrast to aerosil, the silanol groups in aerogel are arranged in a sequence where they adjoin one another at a distance of ~ 3.5 Å, so that several groups participate in the interaction of the chain-strip with water. Another cause is the significant different between the core chain structure of the siloxane bonds of aerogel and the close-packed aerosil structure. As a consequence of this, the small cluster, needed according to Khavryuchenko and Sheka[35] for the modelling of the functional groups and for the consideration of the interaction of aerogel with water, must have a fairly complex structure. One of the possible models of this cluster is illustrated in Fig. 25.

The model structures of aerogel presented here agree well with the existing ideas about its structure[3] specified in detail at the atomic level. At the same time, they make it possible to explain a distinctive feature of the vibrational spectra of its components — the narrowness of their bands. This form of the spectra is known to be characteristic of polymers,[89] which yet again confirms that the model presented for this silica is reasonable.

* * *

The physicochemical phenomenon examined above has been called technological polymorphism. This verbal construction does not imply simply following the fashion for new terms but has proved to have a rich inner significance. The polymorphism of amorphous silicas has been established reliably from the vibrational spectra which constitute 'fingerprints' of the structure of the substance. The existence of such polymorphism is well known for labile systems.[113] One could confine oneself to this reference and attempt to describe qualitatively the disperse amorphous silicas investigated in terms of the degree of their lability. However, the path based on the properties of the substance which are characteristic of it alone and which permit the introduction of a characteristic numerical parameter (or parameters), with the aid of which it is possible to achieve their classification, proved much more productive. Thus, in the case of amorphous substances with a molecular structure, success in the understanding of the polymorphic modes of the amorphous state was achieved by considering these modes as the corresponding prototypes of the mesophases in the liquid crystal state.[113] The classification of the amorphous phases made it possible to discuss immediately specific structural models of the substance. In the case of disperse silicas, such a classification guide proved to be the technology of the preparation of the products and the classification parameters were the dimensionality and multiplicity of the structures formed on packing the silicon–oxygen tetrahedra. The structural classification modes established made it possible not only to take a new look at various representatives of the substance considered, but also to propose a fairly unambiguous algorithm for the modelling of the corresponding structures.

Another indication of the fruitfulness of the terminology introduced here is the possibility of extending it to the entire class of nanomaterials to which the silicas presented above belong. A characteristic feature of these substances is the considerable contribution of surfaces and interfaces to their structure. This factor renders, in its turn, the nanomaterials exceptionally sensitive to the technology of their preparation and to the conditions under which they are kept. As is well known to technologists, because of this the chemical formula of the substance in reality describes a whole family of nanoproducts. The situation frequently arises where the investigator of the fundamental effects in such materials is extremely concerned by the 'dirt' on the surface of the specimen. However, this 'dirt' on the surface and on the interfaces of the nanomaterials obeys strictly the laws of chemical interaction and can be identified or predicted with the aid of a combined study of the same technological polymorphism. This approach has been applied successfully, for example, in the case of the family of silicon nitride powders of different origin.[101] Particular attention should be drawn to the fact that in this combined approach quantum-chemical modelling is converted into an active computational procedure and acquires the importance of an analysing instrument. This is particularly important in connection with the gradual onset of the era of nanotechnology, which brings our accustomed material world to the level of practical manipulation of atoms.

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New applications of van der Waals radii in chemistry

Yu V Zefirov, P M Zorkii

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Abstract. This review is part of a continuing study of the many applications of van der Waals radii (WR) in various fields of chemistry, and especially in crystal chemistry and stereochemistry. An analysis of relevant publications has shown that WR systems are used most often and most successfully in studies of the conformation of molecules, though their original source is usually an analysis of intermolecular contacts. This review will deal with traditional applications of WR and with some new aspects, including the geometrical modelling of chemical reactions and new types of specific intermolecular interactions. The bibliography includes 149 references.

I. Introduction

Our previous review of the application of van der Waals radii in chemistry, published[1] in 1989, dealt with information published between the mid-1930s and 1988. However, for a number of reasons several interesting publications (especially those published in the second half of 1987, when our review had been completed) failed to be included. In recent years the flow of information on the application of WR has grown steadily, and the areas of application have also increased. Because of its universality, simplicity, and objectiveness the WR method is convenient for rapid qualitative estimates, and it is often used in the final solution of many problems of practical importance, though (as we have already pointed out) the detailed features of crystal structures are more satisfactorily identified and explained by using concepts such as molecular orbitals, energy calculations, and atom–atom potentials.

These omissions compelled us to extend our critical analysis of the use of WR radii in chemistry, and resulted in the publication of the present review. But even now we cannot be certain that our review is exhaustive, in spite of the very large volume of information which we have assembled and presented. The theme of this review differs substantially from that of our earlier review.[1] Firstly, the section entitled 'Conformations of molecules' has been enlarged significantly, in keeping with the increasing amount of space devoted to the structure of the molecules (as opposed to the description of the molecular packing in the crystals) and to the effect of the molecular structure on the reactivity of compounds. Secondly, the present review introduces new methods of using the WR, and identifies situations not previously discussed which show, in particular, that steric effects can not only stretch the valence bonds but also initiate bond shortening, and that in some parts of the molecule these effects produce an enforced approach of atoms not joined by a valence bond in other parts of the same molecule, leading (under favourable conditions) to the formation of a valence bond. Thirdly, some already traditional methods of using the WR and the results of their application, which had not been adequately dealt with in Ref. 1, are discussed more fully: these include the geometric modelling of chemical reactions, new types of specific interaction, some new types of hydrogen bond, etc. Because of the very large (and continuously growing) number of studies in which WR are used we cannot claim that the whole of this information has been assimilated into this review. To some extent our choice has been arbitrary, but we have at all times endeavoured to make the choice balanced and representative of the methodological aspects of the problem (by the correct use of the optimum WR values). This task could be adequately satisfied by examining in the first instance the work of Russian workers. It should be noted that successful applications of the WR are more often found in studies carried out in this country than in reports from foreign workers. This is not fortuitous: the science of organic crystal chemistry (and its associated field, the concept of WR) were created largely by the work of Kitaigorodskii in this country).

The WR are most often used to detect contracted (or shortened) contacts between atoms which are not covalently bound. These contacts can be intermolecular or intramolecular. A correct choice of the reference point is important in the determination of the shortening. If the length of the contact (whether taken as the sum of the WR or as twice the geometric mean, $2\sqrt{R_i R_j}$) is close to this point the choice of the value from which the difference is calculated assumes an even greater importance. In our work the most probable length of the reference contacts between different atoms (by using the statistically averaged WR values, see below) was determined by giving priority to the doubled geometric mean. Nevertheless in our presentation of published material we quote (following the appropriate authors) a comparison of the length of the atom–atom contacts with the sum of the WR. On the whole no serious discrepancies were found, because the quantities $2\sqrt{R_i R_j}$ and

Yu V Zefirov Kurnakov Institute of General and Inorganic Chemistry of the Russian Academy of Sciences, 117907 Moscow, Leninskii prospekt 31. Fax (7-095) 954 12 79
P M Zorkii Chemistry Faculty, Lomonosov Moscow State University, 119899 Moscow, Leninskie gory. Fax (7-095) 932 88 46

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Table 1. Length of ordinary and of contracted atom – atom intermolecular contacts, in ångströms.

Contact	$2\sqrt{R_iR_j}$	d_{ij}
C···C	3.42	3.27
C···H	2.82	2.52
C···N	3.20	3.05
C···O	2.97	2.82
C···S	3.55	3.40
C···F	3.09	2.94
C···Cl	3.60	3.45
C···Br	3.67	3.52
C···I	3.82	3.67
N···N	3.00	2.85
N···H	2.64	2.34
N···O	2.78	2.63
N···S	3.22	3.17
N···F	2.90	2.75
N···Cl	3.38	3.23
N···Br	3.44	3.29
N···I	3.58	3.43
O···O[a]	2.58	2.43
Br···H	3.02	2.72
O···H	2.45	2.15
O···S	3.08	2.93
O···F	2.69	2.54
O···Cl	3.13	2.98
O···Br	3.19	3.04
O···I	3.32	3.17
S···S	3.68	3.53
S···H	2.92	2.62
S···F	3.21	3.06
S···Cl	3.74	3.59
S···Br	3.81	3.66
S···I	3.97	3.82
F···F	2.80	2.65
F···H	2.54	2.24
F···Cl	3.26	3.11
F···Br	3.32	3.17
F···I	3.46	3.31
Cl···Cl	3.80	3.65
Cl···H	2.97	2.67
Cl···Br	3.87	3.72
Cl···I	4.03	3.88
Br···Br	3.94	3.79
Br···I	4.11	3.96
I···I	4.29	4.14
I···H	3.14	2.84
H···H	2.31	2.01

Note. $2\sqrt{R_iR_j}$ is the mean length of the normal van der Waals contact; d_{ij} is the boundary between the shortened (by van der Waals interaction) and the contracted contacts, or in other words between the ordinary van der Waals interactions and the specific interactions.
[a] See Section II.

$R_i + R_j$ do not usually differ very markedly. We should note that the term bearing contact refers to interatomic molecule–molecule contacts whose existence is a necessary and sufficient condition for the creation of a three-dimensional system of contacting molecules in the crystal.

There is a group of WR systems for which the difference between the members is determined both by the chosen set of structural data and by the procedure used to define the WR. They were analysed in Refs 1 and 2. However, we should stress once again that in many cases the procedures used by some authors were not followed strictly, or they were approximated to an unacceptable degree, and that occasionally a single standard structure was used to determine the radius, thus invalidating the statistical nature of the WR. An important constituent of each system should be not only the averaged WR values but also a clear statement of the 'normal' van der Waals contact limits. This is because the length of the intermolecular contacts formed by the van der Waals interaction depends on many factors: the size of the molecules, their mutual orientation, the distribution of effective atomic charges, etc. These limits were first stated for contacts involving the H, C, N, O, and Cl atoms (see Ref. 3). The statistically averaged values for these atoms [H (1.16 Å), C (1.71 Å), N (1.50 Å), O (1.29 Å), and Cl (1.90 Å), see Ref. 3], were later supplemented with statistically averaged WR values for the sulfur (1.84 Å),[4] fluorine (1.40 Å),[5] bromine (1.97 Å), and iodine atoms (2.14 Å) (see Ref. 6). In the same study[6] the value for chlorine was redetermined by a different method, and was again found to be 1.90 Å. This is the only system of statistically averaged WR values which quotes the maximum deviations (δ) of the length of van der Waals reference contacts from their average values. For the contacts not involving hydrogen atoms $\delta \leqslant 0.15$ Å, whereas for the contacts involving hydrogen atoms $\delta \leqslant 0.30$ Å.

In this review (as in the previous one[1]) we shall use the terms 'contracted' and 'shortened' contacts. A shortened contact is shorter than the statistically average value for the van der Waals interaction, but does not go beyond the limit

$$d = 2\sqrt{R_iR_j} - \delta, \qquad \text{or} \qquad d = R_i + R_j - \delta,$$

or in other words, it can be defined as a contact of length r_{ij} for which

$$d < r_{ij} < d + \delta.$$

If $r_{ij} < d$ the intermolecular contacts are referred to as contracted.

In our analysis of the length of atom – atom contacts we shall use the parameters listed in Table 1.

In some of the studies examined in this review the noncovalent contacts between silicon and other atoms are discussed. Because of the lack of statistically averaged WR values for silicon in these Si···X contacts we compare them in our discussion with tentative values of the sum of the WR for the corresponding atoms. We take the van der Waals radius of silicon atom to be $\sim 2.1 \pm 0.1$ Å, because the WR of nonmetal atoms of the third period is $\sim 0.4 - 0.5$ Å greater than the WR of the corresponding atoms in the second period, and the WR of the carbon atom is 1.71 Å.

The WR system closest to the system of statistically averaged WR values[3–6] is the Pauling system,[7] except for the radii of oxygen and chlorine. The Pauling system is a system of rounded-off ionic radii (except for the Group V elements), which could be identified (according to Pauling) with the van der Waals radii. Pauling lowered the rounded-off values of the ionic radii of the Group V elements by 0.2 Å. We believe that when statistically averaged values of the WR are not available the best procedure is to adopt the values proposed by Pauling.

Descriptions of structures which are pierced by weak or very weak 'hydrogen bonds' of the X–H···Y type are often met in recent publications. In many of these 'H-bonds' the H···Y distance is equal to or even greater than (by a large amount in some cases) the average length of the normal van der Waals contact. Wherever hydrogen atoms exist these 'contacts' can be found with great ease. In the present review we shall be concerned only with H-bonds which form real associations of molecules, as indicated (when appropriate measurements are carried out) by the physical properties of the crystals.

II. Normal intermolecular contacts

In studies of a new substance, if a comparison of the shortest intermolecular (atom–atom) distances with the sum of the WR or with the parameters $2\sqrt{R_iR_j}$ in conjunction with data on the dispersion of the length of the reference contacts gives the expected molecular packing in the crystals we may call the intermolecular interactions 'normal'. This concept can be formulated in different ways: (1) the intermolecular contacts are similar to the normal contacts; (2) the structure consists of a packing of discrete molecules connected by van der Waals contacts; (3) in the structure the intermolecular contacts correspond to van der Waals interactions, etc. (see, for example, Refs 8–15).

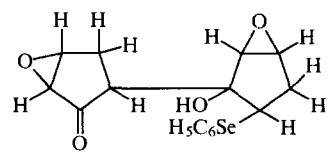
Among the normal intermolecular contacts recognised in the past few years special attention should be paid to the O···O contacts without a hydrogen bond, 2.58, 2.62, 2.68, and 2.72 Å long in different organic crystals.[16] These contacts are among the shortest intermolecular contacts of this type, and are close to twice the statistically averaged value of the oxygen WR (2.58 Å). The latter observation is also of interest, because the 1.29 Å value[3] for the oxygen atom, which 'works' well in intermolecular contacts between oxygen and other atoms, usually involving interactions between atoms with large residual charges of the same sign, appears too low in O···O contacts. This problem has been examined in depth in previous reviews.[1,2]

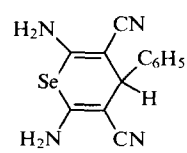
A broader concept of the structure of a van der Waals crystal in terms of the WR is obtained by determining the molecular coordination number (MCN), which is often a useful characteristic of the packing of the molecules in the crystal. In homomolecular crystals a continuous series of MCN between 9 and 18 was reported,[17] the number 9 being found only once (in the pyrene structure), and 18 also only once [in the structure of dichlorobis(vinylbenzotriazole)cobalt(II)].[18] The most widely found MCN are 14 and 12 (in ~50% and ~30% of cases respectively).[17,19] An analysis of the intermolecular contacts in the structure of molybdenum(IV) dioxobispropiohydroxamate, based on the rules laid out in Ref. 17, showed that the MCN for this complex is 8 (see Ref. 20). Thus the MCN series in homomolecular crystals has now been extended slightly and covers the range from 8 to 18.

In order to obtain a more complex picture of the structure of a van der Waals crystal, and to identify the molecules which are most strongly bound and form various types of association (dimers, chains, layers), the geometrical analysis must be supplemented by energy calculations, since the energies of the van der Waals interactions even in the first coordination sphere can be markedly different (in some cases by a large factor).[21] According to a calculation of the intermolecular interaction energies the molecules in a crystal of nickel(II) bis-[4-(n-heptyloxy-*N*-(4′-methoxyphenyl)benzaldimino-2-olate] form layers parallel to the (100) plane; the energy within the layer (54.3 kcal mol^{-1}) exceeds the interlayer energy (11.2 kcal mol^{-1}) about 5-fold.[22] In spite of the well known difficulties associated with the calculation of effective charges on atoms (resulting from the need to reconcile the methods of calculating the different components of the overall energy of the molecular crystal †) the intermolecular interaction energies should be calculated allowing for the electrostatic component, which can have a substantial influence on the total (overall) interaction energy of the molecules.[21]

The role of the steric factor is most clearly seen in the packing of molecules of the fluorine derivatives of *p*-methoxybenzylidene-*p*′-butylaniline in crystals. Combining the WR with an energy calculation showed that the replacement of hydrogen atoms (WR 1.16 Å) by fluorine atoms (WR 1.40 Å) in the $F_3C-C_6H_4-CH=N-C_6H_4-C_4F_9$ molecule increases the volume of the two end substituents, making the packing arrangements which are standard in liquid-crystalline phases seriously unfavourable.[23]

The identification by WR of the unreal (extremely contracted) intermolecular contacts was used in an unexpected way to establish the real structure of partially disordered crystals. The first studies of this type were reported in our previous review.[1] Their further development (for example, in Refs 24 and 25) will be considered here. The fundamental idea of these studies is that by using the WR we can reveal the unreality of the statistical structure given by X-ray structural analysis, in which the benzene rings are located (with assumed equal probabilities) in two mutually perpendicular positions, and in which the true structure of the crystral (domains or layer block) is thus established almost unequivocally.[24] Thus, crystals of the selenium compounds $C_{16}H_{16}O_4Se$ and $C_{13}H_{10}N_4Se$ consist of fully ordered layers each of which displays one of the two possible methods (*a* or *b*) of accommodating the benzene rings which form the core of the layer and are packed (in both cases) in a parquet floor pattern, so that rings having both a primary and a secondary orientation are matched in a well defined way. The surface of the layer, and therefore also the method of superposing the layers, remain unchanged. This creates the possibility of obtaining a special kind of polytype: (1) the crystal consists of *a* layers: (2) the crystal consists of *b* layers; (3) the crystal consists of a random (or a regular) alternation of *a* and *b* layers. The latter situation is seen in these compounds, in which blocks of *a* layers alternate with blocks of *b* layers.





A similar result was obtained for the crystal structure of 3-bromobicyclo{3.3.1}non-2-en-4-one. According to X-ray structural analysis data[25] the oxygen atoms in these crystals are accommodated randomly in two positions (with populations of 2/3 and 1/3 respectively). This means that the substance contains L and D enantiomers, but (as was pointed out[25]) these cannot have a random distribution because it would lead to unrealistic intermolecular contacts. By using the WR and calculating the intermolecular interaction energy it was shown[26] that the crystal most probably consists of an assembly of domains of two types: (1) racemic [L, D] domains, containing equal amounts of the L and D enantiomers, and (2) [L] (or [D]) domains, consisting of L (or D) enantiomers. A domain structure of the [L], [D] type, in which each domain contains only enantiomers of one type, must of course be excluded.

In addition to the above comments many examples of the use of WR to identify the normal intermolecular contacts in problems of structural biology and to interpret the physicochemical properties of substances are discussed in our previous review[1] and in Section V of the present review.

III. Contracted intermolecular contacts

Contracted intermolecular contacts usually denote the presence of specific interactions (SI), which are much stronger than ordinary van der Waals interactions. Specific interactions are of the attractive type, and they have a marked effect on the structure and properties of molecular crystals. Unlike contracted intermolecular contacts, contracted intramolecular contacts are only seldom associated with attractive interactions, and they are much more frequently the result of steric stress. In the present review we shall examine, in addition to the types of SI previously discussed, other types of SI not considered in Ref. 1.

† See the review by T V Timofeeva et al. in *Uspekhi Khimii* **49** 966 (1980) [*Russ Chem. Rev.* **49** 509 (1980)]

The validity of the conclusions on the contraction of intermolecular contacts and on SI of the O···X type can be tested by using 1.29 Å as the WR of oxygen (i.e. the value recommended by the present writers[3]): this value is substantially lower than the values proposed by other workers. Its use has allowed the SI to be identified in the packing of 2-bromo-1,4,8-trinitro-6(5H)-phenanthridinone molecules.[27] In this case we have the Br···O contact 2.967 Å long (for an average length of the normal contact of 3.19 Å and a lower limit d of the normal van der Waals interaction for these atoms of 3.04 Å). The C–Br···O angle (171.1°) probably denotes the direction of the SI.[27]

The contracted intermolecular contacts, which indicate the presence of SI, justify the conclusion that molecular associations of various types are present in the various structures. Thus, in the crystal structure of 4-methylbenz-2,1,3-thiadiazolecopper(I) iodide a strongly contracted N···S intermolecular contact (3.01 Å) has been detected,[28] whereas the length of the normal contact between these atoms is 3.32 Å, and $d = 3.17$ Å.[29] In this structure we have chains of molecules connected by pairs of antiparallel contracted intermolecular contacts of this type.

Among the crystal structures studied in recent years we again find structures with strongly contracted Cl···Cl intermolecular contacts. They include the 1,3-dichloro-2,2,4,4-tetrachlorodiphosphethane structure,[30] with contracted (3.311 Å) Cl···Cl intermolecular contacts, and the *O*-carbamoylacetohydroximoyl chloride structure with contracted Cl···Cl intermolecular contacts 3.333 Å long, which is much less than double the WR of chlorine (3.800 Å). These contacts lie at the very beginning of an almost continuous series of contracted Cl···Cl intermolecular contacts, beginning with 3.26 Å. In a crystal of the dichloroneopentylglycollic ester of 3,4-dichloro-1,3-butadiene-2-chloro-2-butene-2-phosphonic acid we can distinguish chains of molecules which contain contracted (3.386 Å) Cl···Cl contacts,[32] and in the structure of the dichloroneopentylglycollic ester of 1,3,4-trichloro-2-butene-2-phosphonic acid the contracted Cl···Cl intermolecular bonds (3.408, 3.540, and 3.550 Å) are said[32] to be retained in the structure of the corresponding polymer, thus creating bonds between the units of one polymer chain or of neighbouring polymer chains.

A recent paper from our laboratory[33] describes an extension of an earlier study[34–36] of the geometric aspects of halogen···halogen intermolecular contacts in organic crystals. A statistical analysis of the geometric characteristics of 330 Cl···Cl intermolecular contacts in organic crystals without hydrogen bonds was carried out. The contacts were divided into four groups: strongly contracted in comparison with double the WR of chlorine, weakly contracted, normal, and stretched.

Occasionally contracted Cl···Cl intermolecular contacts can coexist with hydrogen bonds. In this case the Cl···Cl contacts and the hydrogen bonds jointly give rise to complex associations of molecules. In crystals of the Graw salt $[Pt(NH_3)_4Cl_2]Cl_2$ the $Pt(NH_3)_4Cl_2$ complexes are combined into infinite columns arranged on the tetrad symmetry axis[37] through the axial chlorine atoms, which form contracted Cl···Cl intermolecular contacts 3.54 Å long. the N–H···Cl hydrogen bonds (N···Cl 3.44, N–H 0.9, H···Cl 2.47 Å, NHCl angle 172.6°) connect the columns into a framework through the bridging chlorine atoms. We have discussed[38] the topology of the chlorine derivatives of phenol containing cooperative hydrogen bond systems (CHBS). Three examples of the association of molecules of this type with contracted intermolecular contacts shorter than 3.5 Å were given. In the pentachlorophenol structure the chains containing helical CHBS are connected into a framework by Cl···Cl contacts 3.43, 3.46, 3.48, and 3.54 Å long. The shortest contracted Cl···Cl intermolecular contacts in these structures (3.27 Å) are observed in the 3,4-dichlorophenol structure. There are also clusters containing four chlorine atoms each which are connected by Cl···Cl contacts 3.48 Å long. Paired and fourfold Cl···Cl contacts connect the chains of the CHBS into a framework. In the tetrachlorohydroquinone structure contracted Cl···Cl contacts (3.37 and 3.43 Å) connect the layers containing CHBS into a framework.

In the *p*-bromo-[*N'*-(5-nitrofurfurylidene)benzhydrazide] structure contracted Br···Br intermolecular contacts (3.381 Å)[39] are formed between the molecules of neighbouring chains (double the WR of bromine is 3.94 Å).[6] This contact denotes an intermolecular SI between the bromine atoms in the crystal, which hinders the packing of the ketohydrazone molecules into stacks by the 'head-to-tail' principle, as in crystals where the Br atom is replaced by H or by the SO_2CHF_2 group.

More than 150 symmetrically independent contracted S···S intermolecular contacts have been identified in crystals of cation-radical salts.[40–45] The cations of these salts are usually packed into stacks, often with formation of contracted S···S contacts, and the stacks into layers, often with formation of S···S contacts between the stacks. These contacts are now observed as commonly as the contracted halogen–halogen intermolecular contacts (except the F···F contacts, in which no SI exists).[5] Thus the most recent work has filled all the gaps in the series of S···S contacts from double the WR of sulfur (3.68 Å) to 3.27 Å (a contraction of 0.4 Å).[4]

In the crystals of organometallic compounds contracted intermolecular contacts involving metal atoms can be found. This problem is often very difficult to discuss, because no reliable WR for these atoms are available. For example, the WR values for the mercury atom quoted in the literature vary from 1.5 to 1.9 Å or more.[1] Nevertheless in some cases the presence of SI and of contracted intermolecular contacts in these crystals can be established unequivocally. In the structure of *Z*-1-methyl-2-chloromercury-2-phenylethenyl acetate Hg(B)···Cl(A) contacts (3.110 Å) are observed between the A and B molecules: these can undoubtedly be classified as contracted if the WR of mercury is taken as 1.50 Å and that of chlorine as 1.90 Å.[46] The presence of intermolecular SI in this contact is confirmed by the deviation from 180° of the bond angle C–Hg–Cl (171.2°) in the B molecule. In the A molecule the deviation of the bond angle C–Hg–Cl is smaller (177.4°), and the Hg(A)···Cl(B) contact is longer (3.326 Å), denoting a weaker attractive interaction in this contact. An Hg···Cl intermolecular contact shorter (3.082 Å) than those previously observed[46] was found in the dimethyl ester of *cis-exo*-3-chloromercuro-4-azidotricyclo-[4,2,2,$0^{2,5}$]dec-7-en-*cis-endo*-9,10-dicarboxylic acid.[47] In this molecule the Cl–Hg–C bond angle has fallen to 173.2°. In the structure of the monohydrate of the *N*-phthaloylglycinate of trimethyltin the SI between the tin atom and the oxygen atom of a water molecule (contracted Sn···O contacts of 2.385 Å and 2.520 Å for a tin WR of 2.122 Å[49] and an oxygen WR of 1.29 Å)[3] replaces the tetrahedral coordination of the Sn atoms by a distorted trigonal bipyramid.[48] The contract Sn···O intermolecular contact (2.385 Å) is the shortest of the contacts of this type known when the paper by Ovsetsina et al. was published.[48]

In the research on intermolecular SI a special place must be given to studies of hydrogen bonds, because their presence (or absence) in the structure is often postulated to account for the different methods of packing molecules in crystals, for some conformational properties of the molecules, and even some physicochemical properties of substances. We have previously discussed[1] the geometrical criteria of the H-bond, and in particular we have pointed out that conclusions based on geometrical criteria obtained from structural data and from IR spectral data are often inconsistent. Therefore the criteria for the existence of hydrogen bonds are still an active topic of discussions (see, for example, Refs 50 and 51).

In this context we shall discuss only the relatively short hydrogen bonds which have a marked effect on the methods of packing molecules in crystals or on their physicochemical properties. From the very large number of new methods of using WR to describe H-associations of molecules we shall choose only examples which unambiguously characterise the different types of associations.

Crystals of 1-(2-methylphenyl)-3-methyl-5-(benzothiazol-2-yl)formazane contain A and B conformers (the contact conformation phenomenon).[52] In this structure two intermolecular H-bonds of the N–H···N type have been detected: N···N 2.910, N–H 0.89, H···N 2.08 Å, NHN 155°, and N···N 2.991, N–H 0.85, H···N 2.16 Å, NHN 165° (for d=2.34 Å), which combine the A and B molecules into dimers.‡ As a result of the presence of N–H···O bonds (N···O 3.00, N–H 1.05, H···O 2.01 Å, NHO 155° for d=2.15 Å) the molecules in the $C_{39}H_{56}N_2OBP$ crystal (see Litvinov and Naumov[53]) form centrosymmetrical dimers. In the α-diphenylphosphoryl-*o*-cresol crystal the molecules are connected into 16-member dimeric associations by pairs of P=O···H–O bonds in which the O···H distances are 1.81 Å,[54] and in the β-diphenylphosphorylethyl alcohol crystal three independent molecules are connected into an overall chain by P=O···H–O bonds (H···O distances 1.80, 1.84, and 1.86 Å).[54] Because of the presence of N–H···N bonds (N···N 2.828, N–H 0.94, H···N 1.96 Å for d=2.34 Å, NHN 165°) the molecules of 3,5-dichloro-1*H*-1,2,4-triazole form strong rings of three molecules arranged round the six-fold inversion axis of the crystal. Contracted N···Cl intermolecular contacts (3.149 Å for a sum of the WR of nitrogen and chlorine of 3.40 Å)[3] connect these rings into layers.[55] The existence of these layers, i.e. the fact that the most strongly bound molecules are combined, is confirmed by the anisotropy of the thermal deformation of these crystals (see Section V).

In the structure of *N*-(3-nitrocinnamoyl)-*N*-(2-chlorophenyl)-hydroxylamine a system of H-bonds often seen in hydroxamic acids has been detected: it includes two crystallographically independent O–H···O bonds (O···O 2.617, O–H 0.99, H···O 1.63 Å, OHO 176°, and O···O 2.634, O–H 0.81, H···O 1.82 Å, OHO 179°).[56] These hydrogen bonds connect the molecules into chains. O–H···Cl hydrogen bonds (O···Cl 3.00, O–H 1.04, H···Cl 2.02 Å for d=2.67 Å, OHCl 155°, and O···Cl 3.00, O–H 1.16, H···Cl 1.88 Å, OHCl 158°) were found in the complex anion $[2Cl^- + H_5O_2^+]^-$ of the $(BT)_2 \cdot 2Cl \cdot H_5O_2$ structure, where BT is bis-(butylenedithio)tetrathiafulvalene.[57] In the hydroxonium ion $H_5O_2^+$ a symmetrical O–H···O bond is formed (O···O 2.475, H···O 1.24 Å, OHO 168.1°). The hydroxonium ions are arranged on the diad symmetry axis and are interconnected through bridging Cl^- ions into an infinite chain by O–H···Cl hydrogen bonds.

A slightly different behaviour is observed in the cation···anion contacts of complex ions consisting of twenty or more atoms over which an excess of charge is distributed. In these contacts the distance between the X and Y atoms is not necessarily shorter than the average normal van der Waals contact. In the 1,2-dimethylacenaphthylene-1,2-*S*-phenylepisulfonium tetrachloroaluminate structure the $C_{20}H_{17}S^+$ cations and the $AlCl_4^-$ anions are grouped into stacks arranged in a checkerboard pattern, and the S···Cl contacts are found to be longer than the sum of the WR for sulfur and chlorine (3.74 Å).[58] The cation···anion contacts are occasionally shortened within limits acceptable for van der Waals interactions: for example, the S–Cl contacts of 3.602 and 3.691 Å,[40] 3.635 Å (see Ref. 59), and 3.65 Å[60] (for a sum of WR of 3.74 Å). However, in cation-radical salts we also find contracted cation···anion contacts, including strongly contracted contacts. Thus, a group of strongly contracted S···Cl cation···anion contacts forming in almost continuous series from 3.25 to 3.49 Å has been observed[40,42,59,60,61] in cation–radical salts (d=3.59 Å). In the $(ET)_3(ZnCl_4)_2$ structure, where ET is bis(ethylenedithio)tetrathiafulvalene, the strongly contracted S···Cl contacts of 3.253, 3.261, 3.295, 3.367, 3.371, and 3.424 Å have been observed,[60] in $(ET)_3Cl_2 \cdot 2H_2O$ the 3.328, 3.434, and 3.485 Å contacts,[61] in $(ET)_4ZnCl_4 \cdot C_6H_5CN$ the 3.356 and 3.488 Å contacts,[40] in $(ET)_4PtCl_6 \cdot C_6H_5CN$ the 3.410, 3.433, and 3.474 Å contacts[59] at T=293 K and 3.404 and 3.413 Å at T=218 K, and in the $(ET)_3CuCl_4 \cdot H_2O$ structure the 3.372 Å contact.[42]

Contracted S···Br cation···anion contacts of 3.536 and 3.614 Å,[45] and also of 3.625 and 3.638 Å (d=3.66 Å)[62] were found in the $(ET)_4PtBr_6$ and $BT \cdot IBr_2$ structures respectively.

As reported,[60] in $(ET)_3(ZnCl_4)_2$ the presence of a series of strongly contracted S···Cl contacts (see above) and also of a strongly contracted C···Cl contact (3.34 Å, d=3.45 Å)[60] can account for the nonequivalence in the $(ZnCl_4)_2^{4-}$ dianion of both the bond angles (from 105.9° and 115.6°) and the Zn–Cl distances (from 2.258 to 2.305 Å). We should stress the fact that these anomalies are produced not by internal steric stresses, which will be discussed in the next section, but by strong attractive external interactions. Similar phenomena were discovered in crystals of chlorine trifluoride at −100 °C (see Antipin et al.[63]) and of bromine trifluoride at −120 °C.[64] In the ClF_3 structure Cl···F contacts were found at 2.706 and 2.740 Å, shortened as compared with the normal Cl···F van der Waals contact (3.26 Å) by 0.52–0.55 Å but causing an extension of the Cl–F bridging bonds of 0.03–0.05 Å with respect to the axial bonds and of 0.16 Å with respect to the equatorial. In the BrF_3 structure we find Br···F contacts (2.45 Å) shortened by 0.87 Å with respect to a normal contact (3.32 Å) and extending the Br–F bridging bonds by 0.11 Å with respect to the axial and by 0.18 Å with respect to the equatorial Br–F bonds. Judging by the size of the contacts the stronger intermolecular SI in BrF_3 as compared with ClF_3 is responsible for the more substantial extension of the bridging bond in the former. By means of the SI mentioned above the molecules in crystals of ClF_3 form centrosymmetric cyclic tetramers, and in BrF_3 crystals they form chains. The strongly contracted B···F intermolecular contacts (2.663–2.705 Å) previously observed[65] in the BF_3 structure at 145 °C interconnect the molecules into infinite layers.

The above examples show that fluorine atoms tend to undergo strong attractive interactions with many other atoms (B, Cl, Br, and others). An example of the F···S intramolecular specific interaction is given below. However, as has already been pointed out, fluorine does not produce contracted F···F intermolecular contacts, and therefore specific F···F interactions are atypical.[5]

These effects of intermolecular SI on covalent bonds are well known in the case of intermolecular hydrogen bonds, and in particular of O–H···O symmetrical H-bonds.

A complex system of three types of SI has been observed[66] in 1,2-dimethyl-4-amino-5-ethoxymethylpyrimidinium iodide. In these crystals the cations are connected into dimers by pairs of antiparallel N–H···N hydrogen bonds (N···N 3.10, H···N 2.32 Å for d=2.34 Å, NHN 155.8°) The bridging $I^-(2)$ anions, which occupy individual positions at the inversion centres, form strong N–H···I H-bonds (N···I 3.66, H···I 2.58 Å for d=2.84 Å, NHN 156.6°) which connect the dimers in the direction of the a axis. The bridging $I^-(1)$ anions, which occupy individual positions on the 2 axes, interconnect the dimers in the direction of the b axis as a result of I···C specific interactions (3.573 Å for d=3.67 Å and a sum of WR of the iodine and carbon atoms of 3.85 Å). The resulting corrugated layers create the crystal structure by superimposing in the direction of the c axis in response to the van der Waals interaction.

IV. Conformations of molecules

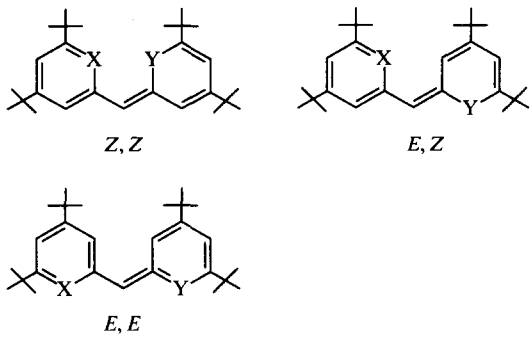
The classical conformational analysis[67–69] has recently undergone some far-reaching developments, and is now usually called 'molecular mechanics'.[70] It is based on the postulate that the conformation of a molecule is a compromise between the tendency for covalent bonds and bond angles to optimise their value (in the additive approximation corresponding to a minimum energy) and the tendency to minimise the resulting

‡ Here and elsewhere we shall use the term H-bond to denote the d value of the H···Y contact.

steric stresses, which create a repulsion between excessively close atoms which are not covalently bound and make a positive contribution to the energy of the molecule; at the same time the fragments of the molecule can rotate round ordinary bonds and thus lower the energy of the non-covalent interactions.

This model relies on the use of isotropic atom–atom potentials and, for approximate calculations based on the same idealogy, it can call upon the WR system. However, in practice isotropic atom–atom potentials are often inadequate. This situation is very well seen, for example, in the presence of both intermolecular and intramolecular SI. Intermolecular SI have been discussed in the previous section. Here we shall be concerned with intramolecular SI, and we shall examine some examples of their effect on the conformation of molecules.

The cation of 4,6,4′,6′,tetra-*tert*-butyl-substituted thiopyrylo-2-monomethenecyanine perchlorate adopts a *Z,Z* conformation.[71,72]



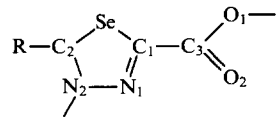
Under these conditions we find a strongly contracted S···S intramolecular contact (ClC) of 3.1 Å (taking 3.68 Å as double the WR of the sulfur atom). Obviously, this close approach of the sulfur atoms is due to their attractive interaction, which exceeds the repulsion between the residual charges of the same sign (+0.053 electronic units).[72] A closer approach is also favoured by the tendency towards conjugation in the carbon skeleton of the cations and symmetrical localisation of the ClO_4^- anions in the cavities between the heterocyclic rings. The stress in the cation is revealed by the increase (to 133.8° as compared with the ideal value of 120°) of the bond angle at the carbon atom which connects the heterocycles, and also by the increase to 122.1° in the exocyclic SCC and S′C′C angles (see Tolmachev et al.[71]).

An even shorter intramolecular S···S contact of 2.960 Å (i.e. a shortening of 0.72 Å) has been found in *Z*-4-methyltetrafluoroethyl-2-(tetrafluorothioacetylmethylene)-2*H*-thiopyran.[73] The sulfur atom lies in the plane of the thiopyran ring on the extension of the C–S bond of this ring; the CS···S angle is 174.7°. As reported,[73] this geometry of the –S···S= fragment is the most favourable to the formation of a CIC. As was pointed out above, SI of the S···S type are often met in intermolecular contacts: as we have seen, they are quite common also within molecules.

Replacing one of the sulfur atoms by oxygen in the cation studied by Tolmachev et al.[71] also produces a *Z,Z* configuration.[72] This creates a contracted intramolecular S···O contact of 2.74 Å ($2\sqrt{R_S R_O}$ = 3.08 Å, $\Delta r = r - 2\sqrt{R_S R_O}$ = −0.34 Å). The spatially unfavourable *Z,Z* conformation of this dye can be stabilised by the electrostatic attraction between the oppositely charged oxygen (−0.147) and sulfur atoms (+0.063). Furthermore, according to Sereda et al.[72] the length of the S···O contact (2.74 Å) allows specific interaction due to electronic factors which also stabilises the *Z,Z* conformation. A similar effect has been observed in the cyclohexane fragment 2,8-disulfonate-5,7-bis(dimethylsulfonium)bicyclo-[4,2,0]-oct-3-ene,[74] in which we find a *cis* configuration of the substituents stabilised by the CIC of the S′ atom with the oxygen of the sulfonate group; the S′···O distance is 2.854 Å.

Attractive interaction of nitrogen and oxygen atoms has been detected in one of the *O*-tosylhydroxylamines.[75] This interaction produces a strongly contracted intramolecular contact of 2.526 Å (as compared with the sum of WR of nitrogen and oxygen atoms of 2.79 Å). The attractive nature of the interaction of the nitrogen and oxygen atoms in this contact was confirmed by an analysis of the bond angles in the molecule. In 3,4-difluoro-8-*exo*-fluoro-12-*syn*-(2′-nitrophenylthio)-tetracyclo-[4.4.0.1^{2,5}.1^{7,10}]-dodec-3-ene the S···F distance (2.942 Å) was shorter[76] by 0.27 Å than the normal noncovalent S···F contact[5] of 3.21 Å. This shows that specific attractive interaction can exist between sulfur and fluorine atoms.[76]

Various examples in which the CIC denote conjugation of the bonds in various fragments of the molecule were quoted in our previous review.[1] Similar observations were made in more recent X-ray structural studies. Thus, in the 2-(*p*-ethoxybenzylidene)-3-phenyl-5-ethoxycarbonyl-1,3,4-selenadiazoline molecule[77]



in spite of the short Se···O distance (2.87 Å) as compared with the sum of the WR, the $C_1C_3O_1O_2$ plane makes an angle of 5° with the $SeC_1N_1C_2$ plane (the $N_1C_1C_3O_2$ torsion angle is −6°). This suggests[77] the presence of conjugation in the $N_1=C_1-C_3=O_2$ system. Similar examples are given in papers[71,72] on the structure of monomethinecyanines.

By analogy with the halogen···halogen contacts, in which the SI increase from chlorine to iodine, it may be assumed that similar effects take place in a contact between Group VI atoms and that the shortened Se···Se contacts denote the presence of SI in these materials. An analysis[78] of the complex bis-(1-isopropyl-3-methyl-4-cyclohexylaldimino-5-selenopyrazolato)nickel(II) supports this assumption. For steric reasons the *cis* compression of the NiN_2Se_2 observed in this complex is less favourable than the *trans* compression. The evidence for this conclusion is the intramolecular Se···Se′ distance (3.667 Å), which is less than double the WR of selenium (4.00 Å).[7] Nevertheless a *cis*-compressed NiN_2Se_2 tetrahedron is observed: as suggested,[78] this effect may be attributed to a Se···Se′ attractive interaction between not covalently bound atoms.

Specific interactions identified by using WR in crystals containing the cluster groups $M_3X_7^{4+}$ and $M_3X_4^{4+}$ (M = Mo, W; X = O, S, Se) are discussed in a recent paper.[79] It was noted that the $M_3X_7^{4+}$ derivatives form interionic contacts substantially shorter than the sum of the van der Waals or ionic radii of the X atoms, which occupy axial positions with respect to the M_3 plane, and the nitrogen, chalcogen, or halogen atoms of the counter ion or of the ion of the same sign. In some derivatives of $M_3X_4^{4+}$ these workers observed the formation of centrosymmetric dimers with the participation of (μ_2-X_2) ligands, in which the X···X distances were also markedly lower than the sum of the WR. These SI are often realised in spite of the coulombic repulsion between particles carrying charges of the same sign. These workers[79] consider that the criterion of the sum of WR[3,4,6] is also applicable to ionic radii in calculations of the degree of 'shortening' of a noncovalent contact.

In the crystal structure of 3-methyl-2-azoniafluorene tetrachloroaurate(III) a short Au···Cl distance (3.510 Å) was detected (for a sum of WR of 4.1 Å), corresponding to a noncovalent contact.[80] Allowing for this contact we can consider the coordination of the gold atom to be tetragonal–pyramidal.

The conformation of the molecules can also be strongly influenced by hydrogen bonds. We shall choose some examples from recently published work in which the presence of contracted intramolecular contacts is confirmed by the presence of an intramolecular H-bond. In the structure of diaqua-bis(nitroaminoguanidine)nickel(II) perchlorate stable N–H···O hydrogen bonds have been observed within the cations between the oxygen atoms of the nitro groups and the coordinated amino

groups; these bonds have N···O distances of 2.56–2.68 Å.[81] In the central fragment of the *N,N'*-di-(2,2,6,6-tetramethyl-1-oxyl-4-piperidyl)-*N*-diethylphosphorylurea molecule[82] we find a six-membered ring (···HNCNPO···) formed by an intramolecular H···O hydrogen bond 1.96 Å long (the Zefirov criterion[83] is $d_{O\cdots H} < 2.1$ Å). This hydrogen bond is retained in solution at moderately high temperatures, as shown by the IR spectrum of the substance.[82] A geometrical modelling of the reaction of ammonia with perfluoro-2-methyl-2-pentene-3-thiocyanate showed that in one of the intermediate products of this reaction (the carbanion A^1) an N–H···F intramolecular hydrogen bond is formed (H···F 1.71 Å for $d_{H\cdots F} = 2.2$ Å,[5] N···F 2.59 Å, NHF 141°).[84]

There can be no doubt (according to the geometrical criteria established for intermolecular hydrogen bonds) that an unusual intramolecular O–H···P H-bond is present in the ···PC=CBOH··· six-membered ring of the $C_{39}H_{56}N_2OBP$ structure (see Ref. 53). In this molecule the OH group has a short contact with the phosphorus atom (O···P 3.103, O–H 0.93, H···P 2.30 Å, OHP 145°). As reported,[53] this contact can be taken as a proof of the formation of an intramolecular O–H···P hydrogen bond, since the quoted distances correspond to the H-bond criterion (sum of the WR of the phosphorus and oxygen atoms 3.3, of the phosphorus and hydrogen atoms 3.0 Å),[7] and furthermore the OH group is positioned in the direction of the phosphorus atom. However, in the IR spectrum of this compound the stretching vibrations band of the OH group (3560 cm^{-1}) is not significantly shifted and is not broadened.[53] Therefore the existence of an O–H···P hydrogen bond in this compound remains an open problem.[53] Doubts have also been expressed concerning the presence of an N–H···N H-bond in the thiosemicarbazone of methylglyoxal.[85] In the five-membered $\cdots N_2N_1CN_3H_2\cdots$ ring of this molecule the presence of an $N_3\cdots N_2$ CIC of 2.637 Å suggests an intramolecular hydrogen bond. However, the $N_3H_2N_2$ angle of 104.9° is said by these workers to be 'unfavourable to bonding'.

Unusual C–H···F–C intramolecular hydrogen bonds have been reported[86] in *exo-cis*-2,3-dichloro-5,5-dicyano-6,6-bis(trifluoromethyl)-norbornane. This structure contains two intramolecular H···F contacts (2.16 and 2.30 Å) which are markedly shorter than the sum of the WR of the hydrogen and fluorine atoms (2.56 Å). One of these contacts is less than 2.2 Å long (the parameter corresponding to the criterion of 'guaranteed' existence of an F···H hydrogen bond).[5] These workers have suggested[86] that the short C–H···F–C contacts in this substance "should probably be interpreted as intramolecular H-bonds". A similar state of affairs was encountered[87] in 2-methyl-5α,6β-7,8-tetrakis(trifluoromethyl)-5,6-dihydro-Δ^2-1,3,4-oxadiazolino-[2,3-*a*]-azepine. This structure contains four short intramolecular H···F contacts, of length much smaller than the sum of the WR of the H and F atoms, and one as short as 2.13 Å. It is again suggested[87] that these contacts should be interpreted as intramolecular C–H···F–C H-bonds. Some doubt arises from the fact that in the five-membered HCCCF 'rings' of these compounds the free motion of the atoms within the molecule is limited, and the C–H···F angles are small; 114° in the first structure and 111° in the second. In relation to this work[86,87] it should be noted that according to the criteria formulated by Zefirov and Porai-Koshits[5,83] a hydrogen bond can be confidently identified only in intermolecular contacts, or for intramolecular interactions in which the contacts are not imposed by the rigid conformation of the molecule.

Thus doubts concerning the presence of SI (and in particular of H-bonds) in the system usually arise because a contracted intramolecular contact can denote either an attractive interaction or an imposed steric stress. For example, in 10-bromo-2,4,8-trinitro-6(5H)-phenanthridinone a Br···H intramolecular contact of 2.43 Å has been discovered; it is strongly contracted as compared with the value $2\sqrt{R_H R_{Br}} = 3.02$ Å as a result of substantial steric hindrances.[88] These effects increase the out-of-plane angles of the carbon atoms in the six-membered ···BrCCCCH··· ring. By relying on the geometrical characteristics of the C–H···Br contact (C···Br 3.161, C–H 0.90, H···Br 2.43 Å, CHBr 138°) it could be thought that a bond of the C–H···Br type is present. However, the shortening of the distance may also be induced by the resulting decrease in the steric stress. Often correct conclusions on the shortening of a contact can be reached by allowing for 'subsidiary' factors. However, if even additional information fails to produce a fully definite conclusion we can only assume that the existence of SI is a possibility.

A comparison of the interatomic distances with the sums of the WR is often used to prove the absence of a hydrogen bond. For example, in the 4,4',6,6'-tetranitro-2,2'-dicarboxybiphenyl and 6,6'-dinitro-2,2'-dicarboxybiphenyl molecules the intramolecular distances 3.434 and 3.933 Å (between the oxygen atoms of the carboxylic acid and of the nitro groups respectively) are so much greater than double the WR of oxygen that the presence of any significant hydrogen bond can be excluded.[89]

It was pointed out above that the use of the statistically averaged value (1.29 Å)[3] for the WR of oxygen offers reliable conclusions on the presence of shortened and contracted O···X contacts in the structure, from which reliable deductions can be made. However, the large positive charges on the oxygen atoms usually prevent the formation not only of short intermolecular bonds but also of short intramolecular O···O contacts, even when the conformational conditions appear to be satisfied. The cation of 4,6,4',6'-tetra-*tert*-butyl-substituted pyrylo-2-monomethinecyanine (I) exists in the *Z,E* form,[72] and not in the *Z,Z* form (see above), though the latter is sterically advantageous, since the WR of oxygen is much smaller than the WR of the carbon atom. One possible reason for the existence of the cation (I) in the *Z,E* form is the repulsion between the similarly charged oxygen atoms.[72] According to quantum-mechanical calculations (CNDO/2 method) negative charges are collected on the oxygen heteroatoms (O −0.083, O' −0.137 electronic units), the charge on the O' atom being 0.035 electronic units greater in absolute value than the charge on the C'_1 atom (−0.102 electronic units). In the *Z,E* form of the cation (I) we find the shortened contacts C'···O (2.94) and H'···O (2.29 Å) for WR sums of 3.00 and 2.45 Å respectively. Since the molecule is flat, and the H···O contact closes a six-membered ring, one could conclude that this ring contains a weak intramolecular C–H···O hydrogen bond. However, Sereda et al.[72] reach a different conclusion. In this case the C–H···O contact is constrained, and is created not by an H-bond but by its accommodation in the carbon skeleton of the molecule between the heterocyclic rings. The steric stress within this contact is made evident by the large increase in the exocyclic bond angles at the C_2 and C'_2 atoms (attached to the C_7 atom, which connects the heterocyclic rings) to 129.0°, and the bond angle of the C_7 atom to 128.2°. Nevertheless the shortenings detected in the C···O and H···O contacts do not reach the lower limits expected from the van der Waals interaction (2.82 and 2.15 Å respectively).

To establish the cause of the appearance of a *Z,E* conformation in the above example of 4,6,4',6'-tetra-*tert*-butyl-substituted pyrylo-2-monomethinecyanine a calculation of the effective charges on the atoms of the cation was required.[72] In many other cases of nonrigid molecules the existence of a particular conformation can be explained simply by a geometrical analysis. In the bis-(5,5-dimethyl-1,3-dioxan-2-yl) molecule ($C_{12}O_4H_{22}$) the H···H and O···H contacts (which determine the degree of steric stress) are 2.335 and 2.646 Å long, and exceed the normal van der Waals contacts (2.31 and 2.45 Å), i.e. we observe[90] an unstressed *E*(⊥) conformation § with $\varphi = 90°$.

§ φ is the angle between the plane of symmetry of one dioxan ring and the orientation (averaged atomic plane) of the other. For a parallel orientation of the two rings $\varphi = 90°$.

A geometrical analysis was carried out in order to identify the steric stress in other conformations of the $C_{12}O_4H_{22}$ molecule, i.e. the shortest noncovalent contacts were calculated on the assumption that the conformation of the rings remains unchanged. It was found that the intramolecular contacts are always shortened except in bisequatorial conformers with φ between 90° and 45°.[90] It was suggested that the advantage of the parallel orientation of the dioxan molecules ($\varphi = 90°$) over the crossed orientation ($\varphi = 45°$) is due mainly to the effect of the crystal field (the tendency for the molecule to retain its centre of symmetry in the crystal). In *P*-methoxy-*C*,*C*-bis(trimethylsilyl)methylen-*N*-(2,4,6-tri-*tert*-butylphenyl)-imino-σ^3,λ^5-phosphorane we find a *cis* orientation (torsion angle 5.1°),[91] whereas the characteristic orientation for the original iminophosphines is the *trans* (torsion angle 180°). This orientation is due to steric causes: the difficulty of bringing the methyl group bound to the oxygen atom close to the bulky $SiMe_3$ substituent. The geometrical analysis showed that the rotation of this group round the P–O bond by 180° relative to the position found in the molecule leads to impossibly short C···C contacts (2.152 and 2.614 Å).

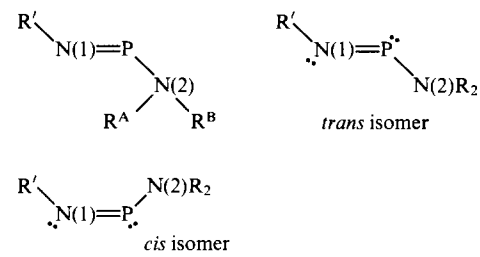
In four biphenylcarboxylic acids (4,4′-dinitro-2-carboxybiphenyl, 2′,4-dinitro-2-carboxybiphenyl, 2′-nitro-2-carboxybiphenyl, and 2′,4,4′-trinitro-2-carboxybiphenyl) the dihedral angle between the aromatic rings takes the values[92] −57.9°, −67.3°, +78.6°, and +89.4° because of the repulsion between the substituents. As a result of internal rotation round a single bond the intramolecular distances between not covalently bonded atoms and atomic groupings in all these molecules exceed the distances corresponding to normal van der Waals contacts.

Furthermore, steric hindrances often produce a distortion of the bond angles and an extension of the valence bonds. The distortion increases the probability of bond breaking, and therefore many workers place special emphasis on these sources of instability. Shortened contacts resulting from the distortion of the bond angles have been observed recently[93–98] in various structures by using statistically averaged values of the WR. In some cases inflections in the heterocycles of the molecule are accompanied by repulsion of the atoms which are not covalently bonded, as shown by the WR values,[99] and in other cases the CIC is accompanied by the loss of coplanarity of various fragments of the heterocycle.[100] In the [*N*,*N*,*N*′-tris-(trimethylsilyl)-diamido-*N*″-trimethylsilyl-*P*-phenyl-phosphon-imidato]phenylzinc molecule the presence of bulky trimethylsilyl substituents produces marked steric overloading with CIC (Si···C 3.274, P···C 3.352, C···C 3.166 Å), which leads to substantial nonequivalence of some covalent bonds of the same type on the nitrogen atoms and to a strong distortion of the tetrahedral coordination of the silicon atoms.[101] In the 2-methylphenyl ester of *N*-[2,4,6-tri(*tert*-butyl)phenyl]imidophosphenous acid we find a whole group of contracted intramolecular C···C contacts (2.801–2.882 Å) and N···C contacts (2.942–3.035 Å), which lead to an increase of the CCC bond angles in the 2,4,6-$(Bu^t)_3C_6H_2N$ fragments by ~3° with respect to the ideal values.[102]

The stress generated by steric hindrances in any part of the molecule becomes distributed (if possible) more or less uniformly over the whole of the molecule. A clear example of this behaviour is seen in 3,4′-difluoro-8-*exo*-fluoro-12-*syn*-(2′-nitrophenylthio)-tetracyclo[4.4.0.$1^{2,5}$.$1^{7,10}$]dodec-3-ene, in which the stress due to C···C intramolecular contacts (3.118 Å) and magnified by the H···H contacts (1.88 Å) leads to a fairly uniform distribution of the distortion of the six bond angles in the polycyclic framework of the molecule.[76]

As we know, the deformation of the bond angles is associated with much smaller energy losses than the extension of bonds in the molecule. Therefore bond stretching effects produced by steric hindrance in overloaded molecules are met more rarely than the distortion of bond angles produced by the same effects. Recent X-ray structural studies produced new examples of this behaviour. In 2-amino-5-methyl-3-(1-methylisopropoxyallyl)-1-formyl-3,4,4-tricyanocyclopentene[103] we observe a whole group of CIC with C···C values 3.022, 3.037, 3.048, and 3.057 Å and C···H values of 2.66 Å. The C_2-C_3 and C_3-C_{11} bonds, 1.542 and 1.571 Å long, are elongated by 0.03 Å with respect to the corresponding standard values of the $C(sp^3)-C(sp^2)$ and $C(sp^3)-C(sp^3)$ distances. According to the authors[103] this is probably due to steric overloading. In bicyclic iminoester molecules we find a group of intramolecular contacts shorter by 0.6 (C···C) and 0.4 Å (C···H) than the sum of the corresponding WR. These steric effects lengthen some of the covalent C–C bonds to 1.56–1.59 Å,[104] which increases the reactivity of these compounds (see also Section VI).

An analysis of the influence of steric and electronic factors on the conformation of three sterically overloaded λ^3-aminoiminophosphines [2,4,6-$(Bu^t)_3C_6H_2N{=}P-NR_2$, where R = Me (I), (Pr^i) (II),[105] and $SiMe_3$ (III) [106]] showed that the realisation of *cis* and *trans* forms in these materials is determined by a fine balance between these factors, and that the steric factors revealed by WR calculations have a strong effect on the length of the covalent bonds.



The predominant influence of the R···R′ repulsion following an increase in the volume of the R substituent favours the *trans* isomers. In the *trans* isomers of II and III the N(1)···C(19) (2.934 Å) and N(1)···Si(2) distances (3.227 Å) are greatly shortened with respect to the sums of WR (3.20 and ~3.60 Å); the stronger repulsion between the N(1) atom and the closely accommodated substituent R produced by replacing isopropyl by the bulkier substituent $SiMe_3$ is accompanied by an increase in the N(1)PN(2) bond angle from 105.6° to 109.3° and by an elongation of the P=N(1) bonds from 1.555 to 1.566 Å and of the P–N(2) bonds from 1.656 to 1.668 Å [though the lengthening of the P–N(2) bond may be due at least partially to the effect of the $SiMe_3$ acceptor groups], and also by an increase in the distortion of the configuration of bonds at the N(2) atom.

Steric effects in overloaded molecules can produce not only an elongation but also a shortening of the covalent bonds. The *cis* isomers of λ^3-aminoiminophosphine is energetically more favoured when the volume of the R substituent is small (i.e. for R = Me), when the electronic factors become predominant.[105,106] Nevertheless in the *cis* isomer I the N(1)PN(2) bond angle increases (for steric reasons) to 115.9° as compared with 105.6° in II and 109.3° in III, and the PN(1)C(1) angle increases to 140.7° as compared with 117.6° in III and 129.6° in II. This increase in the bond angles ultimately leads to a shortening of the P=N bond to 1.539 Å as compared with 1.555 Å in II and 1.566 Å in III. The shortening of the P=N bond is due to electronic factors: an increase in the *s*-character of the hybrid atomic orbitals which form this bond and an increase in the *p*-character of the unshared electron pairs in the nitrogen and phosphorus atoms, which favours the $n-\sigma^*$ interactions.

An even stronger shortening of the P=N covalent bond (by 0.04–0.08 Å, i.e. to 1.500 Å) is stimulated (for steric reasons) by the marked increase in the CNP angle in molecules of derivatives of two-coordinated phosphorus in which the –N=P–N< group is replaced by –N=P–O–. This is observed in molecules of 2,4,6-$(Bu^t)_3-C_6H_2N{=}P-OR$, where R = 2-MeC_6H_4 (IV)[102] and 2,6-$(Bu^t)_2$-4-MeC_6H_2 (V).[107] A geometric analysis has shown that the main cause of the increase in the CNP bond angle to 164.1° in IV and to 170.9° in V is the repulsion between the aryl

substituents on the nitrogen and the oxygen atoms; the decrease in the angle at the nitrogen atom to 140° reveals the formation of a strongly contracted C···C intramolecular contact (3.048 Å).[102] The CPN bond angles are increased by steric hindrances to 164.1° in IV and 173.7° in V, i.e. they go beyond the limits of 107.7° – 140.7° previously established for these iminophosphines. The increased bond angles also induce a shortening of the P=N bond to 1.497 Å in IV and to 1.500 Å in V (the P – N distance in the previously studied iminophosphines lay in the 1.539 – 1.575 Å range).

The influence of the steric factor on the electronic factor has been demonstrated[108] for the so-called aroylotropy of 2-substituted carboxylic acids. Here the steric effect of the F, Cl, Br substituents produces a rotation of the carboxy group round the C – C single bond and destroys its conjugation with the benzene ring: this group experiences only the inductive electronic effect of the substituent.

The contracted intramolecular contacts in overloaded molecules are often the cause, and sometimes also the consequence, of the stress in the intramolecular contacts in other parts of the molecule, and are also used to explain some anomalies in the geometric characteristics of these parts. These anomalies, in their turn, account for some of the physicochemical or chemical properties of the substance (see Section VI). Therefore the CIC in nonrigid molecules, offering the possibility of rotation round single bonds, have claimed the widest interest of research workers.

In the *N*-trimethylsilyl-2,4,6-tri-*tert*-butylphenylamidochlorophosphite molecule [$Me_3Si(Ar)N-PClOR$, where Ar = 2,4,6-$(Bu^t)_3C_6H_2$ and R = 2,6-$(Bu^t)_2$-4-MeC_6H_2] the Si and Cl atoms in the planar SiNPCl group are drawn together to within 3.330 Å by steric effects.[109] This is much shorter than the normal distance, since the normal van der Waals Si···Cl contact should be substantially longer (3.60 Å is observed in the normal C···Cl contact, and the WR of the atoms of the third-period elements, P, S, and Cl are 0.4 – 0.5 Å longer than the WR of the corresponding second-period element atoms N, O, F). The formation of the strongly contracted Si···Cl contact in this molecule is due to the presence (near the oxygen atom) of the bulky 2,6-$(Bu^t)_2$-4-MeC_6H_2 substituent, which prevents the perturbation of the planarity of the SiNPCl group. Indeed, as was shown by a geometric analysis,[109] the rotation of this substituent round the P – N bond by +30° relative to the position found in the molecule produces the unacceptably short C···Cl 2.711 and C···C 3.044 Å contacts, and the rotation through −30° produces the short C···C 2.841, 3.294, and 3.299 Å contacts. In two other phosphites of this type, where the 2,6-$(Bu^t)_2$-4-MeC_6H_2 radical is replaced by the phenyl (Ph) and by the adamantyl (Ad) radical, there are no spatial effects opposing the mutual repulsion of the Si and Cl atoms, and therefore the SiNPCl torsion angle in these materials is 68.6° and 67.7° respectively, and the Si and Cl atoms are 3.932 and 3.916 Å apart.[109] A similar case has also been described.[110] In the *N*-(2,4,6-trinitrophenyl)-*N,N'*-di-*p*-anisylbenzamidine structure the intramolecular N···C distance (2.66 Å) between the amidine nitrogen atom and the carbon atom of the picryl group is strongly shortened as compared with the normal van der Waals distance, which could be taken as evidence of both SI and of a strong steric stress. However, as was shown by a detailed analysis of noncovalent contacts carried out during an X-ray structural investigation, this shortening is due to the steric overloading of the molecule, produced by the presence of four benzene rings in the molecule. In both the structures described above the CIC directly affect the chemical properties (reactivity) of the molecules which contain them: this important problem is examined in Section VI.

V. Physicochemical properties of substances

The interpretation of the physicochemical properties of crystalline substances is often treated as the ultimate goal of crystal chemistry. Therefore the possibility of using WR to solve these problems undoubtedly confirms their effectiveness. The WR are most often used in discussions of the structural properties of crystals and molecules, but sometimes these features are directly related to the properties being discussed. In these cases we can directly attempt the interpretation, and even the predictive calculation, of the physical and physicochemical properties. Examples of this kind are discussed below.

Statistically averaged values of the WR were used as Onsager radii of the hydrogen atoms (1.16 Å) and of the CH_3 radicals (2.0 Å) in calculations of the band structure on the surface and in the bulk of polyethylene.[111] The band structure of the polyethylene molecule was calculated by semiempirical CNDO method on the surface of and within a polyethylene mass, treated as a uniform dielectric medium. The energy of the interaction of the polymeric molecule with the medium is expressed through the Onsager radii of the atoms, their average charges, valences, and bond indices. It was established that the immersion into a polyethylene mass lowers the ionisation potential of the polyethylene molecule by 0.87 eV, narrows the band gap by up to 1.9 eV, and raises the bottom of the valence band by 1.2 eV (see Semenov[111]).

As was pointed out above, the use of WR allows the detection in molecular crystals of associations of the molecules which are most tightly interconnected as a result of SI effects. The presence of these true associations must, of course, affect the physicochemical properties of the crystals. Thus, in the 3,5-dichloro-1*H*-1,2,4-triazole structure contracted intermolecular N···Cl contacts (3.149 Å for $d = 3.23$ Å) unite the cyclic trimers formed by hydrogen bonds into layers parallel to the XY plane.[55] The distance between these layers is 3.33 Å. The layer character of this crystal structure accounts for the sharp anisotropy of its thermal deformations,[55] the thermal expansion coefficient being greater in the direction perpendicular to the layers [$\alpha_3 = (161 + 0.29t) \times 10^{-6}\ K^{-1}$] than it is within the layer [$\alpha_1 = (34 + 0.19t) \times 10^{-6}\ K^{-1}$].

An analysis[112] of the intra- and intermolecular interactions in $(CCl_3)_2PCl_3$ and $Cl_3P{=}N-C(CF_3)_3$ crystals led to an interpretation of the differences in the character of the thermal motion of the PCl_3, CCl_3, and CF_3 groups. The rotation of the CCl_3 group in the $(CCl_3)_2PCl_3$ crystal is obstructed by strong intramolecular $CCl_3\cdots Cl_3P$ interactions which limit the mobility of these groups to small librations about the long axis of the molecule; the lengths of the intramolecular Cl···Cl contacts between the CCl_3 and the PCl_3 groups are 3.21 and 3.22 Å (for $d_{Cl\cdots Cl} = 3.65$ Å and $2R_{Cl} = 3.80$ Å). Furthermore the intermolecular contacts formed by the two groups $C(1)Cl_3$ and $C(2)Cl_3$ in the molecule are substantially different, the chlorine atoms of the $C(2)Cl_3$ group [unlike those of the $C(1)Cl_3$ group] having no contracted contacts. As a result of 300 K the mean square amplitude of the libration $\langle\varphi^2\rangle$ is 32 deg^2 for the $C(2)Cl_3$ group and only 3 deg^2 for the $C(1)Cl_2$ group. A decrease in temperature freezes out the enhanced libration of the $C(2)Cl_3$ group, and at 153 K the parameter $\langle\varphi^2\rangle$ for both groups is 0.5 deg^2, i.e. the molecule behaves effectively as a rigid body. A similar state of affairs exists in a $Cl_3P{=}N-C(CF_3)_3$ crystal, where we find an intermolecular Cl···F contact (3.07 Å) and three shortened Cl···F contacts (two intermolecular and one intramolecular). The $\langle\varphi^2\rangle$ values are 41 deg^2 at 208 K and 0.4 deg^2 at 153 K, i.e. the libration of the PCl_3 group is frozen by the decrease in temperature.

Great interest has been stimulated by shortened and by contracted contacts in organic conductor structures, as was pointed out in several reviews.[113–115] A large group of workers[40–45,57,59–62,116,117] attempted to interpret these contacts as factors determining the conductivity.

The organic metal $(ET)_4Cl_2 \cdot 4H_2O$ contains cation–radical layers alternating along the Z axis with layers of the complex anions $Cl_2 \cdot 4H_2O$ (see Shibaeva et al.[117]). The cation–radical layer is formed from ET stacks stretched along the Y axis, and the intermolecular S···S contacts contracted between stacks (3.451, 3.475, 3.489, and 3.541 Å) are aligned with the X axis: the maximum conduction is observed along this axis. A calculation of the conduction anisotropy (from the band structure) gives the ratio $\sigma_a/\sigma_b \approx 7$ (the anisotropy could not be determined experimentally because of the small size of the crystals). The conductivity of $(ET)_4Cl_2 \cdot 4H_2O$ crystals at room temperature is $10-50\ \Omega^{-1}\ cm^{-1}$; at ~ 20 K the material passes into the dielectric state. In the $(ET)_3Cl_2 \cdot 2H_2O$ structure the cation–radical layers along the Z axis alternate with layers of $Cl_2 \cdot 2H_2O$ complex anions, and the cation–radical layer is formed of ET stacks stretched along the X axis.[61] The anisotropy of the conductivity in these crystals is characterised by the ratio of the specific conductances $R_b : R_a : R_c = 1 : 7 : 1000$. The authors[61] suggest that the crystals should have a maximum conductivity along the Y axis; strongly contracted S···S contacts between the stacks (3.343–3.431 Å long) are stretched in this direction, and are complemented by less strongly contracted contacts (less than 3.53 Å). The average conductivity ($\sim 40\ \Omega^{-1}\ cm^{-1}$) should correspond to the X axis, i.e. to the direction of the cation–radical stacks, and the minimum conductivity to the Z axis. The anisotropy of the conductivity in crystals of $(ET)_3CuCl_4 \cdot H_2O$ (see Shibaeva et al.[42]) and of $(BEDOTTF)_2ReO_4 \cdot H_2O$, where BEDOTTF is the symmetrical bis(ethylenedioxy)tetrathiafulvalene,[44] can also be explained in terms of the length of the S···S contacts.

However, as could have been expected, the electric conductivity of these cation–radical salts does not show a direct relationship to the length of the S···S contacts. Thus, in crystals of the cation–radical salt $(ET)_4ZnCl_4 \cdot C_6H_5CN$ we find a whole series of short S···S lengths, including contracted ones,[40] but the complex internal structure of the conducting cation–radical layer gives a conductivity of only $\sim 0.9\ \Omega^{-1}\ cm^{-1}$ at room temperature; the substance is a semiconductor. But in $(BT)_2 \cdot 2Cl \cdot H_5O_2$ crystals the S···S contacts were found to be not contracted but merely shortened (lying between limits of 3.68 and 3.53 Å). Nevertheless the substance has a conductivity of $\sigma \approx 100\ \Omega^{-1}\ cm^{-1}$ and is a quasiunidimensional organic conductor.[57]

Some features of the IR spectra of chemical compounds are sometimes attributed to specific interactions. Thus, Br···Br contacts 3.55 and 3.75 Å long ($2R_{Br} = 3.94$ Å) are found in the $[(Me_2S)AuBr_3]$ structure. The authors suggest[118] that these interactions are responsible for the broadening of some bands in the IR spectrum of the complex.

By using the WR we can study the size and form of the cavities and channels in crystal structures, and in particular in zeolites. The volume and shape of the free space in zeolites strongly affect the diffusion processes in these materials and their adsorption and catalytic properties. The geometry of the free space in the pentasil ZSM-5 has been determined[119] by using the WR: the composition of this material (not allowing for the water) is described by the formula $M_xAl_{1.1}Si_{94.9}O_{192}$, where M_x is a mixture of sodium and tetraalkylammonium cations. The van der Waals radii were taken to be 1.80 Å for the Al and Si atoms and 1.29 Å for oxygen. A calculation showed[119] that all the free space in the pentasil forms an interconnected region with channels and connecting bridges of various sizes. The most favourable sites for the adsorption and diffusion of molecules are the infinite channels with a radius of 2.70–3.30 Å separated by bridges having radii of 2.64 and 2.68 Å.

Very different physicochemical properties directly related to the effective volume, size, and shape of the molecule are often found in substances.[1] Special attention is devoted to the volume of the molecules in this context. In particular, by inserting into the formulae the volumes of the self-repeating units of the polymer a large number of physical characteristics were calculated: density, coefficient of volume expansion, melting point, and many others.[120] By using the volume of the molecules of compounds to be separated a model was made of the chromatographic separation of cyclopentadienylcarbonyl complexes of the transition metals.[121] It has been reported[122] that in the similar structures $Cu(C_9H_{13}N_2O_2CH_3)_2$ and $Cu(C_9H_{13}N_2O_2CF_3)_2$ which differ only by the replacement of the CH_3 by the CF_3 radicals, the difference in the volume ascribed to one formula unit is completely explained by the difference in WR of the F (1.40 Å) and the H atom (1.16 Å).

By combining previous X-ray structural studies[124] with an allowance for the WR of the atoms the shape of several mesogenic molecules containing metal atoms with a square coordination has been described:[123] it can be adequately approximated by an anisometric prism $30 \times 10 \times 6$ Å in size. WR have been used[125] to study the structure of aqueous solutions of electrolytes, and in the analysis of structural solvation effects.

Sets of volume increments for the atoms and atomic groups present in molecules had been proposed to facilitate the calculation of molecular volumes.[120,126] The common foundation of all these calculations were the WR. More recently new methods of calculating the volumes and surface areas of molecules from the WR (as well as the density of substances) have been published.[127–131] A paper by Gavezzotti[128] (like the earlier publications of the same author) discusses the correlation between the volumes and surfaces of molecules and the energy of sublimation of the crystal. The method of calculating the atomic volume increments described by Shil'nikov et al.[129] is carried out in three steps: an analysis of the intersection of interpenetrating spheres whose size is determined (fixed) by the WR, a calculation of the increments for atoms with surroundings compatible with the use of analytical expressions, and a Monte Carlo calculation of the increments for the other atoms. Kuz'min and Katser[130] obtained the statistically averaged volume increments of individual atoms and molecular fragments by least squares. Koch and Fischer[131] used the method of constructing Dirichlet regions for the same purpose.

An empirical model which allows the density of a substance to be predicted from approximate data on the geometric structure of the molecule has been proposed.[132,133] The model is based on the concept of the WR, but in this model a special modelling function allows for the effect of the immediate surroundings of an atom on its WR. Furthermore in the calculation of the molecular volume the WR of the end atoms are artifically increased; in liquid substances this produces a more correct allowance for the vibrational motions of the molecules.

It should be noted that the dependence of the effective WR of an atom on the individual properties of the molecule which includes that atom has been discussed previously. Kitaigorodskii suggested[126] distinguishing between the WR of carbon atoms in aliphatic and in aromatic compounds (1.80 and 1.72 Å), but in subsequent publications he did not adopt this differentiation. It was postulated[134] that sterically overloaded molecules are more loosely packed in a crystal, i.e. that the atoms in these molecules have effectively larger WR (the authors called this effect the 'saturability of van der Waals bonds'). This concept was tested[135] by calculating the energies of noncovalent interactions and the packing density coefficients (K) for 159 substances. The van der Waals volumes of the molecules were calculated by using the Pauling WR.[7] This study revealed a tendency for K to decrease with increasing 'density of the molecule' (which is generally consistent with the model proposed by Atovmyan et al.[134]). However, it was concluded[135] that the straight line giving the average dependence of K on ρ_{mol} (the mass of the molecule related to its volume) cannot be used directly to determine the density of the crystal.

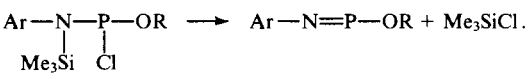
It should be noted that conclusions on the looseness of packing are sometimes reached too hastily. The fact that some intermolecular bearing contacts in the crystal exceed the conventional values is not sufficient to justify such a conclusion.

Thus, in a crystal of 2-methylthio-3-phenyl-5-methylthiocarbonyl-1,3-thiazolium-4-olate the molecules are located at a distance generally exceeding the sum of the statistically averaged WR of the atoms in contact, and this (as suggested[136]) accounts for the loose packing. However, these conclusions need to be reconsidered if they were made without allowance for the natural dispersion of the bearing contacts.

VI. Chemical reactions

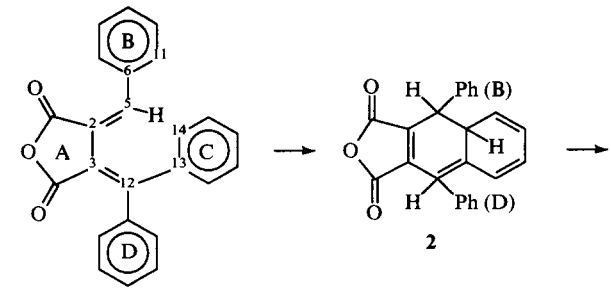
We have previously discussed[1] the steric effects of various types (discovered by using WR) which influence the reactivity of a substance: (1) steric hindrances, leading to the extension of covalent bonds or to the distortion of bond angles; (2) the shielding or complete blocking of the active centre of the molecule; (3) steric factors, which determine the angle of nucleophilic or electrophilic attack, and some other variants of the effect of steric factors on chemical processes. In the present review we shall examine, in addition to recently reported new studies in some of the directions mentioned above, examples of the use of WR in one direction not discussed in Ref. 1.

In some cases the steric effects in overloaded molecules force closer together the not covalently bound atoms: as a result the activation energy of the chemical reaction leading to the establishment of covalent bonds between these atoms is substantially lowered. Thus, in the amidochlorophosphite molecule $Me_3Si(Ar)N-P(Cl)OR$, where $Ar = 2,4,6\text{-}(Bu^t)_3C_6H_2$ and $R = 2,6\text{-}(Bu^t)_2\text{-}4\text{-}MeC_6H_2$ (I), the Si and Cl atoms are drawn together to a distance of 3.330 Å, whereas in other phosphites, where R = Ph (II) or R = Ad (III), there are no obstacles such as those found in (I), and the silicon and chlorine atoms lie at distances of 3.932 and 3.916 Å from each other respectively.[109] The covalent Si–Cl bond is 2.03 (±0.03) Å long.[137] In order to reach this value in the case of the molecule I we must contract the distance between the atoms by ~1.3 Å, and in the case of molecules II and III by ~1.9 Å, i.e. by a much greater amount. Not surprisingly the amidochlorophosphite I easily splits off trimethylchlorosilane (even at 20 °C) in a solution of tetrahydrofuran: this converts it into the λ^3-iminophosphine

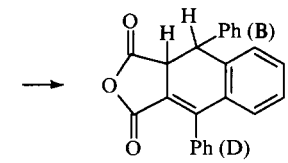


Conversely, the compounds II and III are stable up to 180 °C, and they cannot be converted into iminophosphines even by lengthy heating.[109] Similarly, in the *N*-(2,4,6-trinitrophenyl)-*N*,*N*′-di-*p*-anisylbenzamidine molecule[110] the distance between the amidine nitrogen atom and the ipso carbon atom of the picryl group (N···C 2.66 Å) is shortened by 0.54 Å in comparison with the normal van der Waals contact. This close approach of the atoms assists the migration of the picryl group towards the amidine nitrogen atom in solution.

An X-ray structural study has shown[138] that the direction of the photo- and thermochromic cyclisation reactions of *E*-benzylidene-(diphenylmethylene)succinic anhydride **1** is controlled by steric factors. The molecule of this compound is sterically overloaded (especially its diphenylmethylene fragment). In this fragment the C(3)=C(12) double bond (1.37 Å) is 0.02 Å longer, as a result of steric hindrances, than the C(2)=C(5) double bond (1.35 Å) in the benzylidene fragment. For the same reason the C(12)–C(13) bond (1.48 Å) is 0.02 Å longer than the corresponding C(5)–C(6) bond in the benzylidene fragment (1.46 Å). Furthermore the C(3)=C(12) double bond is twisted by 9.4° more strongly than the C(2)=C(5) bond (the torsion angles are 24.4° and 15.0° respectively). As a result the noncovalent distance between the C(5) and C(14) atoms, which are potential reaction centres, is 3.30 Å, which is 0.12 Å less than double the WR of carbon and 0.16 Å shorter than the distance between the atoms C(11) and C(12), (3.46 Å). Thus in the



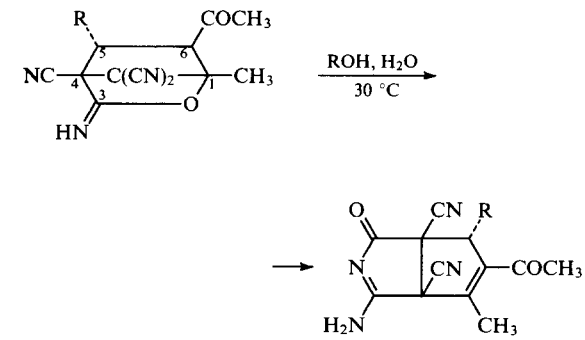
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sterically more overloaded diphenyldimethylene fragment the benzene ring C is more closely connected to the methylene centre C(5), and because of the lower barriers to rotation round the extended C(3)=C(12) and C(12)–C(13) bonds it should be more mobile than the benzene ring B in the benzylidene fragment. It was pointed out[138] that in the molecule I the noncovalent distance between the atoms H(14) and C(2) (2.76 Å) is much shorter than the H(11)···C(12) distance (3.00 Å), which can account for the fast migration of the H(14) atom (in the intermediate **2** formed by cyclisation) towards the C(2) atom, and to the formation of the stable product **3**.

In the 3-imino-4,7,7-tricyano-2-oxabicyclo[2,2,1]-heptanes,[104] which belong to the series of bicyclic iminoesters, we find several CIC between the substituent in position 5, the *gem*-dicyano group, and the C(3) atom. These CIC are 0.6 Å (C···C) and 0.4 Å (C···H) shorter than the sum of the statistically average WR of the corresponding atoms. Steric strain lengthens the C(4)–C(5) bonds to 1.58–1.59 Å and the C–$C(CN)_2$ bonds to 1.56–1.57 Å, which increases the reactivity. When kept in aqueous ethanol (or in ethanol) this compound is converted into a mixture of 3-azabicyclo-[3,3,0]octadienes even at slightly elevated temperatures:[104]



The site of the initial nucleophilic attack on one of the carbon atoms of the cyano group in the 3-(*N*′,*N*′-dimethyl-*N*-acetylhydrazino)-1,1,2,2-tetracyano-5-methylcyclopentane was investigated by a calculation[139] of the role of the steric factor based on a geometrical modelling relying on published values[3] of the WR. It was established that only the *trans* C≡N group (in the β position with respect to methyl) is accessible to nucleophilic attack: large steric hindrances are met in other positions. This conclusion was confirmed experimentally: nucleophiles are added selectively to this cyano group.

A geometrical modelling of one of the Ugi reactions for an N···C=S angle of attack of 90° in the initial stage of the nucleophilic addition for $R' = CH_3$ and $R' = CH_2R$ to 1-methyl-2-thio-4-benzylimino-5-spirocyclohexanehydantoin was carried out[140] by using statistically averaged values[3] of the WR. It was found that for $R' = CH_3$ contacts much shorter than the sum of the corresponding WR are not formed in the initial stage of the nucleophilic addition, whereas for $R' = CH_2R$ the system is highly stressed and a closer approach of the atoms is unlikely. The stereochemical features of the reaction of ammonia with perfluoro-2-methyl-2-pentene-3-thiocyanate have been analysed by the same procedure.[84] The parameter δ, defined as $R_A+R_B-d_{AB}$, where R_A and R_B are the WR of the A and B atoms and d_{AB} is the distance between them (in this case, contracted), was used as a criterion of the possible existence of various stages in the reaction. The geometrical modelling demonstrated the dominant role of the lower steric factor and led to the prediction of the following conformational consequences: for $\delta > 0.35$ Å the stresses are removed by the distortion of valence and torsional angles and of bond lengths, for $0.55 < \delta < 0.65$ Å the stresses are partially relieved by the same factor, but the system remains stressed and the probability of encountering this conformation is small, and for $\delta < 0.85$ Å the system cannot exist in this conformation. Thus the stereospecificity of the reaction indicated by the formation of only one *E*-stereoisomer (2-aminoperfluoro-4,4-dimethyl-4,5-dihydro-5-ethylidene-1,3-thiazole) is due to the lower steric stress in the anion leading to the *E*-isomer than in the anion leading to the *Z*-isomer. Strong steric stresses prevent the cyclisation on heating of *E*-3,4-diaminoperfluoro-4-methyl-2-pentene-3-thiocyanate (through the amino group of the double bond) with formation of a thiazole ring.

In a special program assembled[141] for calculating the steric shielding of the metal atom in complexonates the complex is modelled as a coordination centre with its surrounding ligands (consisting of atoms with known WR). Another program[142] for calculating the shielding of the metal atom in compounds of the MR_n type in terms of WR has been discussed.[1]

The WR method is often used to account for the spatial conditions consistent with various solid-state reactions. Let us examine a new example of this application. An X-ray structural analysis of 4,4'-methylene-bis(phenyl isocyanate) has shown[143] that N···C intermolecular contacts (3.146 Å) are formed in the packing of molecules in a crystal between pairs of isocyanate groups connected by the centre of symmetry. Though this distance is only 0.05 Å shorter than the sum of the WR of the nitrogen and carbon atoms the optimum orientation of the NCO group in the structure is compatible (as suggested[143]) with dimerisation reactions between these groups in the solid phase. This assumption agrees with the conclusion by Shklover et al.[144] that solid-phase polymerisation which produces a bond between the A and B atoms of neighbouring molecules is possible if the r_{AB} distance is not greater than $R_A + R_B + 0.5$ Å, where R_A and R_B are the van der Waals radii of the A and B atoms.

An updated method[146] of calculating the rate constants and the heats of some gas-phase reactions over a wide temperature range by using internuclear distances, WR, and the vibrational energies of molecules has been proposed in a development of a previous method.[145]

The van der Waals radii have been used also for mapping chemical reactions from X-ray diffraction data. We have already discussed[1] in depth the mapping of the tautomeric transition[147] of tropolone derivatives in terms of four aryl-substituted tropolones. A more recent study[148] of five other compounds of this series allowed the geometrical changes in the molecules to be monitored more thoroughly.

* * *

The data discussed in the present review show that the van der Waals atomic radii are still finding extensive and varied applications in chemistry. We note that the WR are much more generally used than the covalent radii, since in order to discuss the geometrical aspects of chemical bonds we need a more exact estimate of the interatomic distances, and tabulations of averaged bond lengths are most frequently used. The pathways available for these transformations were the object of both our previous review[1] and of the present work.

However, we must stress that van der Waals radii will 'work' reliably and give useful results only if used correctly.

In conclusion we should remind the reader that the concept of van der Waals radii was formulated in the 1930s and 1940s, and is the central attribute of the classical organic crystal chemistry, based on the postulate of molecular close packing. However, in recent years there has been a rapid production of data indicating the limitations of this postulate. Our increasing understanding of specific (strongly nonisotropic) atom–atom interactions has led to new views on the structure of organic crystals.[149] The results of nonempirical quantum-chemical calculations are playing an increasingly important role in discussions of molecular structures: they are now carried out systematically not only for the simplest but also for relatively complex polyatomic organic molecules. Strictly speaking these concepts leave no room for the van der Waals radii. However, van der Waals radii are a very convenient and correct means of calculating the possible lengths of noncovalent interatomic contacts: they have become an integral part of modern chemistry, and we believe that they will so remain for a long time.

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Complexes of metal chlorides with proton donors — promising polyfunctional catalysts for electrophilic processes

K S Minsker, S R Ivanova, R Z Biglova

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Abstract. The Brønsted acids formed as a result of the interaction of aluminium chlorides with Group I and II metal chlorides in the presence of proton-donating compounds are promising polyfunctional catalysts for electrophilic processes (polymerisation, depolymerisation and degradation of macromolecules, alkylation, desulfurisation, and hydrogenation). The factor determining the electrophilic activity and selectivity of the action of the catalysts is their acidity. This makes it possible to predict the direction of the changes in the activity and selectivity of the catalyst in specific chemical processes in conformity with the opposite variation rule: with increase in the acidity of the electrophilic catalyst, their activity increases but the selectivity of their action diminishes. The bibliography includes 72 references.

I. Introduction

The importance of catalysis in modern chemistry, characterised by the diversity of reactions, the enormous number of compounds, and the possibility of their modification, is very great. Naturally, the search for readily available active and selective combined-action catalysts, which make it possible to achieve under mild conditions many chemical reactions of practical importance and to investigate their properties, is of special interest.

The classical catalysts based on metal chlorides, used in numerous electrophilic reactions, are $AlCl_3$, $FeCl_3$, $SnCl_4$, etc. However, their high relative acidity also when they are combined with cocatalysts (H_2O, CH_3Cl, HCl, etc.) (Table 1, see over) is responsible in many instances for the occurrence simultaneously with the main process of undesirable chemical reactions (side and secondary reactions), such as the decomposition of the catalytic system, tar and coke formation, degradation of molecules, cross-linking of macrochains, etc. On the other hand, for catalysts characterised by a low acidity the very manifestation by the latter of catalytic properties is doubtful. It is therefore useful to consider the catalytic properties of metal chloride complexes with an acidity lower than that of $AlCl_3$, $SnCl_4$, etc. In particular, a relation between the acidity of electrophilic catalysts and their catalytic activity[6–16] and also the selectivity of their action[13–17] has been noted. The acidity of electrophilic catalysts has therefore attracted attention as a possible criterion for the preliminary assessment of their postulated activity and selectivity.

K S Minsker, S R Ivanova, R Z Biglova Department of Macromolecular Compounds and Colloid Chemistry, Bashkir State University, ul. Frunze 32, 450076 Ufa, Russian Federation.
Fax (7-347) 223 67 78 Tel. (7-347) 223 66 08 (K S Minsker)

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II. Cationic polymerisation of alkenes

The complexes of aluminium chlorides with proton-donating compounds, i.e. $H[AlCl_3OH]$, $H[Al(C_2H_5)Cl_2OH]$, etc., are catalysts for electrophilic oligo-, poly-, and co-polymerisation reactions of alkenes.[10–13,18,19] By varying the chemical nature of the Lewis acid and the proton donor (H_2O, ROH, HCl, etc.) and in essence the parameters of the acid strength of the catalyst, it is possible to form complexes with a wide range of activities and selectivities † of their action (Table 2, see over).[2,17,20,21]

The ability of electrophilic catalysts to initiate the process is determined by their acid properties, since cationic polymerisation constitutes an unusual sequence of steps occurring in accordance with the principle of the neutralisation of an acid (the active centre) by a base (the monomer),[22,23] and one has to bear in mind that, in the initiation of polymerisation by H acids, the highly acid protons abolish to some extent the differences between the basicities of the alkene monomers and, conversely, weakly acid centres are distinguished by enhanced selectivity in relation to them. The cause of the low selectivity of strongly acid (hard) centres ($H^{\delta+}$), of 'superstrong' acids is that they can interact with single C–C bonds, inducing their dissociation.[24]

The data presented below[10,25] confirm the conclusion that the activity of 'Lewis acid–cocatalyst' complex systems in the electrophilic polymerisation of alkenes depends on their acidity. For clarity, the 'Lewis acid–electron-donating

† Here and henceforth, the degree of conversion of the reactant (%) has been adopted as a measure of the activity of the catalyst.

Table 1. Acidity indices of electrophilic catalysts based on metal chlorides.

Catalyst	RAI/mequiv. (g cat.)$^{-1}$ (±0.1)	pK_a (±0.1)	q_{H^+} (±0.02)	Catalyst	RAI/mequiv. (g cat.)$^{-1}$ (±0.1)	pK_a (±0.1)	q_{H^+} (±0.02)
$H[AlCl_3OH]$	5.0	−22	0.45	$H[CdCl_2OH]$	0.1	+17.8	0.10
$H[AlCl_4]$	4.4	−16	—	$H[Al(C_2H_5)Cl_3]$	4.3	−16	—
$H[FeCl_2OH]$	3.5	−10	0.34	$H[MgAlCl_5OH]$	2.3	0	0.24
$H[BiCl_3OH]$	2.8	−4.2	0.29	$H[MgAl(C_2H_5)Cl_4OH]$	2.2	+0.9	0.25
$H[InCl_3OH]$	2.6	−2.5	0.27	$H[CaAlCl_5OH]$	2.2	+0.9	0.25
$H[MgInCl_5OH]$	1.9	+3.5	0.21	$H[CaAl(C_2H_5)Cl_4OH]$	1.8	+4.0	0.21
$H[CaInCl_5OH]$	1.6	+4.5	0.22	$H[LiAl(C_2H_5)Cl_3OH]$	1.8	+4.1	0.18
$H[MgCl_2OH]$	1.5	+7.1	0.19	$H[Al_2Cl_4(O)OH]$	—	+4.4	0.21
$H[MgCl_2OH]\cdot H_2O$	1.5	+7.7	0.18	$H[NaAlCl_4OH]$	1.6	+4.5	0.23
$H[Mg(C_4H_9)ClOC_3H_7]$	—	+7.7	0.19	$H[SrAlCl_5OH]$	1.6	+5.0	0.21
$H[AlCl_3OC_2H_5]$	1.5	+7.7	0.19	$H[BaAl(C_2H_5)Cl_4OH]$	1.4	+7.3	0.18
$H[Mg(C_2H_5)ClOH]$	—	+8.1	0.17	$H[NaAl(C_2H_5)Cl_3OH]$	1.4	+7.2	0.19
$H[Mg(C_3H_7)ClOC_3H_7]$	—	+8.5	0.18	$H[Al(C_2H_5)Cl_2OH]$	—	+7.5	0.20
$H[MgCl_2OH]\cdot 3H_2O$	1.0	+10.5	0.16	$H[Al(C_2H_5)_2ClOH]$	—	+8.5	0.18
$H[CaCl_2OH]$	1.0	+10.5	0.16	$H[Al(OH)Cl_2OH]$	—	+8.5	0.18
$[MnCl_2OH]$	1.0	+10.5	0.16	$H[Al_2(CH_3)_3Cl(O)OH]$	—	+8.5	0.18
$H[BaCl_2OH]$	0.9	+11.6	0.15	$H[ZnAlCl_5OH]$	1.1	+9.8	0.16
$H[CoCl_2OH]$	0.6	+13.8	0.13	$H[CdAlCl_5OH]$	1.1	+9.8	0.16
$H[NiCl_2OH]$	0.5	+14.5	0.12	$H[KAlCl_4OH]$	0.9	+11.6	0.13
$H[ZnCl_2OH]$	0.2	+17.0	0.10	$H[KAl(C_2H_5)Cl_3OH]$	0.8	+12.0	0.13

Note. RAI is the relative acidity index (experiment);[1] pK_a is the universal acidity index;[2,3] q_{H^+} is the charge on the catalyst hydrogen atom (quantum-mechanical calculation).[2-5]

Table 2. Polymerisation of isobutene in a mixture of hydrocarbons in the presence of complexes of aluminium chlorides with proton-donating compounds.

Catalyst	Composition of initial mixture of hydrocarbons (mass %)				Degree of conversion of isobutene (mass %)	Selectivity with respect to isobutene (relative units)
	C_3H_8	C_4H_{10}	iso-C_4H_8	Σ(*n*-C_4H_8)		
$H[AlCl_4]\cdot AlCl_3$ [a]	0.6	55.1	14.9	29.5	99	0.3
$H[Al(C_2H_5)Cl_3]$ [a]	0.6	55.1	14.9	29.5	86	0.4
$H[Al(C_2H_5)_2Cl_2]$ [a]	0.6	55.1	14.9	29.5	98	0.6
$H[Al(C_2H_5)Cl_2OC(C_6H_5)_3]$	0.6	55.1	14.9	29.5	90	0.8
$H[Al(C_2H_5)Cl_2OCH_3]$	0.6	55.1	14.9	29.5	95	0.8
$H[Al(C_2H_5)Cl_2OH]$	0.9	45.1	31.1	23.0	99	1.0
$H[Al(C_2H_5)Cl_2OH]$	3.0	55.5	37.9	3.5	96	1.0
$H[Al(C_2H_5)Cl_2OH]$	3.9	67.5	11.3	17.3	98	1.0
$H[Al(C_2H_5)Cl_2OC(CH_3)_3]$	3.0	55.5	37.9	3.5	90	0.8

Note. Reaction conditions: T = 253 K, concentration of hydrocarbons 1.3 M, [Cat] = 5.6×10^{-2} M, solvent — heptane.
[a] [Cat] = 7.3×10^{-3} M, solvent — CH_2Cl_2.

additive' complexes are arranged in series in conformity with their electrophilic activity (the region of active systems is indicated).

$BF_3\cdot R_2O$	$\underline{AlCl_3\cdot R_2O}$	$RAlCl_2\cdot R_2O$	$R_2AlCl\cdot R_2O$	$R_3Al\cdot R_2O$
$BF_3\cdot ROH$	$AlCl_3\cdot ROH$	$\underline{RAlCl_2\cdot ROH}$	$R_2AlCl\cdot ROH$	$R_3Al\cdot ROH$
$BF_3\cdot H_2O$	$AlCl_3\cdot H_2O$	$RAlCl_2\cdot H_2O$	$\underline{R_2AlCl\cdot H_2O}$	$\underline{R_3Al\cdot H_2O}$
$BF_3\cdot HHal$	$AlCl_3\cdot HHal$	$RAlCl_2\cdot HHal$	$R_2AlCl\cdot HHal$	$R_3Al\cdot HHal$

The substituents R in the Lewis acid and in the electron-donating additive can be both the same and different.

With decrease in the strength of the Lewis acids from left to right, the set of activators from isotypical series promoting the formation of the active centres becomes narrower. The strongest acid (BF_3) induces the ionisation of all the activating bases.[26] Owing to their weak electron-accepting properties, weak Lewis acids show a low activity or are inactive. Evidently, the majority of the effective electrophilic catalysts occupy an intermediate position between the two cases examined as regards their activity.

Formal considerations[10,19] show that the mechanism of the cationic polymerisation of alkenes, in particular isobutene (IB), is fairly simple and includes the following elementary stages with participation of carbonium ions:

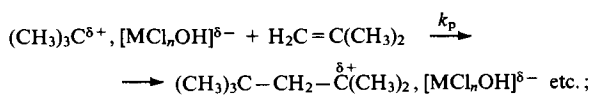
(a) the formation of the catalytic complex:

$$MCl_n + H_2O \longrightarrow [MCl_n\cdot H_2O] \longrightarrow H^{\delta+}, [MCl_nOH]^{\delta-} \text{ (or } H^+, A^-);$$

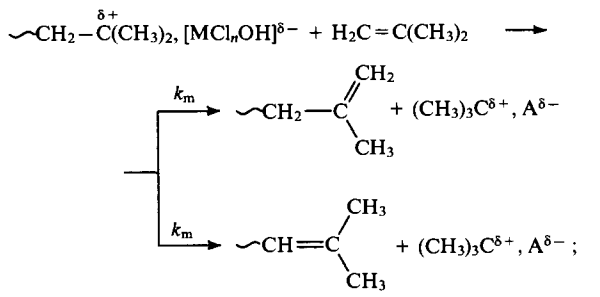
(b) initiation:

$$H^{\delta+}, [MCl_nOH]^{\delta-} + H_2C{=}C(CH_3)_2 \xrightarrow{k_i} (CH_3)_3C^{\delta+}, [MCl_nOH]^{\delta-};$$

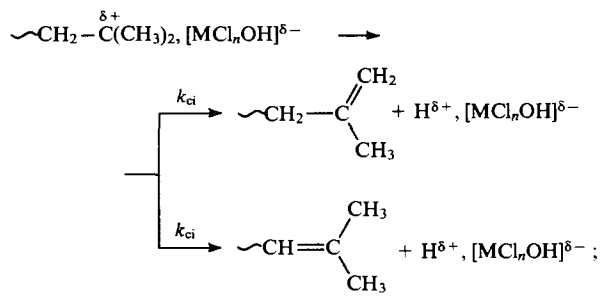
(c) chain propagation:



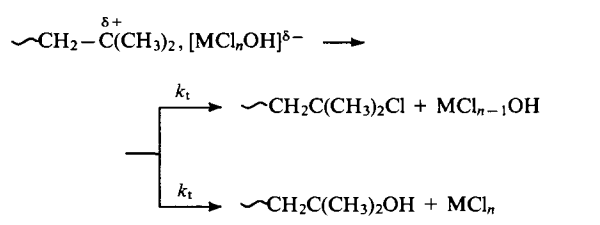
(d) chain transfer to the monomer:



(e) proton transfer to the counterion (probable reaction):



(f) chain termination with capture of a fragment of the counterion.



Like the polymerisation of other alkenes, the polymerisation of isobutene has a series of characteristic features associated with the occurrence of reactions involving the formation and growth of polymeric carbonium ions. The slight internal stabilisation of the growing carbonium ions having the isobutene structure (owing to the absence of strong electron-donating substituents at the cationic centre) is responsible for the significant role of the solvating (electrostatic) function of the monomer despite its low relative permittivities ($\varepsilon = 2-3$). The low degree of solvation of carbonium ions by virtue of their size does not rule out but actually presupposes the effective external stabilisation of the cationic active centre by means of the monomer, associated with its nucleophilicity. This is the reason for the extremely rapid growth of carbonium ions, characteristic of the electrophilic polymerisation of isobutenes, such growth determining in its turn the characteristic features of the isobutene polymerisation reaction in the presence of metal chloride complexes with proton-donating compounds. As a consequence of the high rates of polymerisation and at the same time a fairly pronounced exothermicity of the process (71.9 kJ mol^{-1}), a situation arises such that, even for very slow addition of the initiator and rapid stirring, it is not possible to remove the heat evolved during the reaction in the liquid phase. In this case, the kinetic constants (in particular, $k_p > 10^6$ litre $mol\ s^{-1}$), especially under the conditions involving the formation of a viscous product, may prove to be higher than the diffusion constant (k_D) and the reaction begins almost immediately after the addition of drops of the initiator solution to the liquid monomer, i.e. long before the monomer and initiator drops have been mixed.[19] Hence it follows that, in the cationic polymerisation of isobutene in the presence of metal chloride complexes with proton-donating compounds and a series of other electrophilic catalysts, the principle of a steady-state process cannot be maintained. This means that in reality the molecular masses of the polymer are lower and the molecular distribution (MMD) is broader than expected for an isothermal process (this is in fact observed experimentally[27,28] under industrial conditions). Calculation for the nonstationary polymerisation of isobutene in turbulent streams and modelling of this process have been described in detail in a number of studies[29-35] and will not be discussed in the present review.

III. Degradation of polyalkenes (depolymerisation and degradation of macrochains)

Certain complexes of metal chlorides with a reduced acidity compared with $AlCl_3$, especially catalytic systems such as Brønsted acids based on double salts of aluminium chlorides with Group I and II metal chlorides and proton-donating compounds {H[MAlCl$_4$OH], H[MAlCl$_5$OH], H[MAl(R)Cl$_3$OH], etc.}, are extremely active in processes involving the selective thermocatalytic degradation of polyalkenes, butyl rubber (BR),[8-10,36-46] and petroleum raw material.[47-49] The main gaseous products are then C_4 hydrocarbons (Table 3, see over).

The purely thermal decomposition of polyalkenes is accompanied by the formation of a large set of reaction products (ranging from C_1 to C_6 hydrocarbons), characteristic of the pyrolysis of hydrocarbons. Therefore the concept of selectivity loses its significance when applied to the thermal degradation of polyalkenes.

The electrophilic catalytic degradation of polyalkenes in the presence of H[AlCl$_3$OH] proceeds with a higher yield of low-molecular-mass gaseous products than in the purely thermal decomposition and at lower temperatures. However, this reaction too is insufficiently selective judging from the yield of the monomer (Table 3), because the decomposition of polymeric carbonium ions in the presence of a relatively hard acid involves the formation of a series of gaseous products: ranging from CH_4 (abstraction of methyl substituents) to C_4H_{10} and C_4H_8 (skeletal isomerisation of the macroion with subsequent β-decomposition of the carbonium ion) and also of liquid and wax-like substances, in particular C_5 and other higher hydrocarbons. A major role is attributed in this case to reactions involving random chain transfer to the polymer. Thus the high acidity of the electrophilic polymerisation catalysts promotes an increase in their activity, but reduces the process selectivity. A moderate decrease in the acidity of catalysts of the type H[MAlCl$_4$OH] and H[MAlCl$_5$OH] (compared with $AlCl_3$, etc.) (Table 1) has a favourable effect on the relative contributions of the chain propagation and chain transfer reactions.[37,40] As a result, the process selectivity as regards the yield of C_4 hydrocarbons, in particular iso-C_4 hydrocarbons, increases appreciably (Table 3).

The mechanism of the thermocatalytic degradation of polyalkenes in the presence of catalysts with reduced acidity compared with $AlCl_3$—complexes of metal chlorides with proton donors—differs from the mechanism of the purely thermal decomposition reactions of the alkenes.

The thermolysis of polyalkenes proceeds via a free-radical mechanism,[50] whereas the degradation of polyalkenes in the presence of electrophilic catalysts, in particular Brønsted acids, takes place with participation of carbonium ions.[8,9,51-54]

It has been demonstrated experimentally and theoretically (the LCAO-MO method in the CNDO/2 approximation[8,9,46]) that proton-donating compounds participate in the formation of

Table 3. Thermocatalytic degradation of polyalkenes.

Catalyst	Yield of gaseous products (mass %)[a]	Composition of C_4 hydrocarbons (mass %)			Selectivity of catalyst (relative units)
		iso-C_4H_{10}	iso-C_4H_8	$\sum C_4$	
Polyethylene					
Without catalyst	41[b]	1.1	18.7	47.1	0.57
H[$AlCl_3OH$]	16.2	31.6	2.5	47.5	0.57
H[$LiAlCl_4OH$]	11.1	50.5	18.5	79.8	0.8
H[$NaAlCl_4OH$]	8.4	50.3	24.0	79.3	0.82
H[$KAlCl_4OH$]	3.0	41.7	25.9	83.9	0.85
H[$Li(C_2H_5)AlCl_3OH$]	10.2	39.2	26.5	83.4	0.85
H[$Na(C_2H_5)AlCl_3OH$]	7.0	38.4	27.3	89.8	0.9
H[$K(C_2H_5)AlCl_3OH$]	4.0	39.3	21.2	78.3	0.88
$MgCl_2 \cdot AlCl_3 \cdot H_2O$	88.2[c]	42.5	21.8	85.0	0.85
H[$Mg(C_2H_5)AlCl_4OH$]	54.0	39.9	28.2	89.3	0.89
H[$Ca(C_2H_5)AlCl_4OH$]	42.0	37.8	22.7	89.4	0.89
H[$Ba(C_2H_5)AlCl_4OH$]	31.0	37.3	24.3	91.3	0.9
Polyisobutylene					
Without catalyst	76.0[c]	2.1	16.0	19.1	0.2
H[$AlCl_3OH$]	63.0[c]	2.1	19.1	22.1	0.2
H[$NaAlCl_4OH$]	38.2	7.0	88.8	98.1	1.0
H[$Li(C_2H_5)AlCl_3OH$]	27.0	7.0	87.5	97.5	1.0
H[$Na(C_2H_5)AlCl_3OH$]	24.2	6.9	88.3	98.3	1.0
H[$K(C_2H_5)AlCl_3OH$]	19.8	7.2	87.3	97.8	1.0
$MgCl_2 \cdot AlCl_3 \cdot H_2O$	93.8	24.2	73.4	98.0	1.0
H[$Mg(C_2H_5)AlCl_4OH$]	59.6	7.0	91.3	99.1	1.0
H[$Ca(C_2H_5)AlCl_4OH$]	54.0	7.2	90.5	98.3	1.0
H[$Ba(C_2H_5)AlCl_4OH$]	45.2	8.1	86.5	98.6	1.0
Butyl rubber					
Without catalyst	50.5[c]	traces	3.0	36.7	0.6
H[$AlCl_3OH$]	75.0	58.3	0.5	58.8	0.6
H[$LiAlCl_4OH$]	39.8	23.6	39.1	76.1	0.75
H[$KAlCl_4OH$]	86.0	30.3	24.8	62.3	0.62
$MgCl_2 \cdot AlCl_3 \cdot H_2O$	75.4	2.1	93.8	97.2	1.0

Note. Reaction conditions: $T = 573$ K, process time 1 h, [Cat] = 1×10^{-3} mol g^{-1}, the values of $\bar{M}_n$ for high pressure polyethylene (HPPE), polyisobutylene (PIB), and butyl rubber (isobutene–isoprene copolymer, 1.7 mol.% of BR) are 2200, 1100, and 257 000 respectively. [a] Molecular hydrogen was identified among the gaseous products; [b] T = 673 K; [c] T = 653 K.

the electrophilic catalysts. The influence of H_2O and ROH in the activation of electrophiles is determined by the dissociative adsorption of such a proton-donating cocatalyst on the catalyst surface. Therefore the structure of the electrophilic centres corresponds to the structure of the Brønsted acid: $H^+[AlCl_3OH]^-$, $H^+[AlCl_3OR]^-$, $H^+[MAlCl_4OH]^-$, $H^+[MAl.(C_2H_5)Cl_3OH]^-$, etc. The series of changes in the activity of such catalysts is consistent with the increase in their acidity (Table 1). They are capable of initiating both the random decomposition of macromolecules (degradation of polymer chains) and their decomposition in accordance with the end group route (depolymerisation of polymer chains).[37,40] Depending on the type of process, particular reaction products predominate, the selectivity in the action of the catalyst increasing with increase in the contribution of the reaction initiating process in accordance with the end group route.

It has been suggested that the equation for the rate of degradation of polyalkenes with allowance for the stationary nature of the concentration of the active centres for the depolymerisation of macromolecules and the rapid chain propagation in depolymerisation be used to estimate the rate constants for both random initiation (k_{ic}) and initiation in accordance with the end group route (k_{it}), as well as the corresponding lengths of the kinetic chains (z_c and z_t).[8,9,42]

$$\frac{d[P]}{dt} = z_t k_{it} c + z_c k_{ic} [P], \quad (1)$$

where [P] is the concentration of the polymer and c the concentration of the terminal double bonds varying in accordance with the exponential law

$$c = c_0 \exp(-k_{it} t).$$

Here c_0 is the initial content of the double bonds.

The solution of Eqn (1) yields

$$[P] = \exp(-k_{it} z_t t) + \frac{k_{it} z_t c_0}{k_{it} - k_{ic} z_c} [\exp(-k_{it} t) - \exp(-k_{ic} z_c t)]. \quad (2)$$

The quantities k_{it}, k_{ic}, z_t, and z_c may be determined in the initial stages of the degradation process where $[P] \ll 1$ and $t \ll 1/k_{it}$. In this case, it is permissible to disregard the change in the concentration of the terminal double bonds. The decrease in the amount of the polymer (expressed as fractions of the initial amount) is then described by the equation

$$[P] = 1 - k_{ic} z_c t - k_{it} z_t c_0 t. \quad (3)$$

The kinetic parameters obtained for to the thermocatalytic degradation of polyisobutylene[9] in the presence of a catalyst with a moderate relative acidity (from 1.4 to 2.3 mequiv. per gramme of the catalyst) are presented in Table 4. Regardless of the chemical structure of the catalyst, the numerical values of both k_{it} and k_{ic} hardly change (within the limits of error). This confirms (taking into account the overall yield of the gaseous products and also the content of iso-C_4 hydrocarbons) the conclusion that the activity and the selectivity of electrophilic

Table 4. Principal kinetic parameters of the catalytic degradation of polyisobutylene.

Catalyst	T/K	$10^6 k_{ic}/s^{-1}$	$10^6 k_{it}/s^{-1}$	z_c	z_t
$H[Na(C_2H_5)AlCl_3OH]$	473	0.45	3.50	8	8
	493	0.48	2.50	7	16
	513	1.12	2.10	4	26
	533	1.50	1.90	3	37
$H[NaAlCl_4OH]$	473	0.53	3.50	7	4
	493	0.62	3.30	5	9
	513	0.80	2.90	5	15
	533	1.20	2.50	4	20
$H[Mg(C_2H_5)AlCl_4OH]$	473	0.36	4.90	12	10
	493	0.45	3.10	11	21
	513	0.69	2.40	9	33
	533	0.89	2.20	8	42
$2MgCl_2 \cdot AlCl_3 \cdot H_2O$	473	0.54	4.60	9	7
	493	0.77	2.70	7	17
	513	1.07	2.20	6	28
	533	1.17	2.00	6	39

Note. Reaction conditions: [Cat] = 1×10^{-3} mol (g PIB)$^{-1}$. The errors are $\pm 3\%$ in the determination of k and $\pm 5\%$ in the determination of z.

catalysts, in particular complexes based on metal chlorides, are related to their relative acidity index. The ratio of k_{it} and k_{ic} (Table 4) indicates the preferential initiation of the depolymerisation of the macromolecules in accordance with the end group route at relatively low temperatures of the degradation of the polymeric product. With increase in the process temperature, the contribution of random reactions increases, but the decrease under these conditions in the length of the kinetic chain in the decomposition of polyalkenes for random process initiation (z_c) compared with the length of the kinetic chain for initiation in accordance with the end group route (z_t) may be only apparent. The actual increase in the number of monomer units formed for the random initiation of the process also occurs, since the energy of the β-decomposition of the carbonium ion diminishes under these conditions, but, against the background of the sharp increase in the number of breaks in the macrochains, the degradation of the macromolecules is not manifested.

For low degrees of polymerisation ($\bar{P}_n^0$), the values of z_t are actually equal to the chain length in the depolymerisation of macromolecules. For high values of $\bar{P}_n^0$, z_t becomes constant, which is evidently determined by the relative contributions of the chain propagation and destruction reactions on the carbonium ion active centres formed from the end groups.[8,9]

The presence of a tertiary carbon atom and especially of the C=C double bonds (both terminal and internal) in the macromolecules exerts a signficant influence on the thermocatalytic degradation of polyalkenes. In particular, process initiation predominantly in accordance with the end group route is characteristic of low-molecular-mass PIB specimens with a high relative content of C=C double bonds (Fig. 1), because in the course of the thermocatalytic decomposition of the polymer a slight change in the molecular masses of the polymeric products is observed (in the initial stages of the process, $\bar{P}_n/\bar{P}_n^0 \approx 1$). The ratio $\bar{P}_n/\bar{P}_n^0$ diminishes only for high degrees of conversion. For high-molecular-mass PIB specimens, isobutene–isoprene copolymers containing labile bonds at the junctions between the isobutene clusters and the isoprenyl unit with a C=C bond, and polyethylene (PE) (regardless of its molecular mass) containing internal vinylidene and *trans*-vinylidene C=C bonds, the overall degradation of the macromolecules proceeds simultaneously both as a random process and

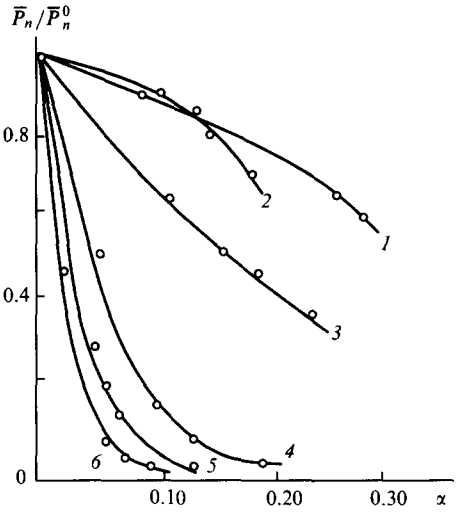


Figure 1. Dependence of the relative degree of polymerisation on the extent of reaction (α) during the thermal catalytic degradation of polyisobutylene (PIB) at 573 K in the presence of $H[NaAlCl_4OH]$. Catalyst concentration 1×10^{-3} mol (g PIB)$^{-1}$. Initial degree of polymerisation of PIB: (*1*) 17; (*2*) 20; (*3*) 49; (*4*) 360; (5) 1790; (*6*) 3570.

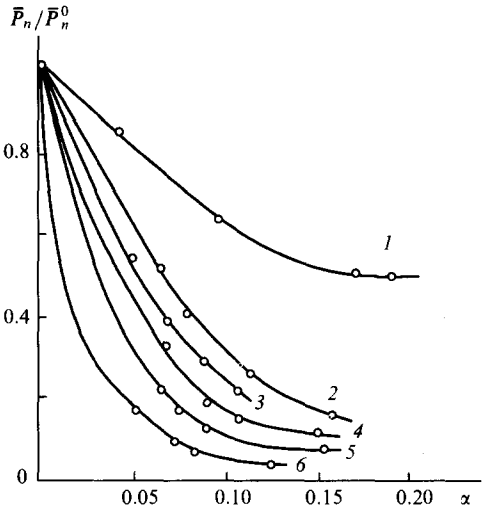


Figure 2. Dependence of the relative degree of polymerisation on the extent of reaction (α) of low pressure polyethylene (LPPE) during thermocatalytic degradation at 633 K in the presence of $H[NaAlCl_4OH]$. Catalyst concentration 1×10^{-3} mol(g LPPE)$^{-1}$. Initial degree of polymerisation of LPPE: (*1*) 2×10^4; (*2*) 6×10^4; (*3*) 1.45×10^5; (*4*) 2.5×10^5; (*5*) 2.7×10^5; (*6*) 8.7×10^5.

in accordance with the end group route, but with different contributions of these mechanisms to the overall process (Fig. 2). The possibility of the initiation of the degradation of macromolecules also via the vinyl end groups cannot be ruled out.

In the general case, the thermocatalytic degradation reactions of polyalkenes are initiated as follows:

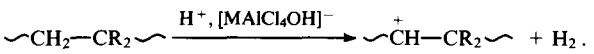
(a) the end group route:

(b) the random route:

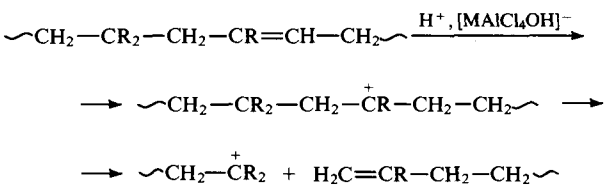
$$\sim CH{=}CR_2 \xrightarrow{H^+,[MAlCl_4OH]^-} \sim CH_2{-}\overset{+}{C}R_2,$$

R = CH_3 (PIB, BR), H (PE);

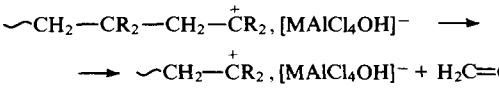
(b) the random route:



The random route in relation to BR and PE:

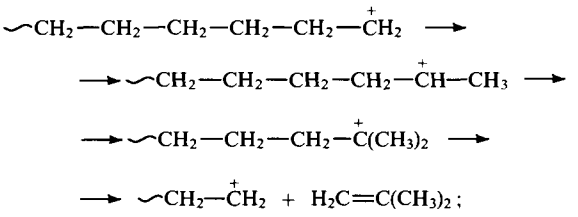


The modes of the chain propagation reactions in the course of the decomposition of macrocations may differ significantly depending on the structure of the selected polymer. For example, in the thermocatalytic degradation of PIB and BR, the carbonium ions formed decompose by β-elimination of the monomer—in the given instance isobutene (Table 3):

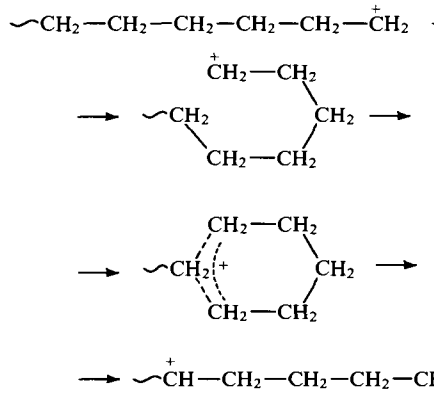


In the thermocatalytic degradation of PE, the linear carbonium ion $R-{}^{+}CH_2$ formed in the reaction can react via two main paths:

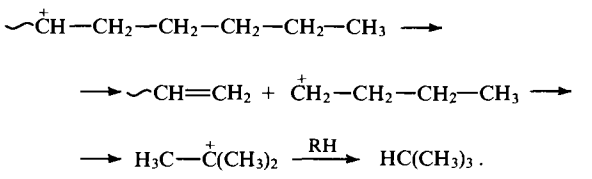
(1) as a result of skeletal isomerisation with formation of a tertiary carbonium ion, which decomposes further into a new carbonium ion and isobutene:



(2) as a result of the isomerisation of the macrocation accompanied by the transfer of the excess positive charge to the sixth carbon atom via an intermediate reaction involving the cyclisation of 'flexible' sequences made up of methylene groups:

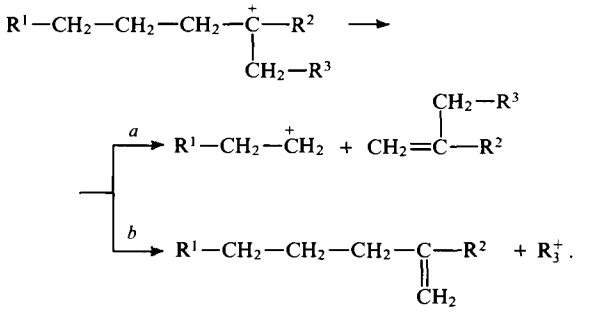


The β-decomposition of the carbonium ion formed and subsequent isomerisation reaction and the reaction involving the abstraction of a proton from the neutral polymer molecule lead to the formation of isobutane (Table 3):



We may note that this reaction does not correspond to the classical mechanism of the PE depolymerisation process, but can be regarded as a coupled reaction involving the degradation of macromolecules and chain transfer.

In the thermocatalytic decomposition of PE, the macromolecules of which contain branches, for example, high pressure polyethylene (HPPE), the carbonium ions may be formed not only from the C=C double bonds but also from a tertiary carbon atom. The subsequent degradation of the polymeric carbonium ions proceeds via two paths: degradation of the main chain (*a*) and decomposition of the polymeric carbonium ion with elimination of the surrounding group (chain branching) (*b*):



A new carbonium ion, undergoing further decomposition, as well as 'dead' polymer, the macromolecule of which contains a vinylidene bond, are formed in both cases.

Thus the presence of a tertiary carbon atom and especially of C=C double bonds in the polymer chains plays an important role in the initiation of the degradation of the macromolecules and in the propagation of the thermocatalytic electrophilic degradation of polyalkenes. The stability of polyalkenes in their thermocatalytic electrophilic degradation diminishes in the following sequence: high pressure polyethylene > low pressure polyethylene > polypropylene > poly-isobutylene > butyl rubber,[42] i.e. an increase in the degree of substitution of the carbon atoms in the macromolecules leads to a decrease in the stability of the latter.

IV. Hydrogenolysis (dehydrosulfurisation) of organosulfur compounds

The complexes of metal chlorides having an acidity lower than $AlCl_3$, in particular $H[MAlCl_4OH]$ (M = Li, Na, K) and other compounds of this type, formed as a result of the interaction of $AlCl_3$ with Group I and II metal chlorides (with H_2O as the cocatalyst),[55] exhibit a fairly high activity and selectivity in the reactions involving the hydrogenolysis of organosulfur compounds of different classes (mercaptans, sulfides, disulfides, thiophene) and accompanied by the elimination of H_2S.[56–61] The process proceeds under mild conditions (450–625 K, atmospheric pressure) and does not require the introduction of molecular hydrogen into the reaction zone (Tables 5 and 6).

The nature and structure of the molecules of the hydrocarbon solvent, which behaves as a hydrogen donor, exert an appreciable influence on the extent of the reaction. The most suitable solvents are naphthene hydrocarbons, which is due to their high proton-donating capacity compared with paraffins having the normal structure and especially arenes.

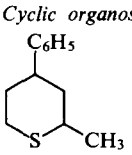
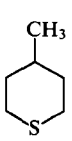
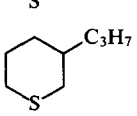
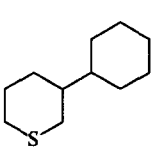
On the basis of experimental data for the hydrodesulfurisation of the naphthene fractions of hydrocarbons[57] and also

Table 5. Gaseous products of the hydrogenolysis of certain organosulfur compounds.

Catalyst	Content of gaseous products (vol.%)											Conversion with respect to S (mass %)	Catalyst selectivity (relative units)
	H_2	H_2S	CH_4	C_2H_4	C_2H_6	C_3H_6	C_3H_8	iso-C_4H_{10}	n-C_4H_{10}	ΣC_4H_8	ΣC_5		
Hexanethiol													
H[LiAlCl$_4$OH]	2.2	15.3	9.91	16.65	17.52	9.30	1.91	11.30	11.32	4.59	—	46	0.7
H[NaAlCl$_4$OH]	2.5	16.84	11.46	11.95	4.99	1.86	11.4	18.0	6.00	11.0	4.0	47	0.9
H[KAlCl$_4$OH]	2.0	20.85	4.43	3.47	traces	6.62	23.78	22.32	11.16	2.53	2.84	23	0.8
Dihexyl sulfide													
H[NaAlCl$_4$OH]	1.38	13.31	6.12	3.90	1.84	6.33	13.0	26.23	19.16	8.39	—	33	0.7
Thiophene													
H[NaAlCl$_4$OH]	5.29	40.19	10.07	4.67	2.07	0.8	1.25	10.23	12.56	0.24	12.63	7	0.3

Note. Reaction conditions: $T = 523$ K, reaction time 30 min, [Cat] = 1 M, solvent — dodecane.

Table 6. Rate constants for the desulfurisation of certain organosulfur compounds.

Compound	Degree of conversion with respect to S (mass%)	$10^4 K/s^{-1}$	Selectivity (relative units)
Acyclic organosulfur compounds			
$C_6H_5CH_2SCH_2C_6H_5$	83	8.5	0.9
$C_6H_5SC_{10}H_{21}$	80	7.8	0.8
$C_6H_5SC_3H_7$	70	5.5	0.7
iso-$C_5H_{11}SC_3H_7$-n	50	3.3	0.6
tert-$C_6H_{13}SC_6H_{13}$-*n*	40	2.3	0.5
n-$C_6H_{13}SC_6H_{13}$-n	33	1.8	0.5
n-$C_6H_{13}SH$	47	220	0.9
n-$C_6H_{13}SH$ [a]	51	170	0.7
n-$C_6H_{13}SH$ [b]	37	230	0.8
Cyclic organosulfur compounds			
	90	6.7	0.9
	60	4.5	0.6
	45	3.3	0.5
	40	2.5	0.5
	35	2.0	0.4
	25	0.3	0.3

Note. Reaction conditions: T = 523 K, catalyst — H[NaAlCl$_4$OH], [Cat] = 1 M, solvent — dodecane.
[a] Catalyst — H[LiAlCl$_4$OH]; [b] catalyst — H[KAlCl$_4$OH].

certain individual organosulfur compounds in hydrocarbon solvents,[58] the catalytic systems H[MAlCl$_4$OH] can be arranged in the following sequence in terms of their activity and the selectivity of their action: H[LiAlCl$_4$OH] > H[NaAlCl$_4$OH] > H[KAlCl$_4$OH]. This sequence agrees with the variation of their acid strength (pK_a, q_{H^+}, RAI) (Table 1).

In all cases, the desulfurisation of organosulfur compounds is accompanied by the formation of gaseous and liquid products (Tables 5 and 7), the main gaseous reaction product at 450–475 K being H_2S (96–98 mass %) under these conditions.

The heterophase, i.e. in the presence of H[MAlCl$_4$OH], hydrogenolysis of organosulfur compounds is complex in view of the occurrence of a series of consecutive-parallel chemical reactions with participation of the hydrocarbon solvent as a proton donor — as a consequence of the polyfunctionality of the action of the catalyst. The process is described by the kinetic equations for topochemical reactions of the Avrami–Erofeev type:[62]

$$c(\tau) = c(\tau_0)\exp[-k(\tau)^n],$$

where $c(\tau_0)$ and $c(\tau)$ are the initial and current concentrations of the reactants respectively, k is the observed rate constant for the reaction of the organosulfur compounds, and n is the reaction order. At the same time, the rate constants for the hydrogenolysis of the organosulfur compounds were estimated from the initial sections of the kinetic curves for low degrees of conversion assuming that the process obeys first-order reaction conditions. The molecular structure of the organic sulfur-containing compounds exerts an appreciable influence on the rate of hydrogenolysis and they can be arranged in the following sequence in terms of their reactivities: hexanethiol > dihexyl sulfide > thiophene. This follows with the strength of the C–S bond in these molecules.[63]

In the desulfurisation of sulfides (Table 6), the reactivity of the compounds investigated varies in the following sequence:
(a) acyclic sulfides:

$$C_6H_5(CH_2)_2-S-(CH_2)_2C_6H_5 > C_6H_5-S-C_{10}H_{21} > \text{iso-}C_5H_{11}-S-C_3H_7\text{-n} > C_6H_5-S-C_3H_7 > \textit{tert}\text{-}C_6H_{13}-S-C_6H_{13}\text{-n} > \text{n-}C_6H_{13}-S-C_6H_{13}\text{-n};$$

(b) cyclic sulfides:

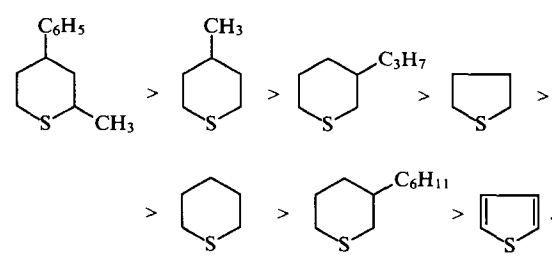
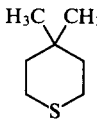
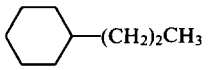
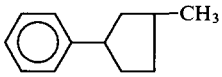
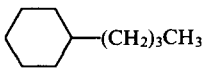
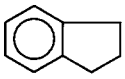
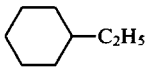
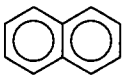
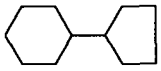
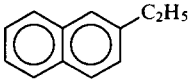
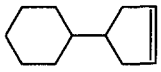
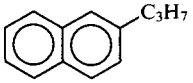
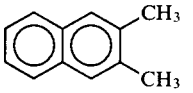
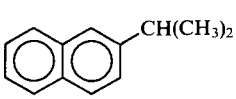
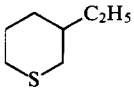
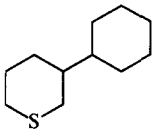


Table 7. Liquid products of the reactions of certain cyclic sulfides (Schemes 1 and 2).

Products of reaction of 3-cyclohexylthiacyclohexane	Content (mass %) at t = 15 min	Content (mass %) at t = 60 min	Products of reaction of 2-methyl-4-phenylthiacyclohexane	Content (mass %) at t = 15 min	Content (mass %) at t = 60 min
$n\text{-}C_9H_{20}$	3.5	1.0	$n\text{-}C_{12}H_{26}$	30.9	26.9
$n\text{-}C_{10}H_{22}$	10.2	2.7	$iso\text{-}C_{12}H_{26}$	34.0	36.8
$n\text{-}C_{11}H_{24}$	10.8	0.8		7.1	—
$n\text{-}C_{12}H_{26}$	29.9	32.6	$C_6H_5C_2H_5$	—	3.4
$iso\text{-}C_{12}H_{26}$	12.5	22.3	$C_6H_5CH(CH_3)_2$	2.2	3.9
$C_2H_5CH(CH_3)(CH_2)_3CH_3$	2.8	4.7	$C_6H_5CH=CH_2$	5.0	1.9
	11.3	11.9		4.9	5.2
	2.5	1.7		6.9	4.7
	1.5	2.0		1.6	—
	8.7	16.2		3.8	6.5
	—	2.8		1.3	2.4
	1.8	—		2.9	4.6
	1.3	—		—	3.7
	0.9	—			
	2.3	1.3			

Note. Reaction conditions: T = 523 K, catalyst — $H[NaAlCl_4OH]$, [Cat] = 1 M, solvent — dodecane (t = reaction time).

Evidently, enhancement of the electron-donating properties of the substituent (taking into account its position relative to the S atom in the cyclic sulfides) weakens the C–S bond. The reactivity of cyclic sulfides diminishes in the presence of bulky substituents capable of giving rise to steric hindrance in the hydrogenolysis of organic thiacycloalkanes. The desulfurisation of organic sulfides is favoured by an increase in the degree of branching in the hydrocarbon fragment, which is also due to the enhancement of the electron-donating functions of the substituent.

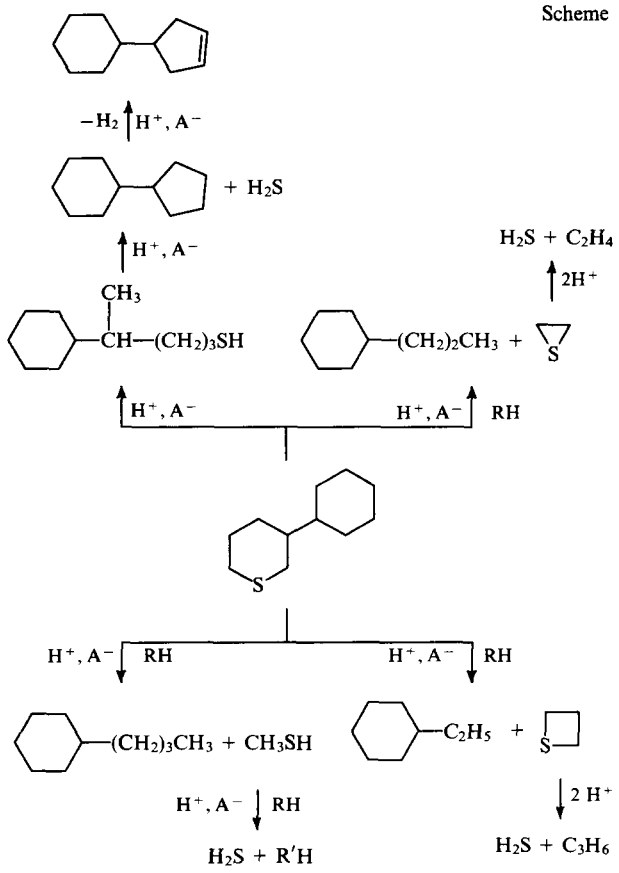
The molecular structure of organic sulfur-containing compounds (both isotypical and belonging to different classes) does not affect the mode and course of the hydrogenolysis. This is seen, in particular, from the comparison of the compositions of the liquid products formed in the desulfurisation of 3-cyclohexylthiacyclohexane and 2-methyl-4-phenylthiacyclohexane in the presence of $H[NaAlCl_4OH]$ (Table 7). The dissociation of the C–S bond in the thiacyclohexane ring and its further reactions, as well as the dissociation of the C–C bond between the thiacyclohexane ring and the surrounding groups with their subsequent reactions are characteristic of the desulfurisation process. The process proceeds as a series of parallel-consecutive electrophilic reactions.

The principal types of the hydrogenolysis of 3-cyclohexylthiacyclohexane in the presence of $H[NaAlCl_4OH]$ (or H^+A^-) in dodecane are presented in Scheme 1.

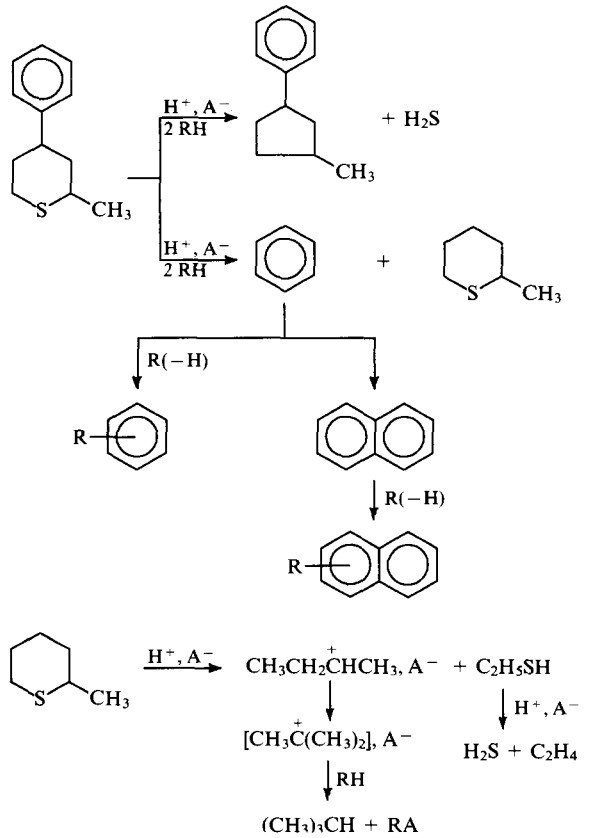
The virtual absence of sulfur-containing compounds 0.5–1 h after the start of the reaction (at 523 K) and the complete absence of mercaptans from the reaction products even in the early stages of the hydrogenolysis of cyclic sulfides (5–10 min) are striking. Furthermore, in the purely thermal decomposition and also in the presence of oxide catalysts, for example alumina–cobalt oxide–molybdenum oxide catalysts, the thiacyclanes react via a stage involving the formation of mercaptans.[64]

The possible types of the hydrogenolysis of 2-methyl-4-phenylthiacyclohexane under the same conditions are illustrated in Scheme 2.

Scheme 1

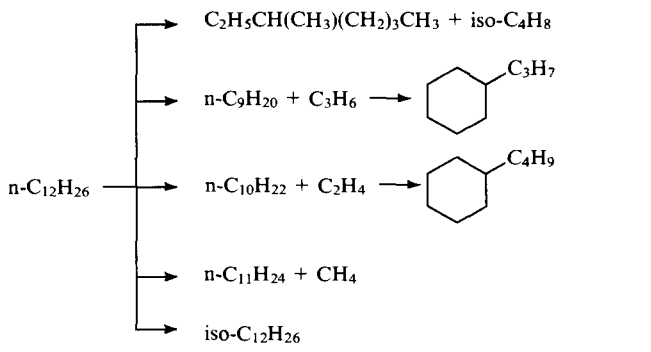


Scheme 2

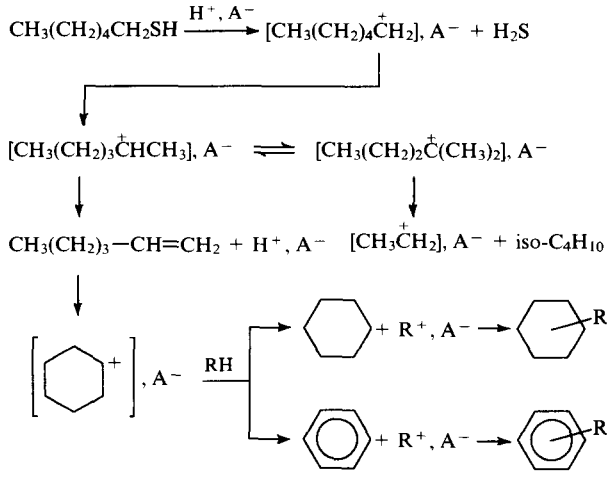


On the basis of these experimental data and also the fact that the rate of hydrogenolysis of mercaptans is 1–2 orders of magnitude higher than that of thiacyclanes (Table 6), one may postulate that mercaptans as well as thiirane, thiacyclopropane, 2-ethylthiacyclohexane, and dimethylthiacyclohexane (Table 7) participate in the process as intermediates. This is reflected in Schemes 1 and 2. Saturated aliphatic C_8-C_{11} hydrocarbons and iso-$C_{12}H_{26}$ are formed as a result of the reactions of the solvent (dodecane). Some of the alkanes are transformed into naphthene derivatives (Scheme 3).

Scheme 3



Thus, in the presence of complexes of metal chlorides with proton-donating compounds, the desulfurisation of cyclic sulfides proceeds via a single mechanism: the hydrogenolysis of the C–S bond with formation of H_2S and the heterolytic dissociation of the C–C bonds between the thiacyclane ring and the surrounding groups and also directly in the ring. The process takes place with participation of ions. The C–S bond and subsequently the C–C bonds of the hydrocarbon fragment dissociate also in the hydrogenolysis of mercaptans.



Thus electrophilic catalysts based on H[MAlCl$_4$OH] exhibit a fairly high activity and selectivity in the catalytic hydrogenolysis reactions of various sulfur-containing organic compounds proceeding via the carbonium ion mechanism at relatively low temperatures (470 ± 50 K). An important factor is that the reaction proceeds at the normal pressure and does not require the additional introduction of molecular hydrogen; the higher the acidity of the electrophilic catalyst, the more active but less selective the catalytic system under these conditions.

V. Dehydrogenation and hydrogenation of hydrocarbons

The complexes of metal chlorides with proton-donating compounds are capable of initiating both dehydrogenation[65] and hydrogenation reactions of hydrocarbons. The study of the hydrogenolysis reactions of sulfur-containing compounds (Table 5) and degradation reactions of hydrocarbons (Table 8) in the presence of Brønsted acids based on $AlCl_3$ and Group I and II metal chlorides showed that the mixture of gaseous reaction products contains as a rule molecular hydrogen. In particular, the thermocatalytic degradation of butyl rubber in the presence of $H[MAlCl_4OH]$ (M = Li, Na, K) is accompanied by the evolution of H_2 (up to 0.7 mass%). At the same time, in many instances anomalously high amounts of isobutane and other saturated hydrocarbons have been detected in the gaseous products (Tables 3, 5, and 8). The foregoing indicates the activity of catalysts of this type in both dehydrogenation and hydrogenation reactions of hydrocarbons under comparatively mild conditions (423 ± 40 K, atmospheric pressure).

The thermocatalytic dehydrogenation of hydrocarbons in the presence of $H[MAlCl_4OH]$ has been studied in fair detail in relation to low-molecular-mass model compounds — dodecane, decene, and cyclohexane (Table 8).[65] It is striking that the yield of molecular hydrogen in the dehydrogenation reactions of saturated and alicyclic hydrocarbons is always higher than in the dehydrogenation of alkenes. A similar conclusion can be reached also as regards saturated C_3-C_4 hydrocarbons (propane, isobutane) (Table 8), which evidently indicates a large contribution of the coupled reaction involving the hydrogenation of unsaturated hydrocarbons formed in situ on decomposition of the initial alkanes in the presence of $H[MAlCl_4OH]$.

Typical H_2 elimination curves for the model dehydrogenation reaction of dodecane in the presence of $H[NaAlCl_4OH]$ are presented in Fig. 3*a*. The extrema on the curves indicate the simultaneous dehydrogenation of dodecane and the hydrogenation of the unsaturated hydrocarbon products catalysed by electrophilic catalysts with reduced acidity compared with $AlCl_3$, i.e. $H[NaAlCl_4OH]$, etc. The curves characterising the variation of the content of unsaturated hydrocarbons in the liquid products formed on decomposition of dodecane in the presence of $H[NaAlCl_4OH]$ (Figs. 3*a* and 3*b*) have a similar shape.

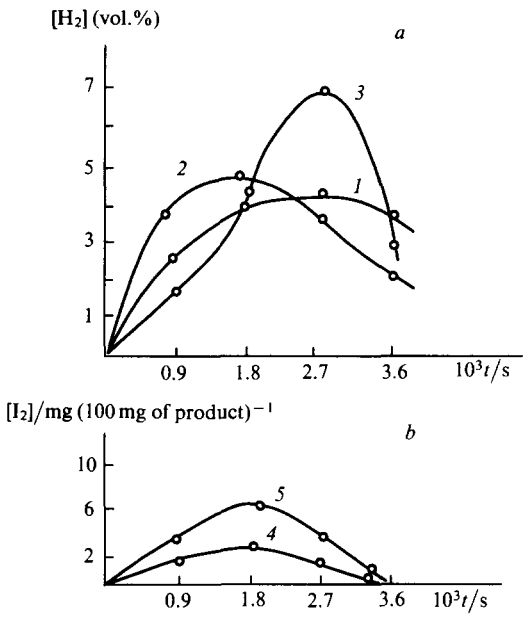


Figure 3. The hydrogen content in the gaseous products (*a*) and variation of the iodine number in the liquid products (*b*) during the catalytic conversion of dodecane in the presence of $H[NaAlCl_4OH]$ as a function of time at different process temperatures (T/K): (*1*) and (*4*) 473; (*2*) 500; (*3*) and (*5*) 525.

The compositions of the liquid products of the thermocatalytic degradation of dodecane, decene, and cyclohexane are presented in Table 9.

Experimental data show that two paths for the formation of molecular hydrogen in the thermal decomposition of hydrocarbons in the presence of $H[MAlCl_4OH]$ are possible: (1) degradation of the hydrocarbon molecules (decomposition via the C–C bonds); (2) cyclisation of unsaturated hydrocarbons with subsequent dehydrogenation of the resulting cyclic compounds. In both cases, the reactions proceed via the carbonium ion mechanism (Scheme 4):

Table 8. Gaseous products of the thermocatalytic decomposition of individual hydrocarbons in the presence of $H[NaAlCl_4OH]$.

Hydrocarbon	Content of gaseous products (vol.%)								
	H_2	CH_4	ΣC_2	C_3H_6	C_3H_8	iso-C_4H_8	iso-C_4H_{10}	ΣC_4	C_5 and above
Dodecane	9.74	1.3	3.30	0.51	10.14	21.35	41.92	74.46	0.55
Dec-1-ene	1.72	0.80	3.52	2.50	1.62	50.22	33.86	88.61	1.23
Cyclohexane	8.25	—	traces	0.22	6.18	15.40	49.54	67.72	17.63

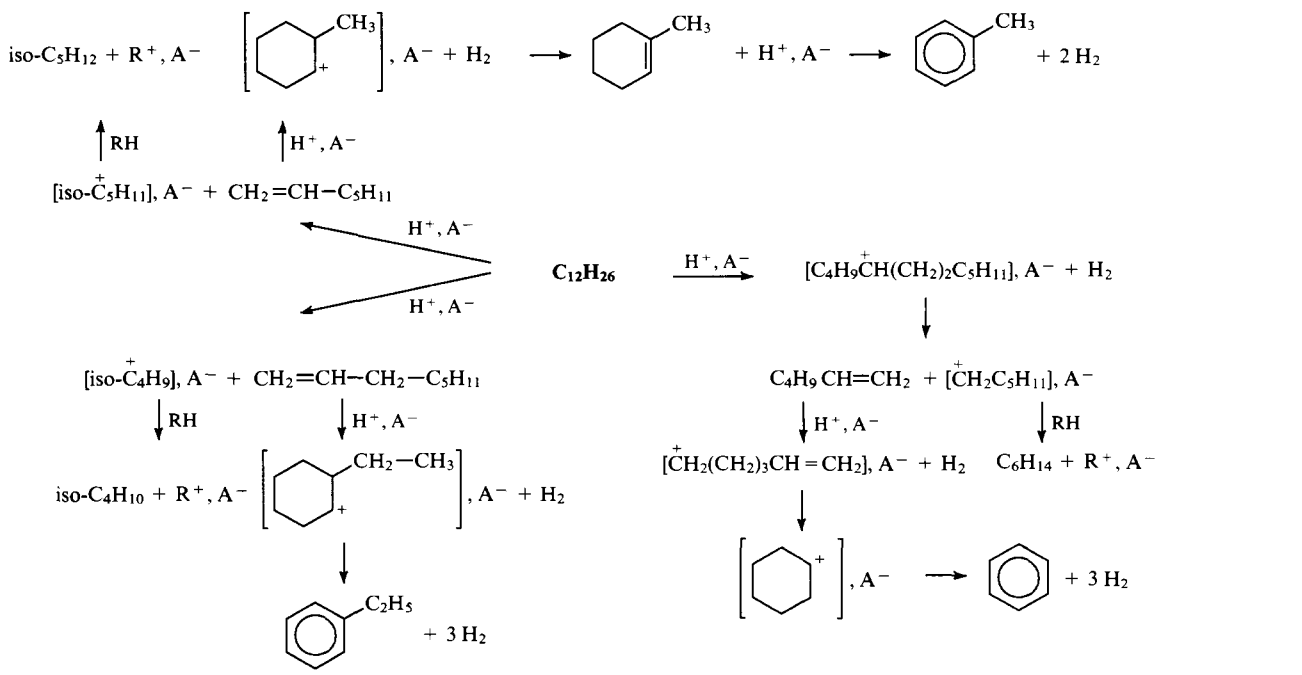
Note. Reaction conditions: T = 523 K, reaction time 30 min, catalyst : hydrocarbon = 1 : 4.

Table 9. Liquid products of the thermocatalytic decomposition of individual hydrocarbons in the presence of $H[NaAlCl_4OH]$.

Hydrocarbon	Content of liquid products (mass%)									
	C_6H_{14}	C_6H_{12}	cyclo-C_6H_{12}	C_6H_6	$C_6H_5C_2H_5$	$C_6H_5CH_3$	$C_6H_4(CH_3)_2$	other products	iso-$C_{10}H_{22}$	iso-$C_{12}H_{26}$
Dodecane	5.0	—	2.3	2.4	0.8	7.9	15.0	36.3	—	30.3
Dec-1-ene	9.5	8.5	7.1	5.5	—	4.1	—	—	65.3	—
Cyclohexane	2.6	—	—	76.3	—	—	21.1	—	—	—

Note. The reaction conditions are indicated in Table 8.

Scheme 4



The formation of anomalously large amounts of unsaturated hydrocarbons in the thermooxidative decomposition of polyalkenes and also of individual saturated and unsaturated compounds in the presence of catalysts — Brønsted acids based on complexes of $AlCl_3$ and Group I and II metal chlorides (Tables 3, 5, 8, and 9) — can be explained by the fact that electrophilic chemical reactions of two types can occur under the given conditions: (1) the interaction of alkenes with alkanes (alkylation); (2) dehydrogenation of the resulting unsaturated hydrocarbons in the presence of H[MAlCl$_4$OH]:

$$CH_2{=}C(CH_3)_2 \xrightarrow{H^+, A^-} (CH_3)_3\overset{+}{C}, A^-$$

$$(CH_3)_3\overset{+}{C}, A^- + \sim CH_2{-}C(CH_3)_2H \longrightarrow$$

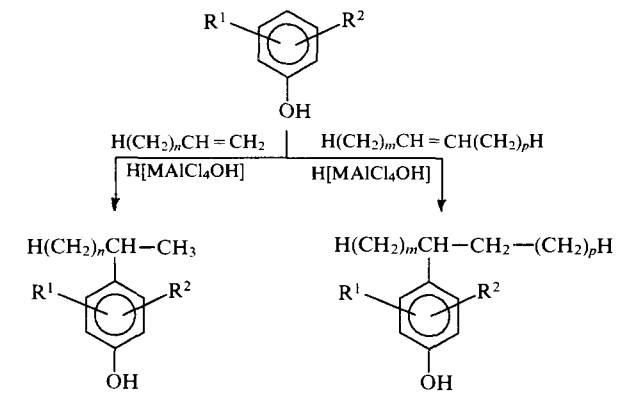
$$\longrightarrow (CH_3)_3CH + \sim CH_2{-}\overset{+}{C}(CH_3)_2, A^-, \text{ etc.}$$

Thus electrophilic catalysts with an acidity reduced compared with $AlCl_3$ are capable of initiating the dehydrogenation and hydrogenation reactions of hydrocarbons proceeding via the carbonium ion mechanism. The active forms of the catalyst are the corresponding Brønsted acids.

VI. Alkylation of phenols by polyalkenes

The Friedel–Crafts alkylation of phenols by alkenes (Scheme 5) belongs to the group of fairly complex reactions involving electrophilic substitution in aromatic hydrocarbons. As a rule the substitution is accompanied by the formation of very appreciable amounts of secondary products, especially when electrophilic reaction catalysts with high relative acidity indices, in particular $AlCl_3$, BF_3, $SnCl_4$, $ZnCl_2$, H_2SO_4, etc., are employed (Table 10). For example, in the reactions of higher α-alkenes with phenols in the presence of $AlCl_3$, the products of the decomposition the phenols (butylphenols, etc.)[66] as well as the products of the interactions of the phenols with $AlCl_3$ (the corresponding salts of HCl)[67] are formed together with alkylphenols.

Scheme 5



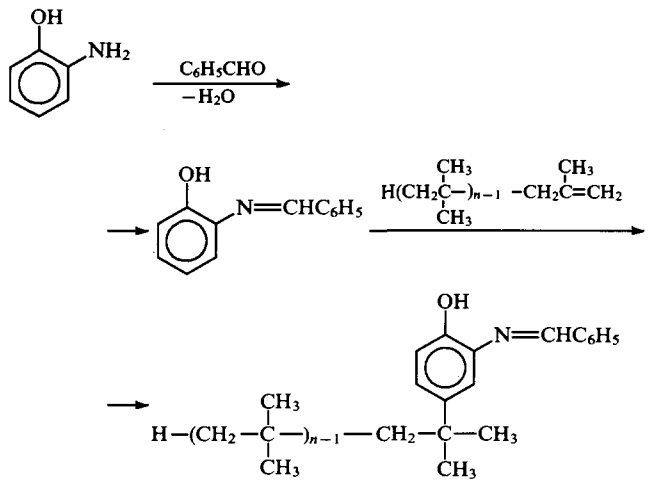
$m + p = n - 1$;
$R^1 = R^2 = H$;
$R^1 = H$, $R^2 = o$-, m-CH_3; $R^1 = H$, R^2 = iso-C_3H_7;
$R^1 = R^2 = tert$-C_4H_9; $R^1 = H$, $R^2 = o$-, m-, p-OH.

The ease of the alkylation of phenols by polyalkenes increases after the introduction of electron-donating substituents (HO, H_2N) into monohydric phenols, but diminishes in the presence of two and more bulky substituents in the aromatic ring, which give rise to steric hindrance.

The kinetics of the alkylation of phenols by alkenes have been investigated in relation to the model reaction of phenol with hept-1-ene — $T = 343$ K, identical concentrations of phenol and the alkene (2.4 M), and H[NaAlCl$_4$OH] concentration 0.24 M. The process follows second-order kinetics and the observed rate constant is $(2.2 \pm 0.2) \times 10^{-5}$ litre mol^{-1} s^{-1}.

The interaction of aminophenols with polyalkenes in the presence of H[MAlCl$_4$OH] and other similar Brønsted acids with a reduced acidity compared with $AlCl_3$ involves the amino-groups and not the aromatic ring. Nevertheless, the possibility of the ring-alkylation of aminophenol derivatives (in particular Schiff bases) by polymers under these conditions has been demonstrated (Scheme 6).

Scheme 6



The alkylation of phenols by unsaturated polymeric hydrocarbons proceeds in an even more complex manner because there is a sharp increase in the number of probable secondary reactions such as isomerisation, depolymerisation, and degradation of the polymeric fragments in the initial (polyalkenes) and final (polyalkenylphenols) products. This had been demonstrated earlier in relation to the interaction of polyalkenes with phenol in the presence of benzenesulfonic acid (Table 10).[68]

Systems of the type H[MAlCl$_4$OH], with a reduced relative acidity (Table 1), proved to be more convenient and effective catalysts of the selective alkylation of phenols by polyalkenes than AlCl$_3$. They exhibit a high activity and selectivity in the reactions of phenols with polyalkenes[69,70] occurring under mild conditions (378 ± 15 K, reaction time 3 ± 1 h), which lead to polyalkenylphenols in nearly quantitative yields (90 mass% and above) (Table 10).

Thus the decrease in the acidity of the metal chloride-based catalytic systems (evidently up to a certain limit) lowers (as in the cases examined above) the contributions of the secondary and

Table 10. Polymer-analogue reactions of polyalkenes in the presence of H[MAlCl$_4$OH].

Phenol	Catalyst	Reaction time/h	Yield of product (mass%)	[C=C]/(mol PIB)$^{-1}$	^{13}C NMR spectrum,[a] δ/ppm	Selectivity (relative units)
Polyethylene ($\overline{M}_n$ = 1300)						
Phenol	H[AlCl$_3$OH]	10	75	—	—	0.7
Phenol	C$_6$H$_5$SO$_3$H	4	46	—	—	0.4
Phenol	H[NaAlCl$_4$OH]	2.5	96	0.012	135.5	0.9
2-Methylphenol	H[NaAlCl$_4$OH]	2.5	96	0.015	135.2	0.9
3-Methylphenol	H[NaAlCl$_4$OH]	3.0	93	0.021	134.8	0.9
4-Isopropylphenol[b]	H[NaAlCl$_4$OH]	3.0	93	0.021	129.6	0.9
2,6-Di-*tert*-butylphenol[b]	H[NaAlCl$_4$OH]	4.0	89	0.033	135.2	0.9
o-Dihydroxybenzene	H[NaAlCl$_4$OH]	2.5	93	0.021	149.0	0.9
m-Dihydroxybenzene	H[NaAlCl$_4$OH]	2.5	96	0.012	122.8	0.9
p-Dihydroxybenzene	H[NaAlCl$_4$OH]	2.5	90	0.030	131.6	0.9
2-Aminophenol[c]	H[NaAlCl$_4$OH]	2.5	93	0.021	—	0.9
4-Aminophenol[c]	H[NaAlCl$_4$OH]	2.5	98	0.006	—	0.9
2-Benzylideneaminophenol[d]	H[NaAlCl$_4$OH]	4.0	98	0.012	136.9	0.9
4-Benzylideneaminophenol[d]	H[NaAlCl$_4$OH]	4.0	96	0.012	131.5	0.9
4-Isopropylphenol	H[LiAlCl$_4$OH]	2.5	91	0.023	—	0.9
m-Dihydroxybenzene	H[LiAlCl$_4$OH]	2.0	95	0.015	—	0.9
4-Isopropylphenol[b]	H[KAlCl$_4$OH]	2.5	93	0.021	—	0.9
m-Dihydroxybenzene	H[KAlCl$_4$OH]	2.0	96	0.012	—	0.9
Polypropylene ($\overline{M}_n$ = 1400)						
Phenol	C$_6$H$_5$SO$_3$H	4.0	36	—	—	0.3
Phenol	H[NaAlCl$_4$OH]	2.5	96	0.037	141.3	0.9
4-Isopropylphenol[b]	H[NaAlCl$_4$OH]	3.0	94	0.056	135.3	0.9
m-Dihydroxybenzene	H[NaAlCl$_4$OH]	2.5	98	0.019	128.5	1.0
4-Isopropylphenol[b]	H[LiAlCl$_4$OH]	3.5	92	0.074	—	0.9
m-Dihydroxybenzene	H[LiAlCl$_4$OH]	2.5	95	0.047	—	0.9
4-Isopropylphenol[b]	H[KAlCl$_4$OH]	3.0	94	0.056	—	0.9
m-Dihydroxybenzene	H[KAlCl$_4$OH]	2.5	97	0.030	—	0.9
Polyisobutylene ($\overline{M}_n$ = 1100)						
Phenol	C$_6$H$_5$SO$_3$H	4	31	—	—	0.3
Phenol	H[NaAlCl$_4$OH]	2.5	98	0.020	143.5	1.0
4-Isopropylphenol[b]	H[NaAlCl$_4$OH]	3.0	96	0.040	137.5	0.9
m-Dihydroxybenzene	H[NaAlCl$_4$OH]	2.5	98	0.020	130.7	1.0
4-Isopropylphenol[b]	H[LiAlCl$_4$OH]	3.0	95	0.050	—	0.9
m-Dihydroxybenzene	H[LiAlCl$_4$OH]	2.0	96	0.048	—	0.9
4-Isopropylphenol[b]	H[KAlCl$_4$OH]	3.0	96	0.040	—	0.9
m-Dihydroxybenzene	H[KAlCl$_4$OH]	2.0	94	0.060	—	0.9

Note. Reaction conditions: T = 383 K, [Cat] = 0.05 mol(mol polyalkene)$^{-1}$.
[a] Signal due to the carbon atom bound to the oligomeric radical; [b] T = 393 K; [c] T = 373 K; [d] [Cat] = 0.10 mol(mol polyalkene)$^{-1}$, T = 393 K.

side reactions, characteristic, for example, of catalytic processes involving the use of $AlCl_3$ or benzenesulfonic acid.[66,67] As a consequence of this, the selectivity of the action of these catalytic systems in these processes also increases.

Depending on the positions of the C=C bonds in the molecule of the initial polyalkene (terminal or internal), the corresponding polyalkenylphenols are formed; the reaction then proceeds via the classical electrophilic addition mechanism and the catalyst is a Brønsted acid: H^+, $[MAlCl_4OH]^-$.

Further reactions involving polyalkenylphenols and their derivatives may be carried out. In particular, polymeric ethers of (4-methyl-5,6-dihydro-2*H*-pyranyl)phenols have been obtained in this way.[69,71] In addition, polyalkenylphenols are of interest as stabiliser-antioxidants and also as additives to oils.

The presence of the benzylideneamino-group in the phenol ring hinders the electrophilic addition of polyalkenes to aminophenols owing to the depletion of the electron density of the aromatic ring. Benzylideneaminophenols therefore interact with polyalkenes under more several conditions than aminophenols or dihydric phenols.

VII. Dependence of the effectiveness of electrophilic catalysts on their acid–base properties

Experimental results obtained for a fairly large number of electrophilic reactions occurring in the presence of Brønsted acids indicate that the degree of conversion and the yield of the target products may vary within extremely wide limits in specific reactions depending on the nature and structure of the metal chlorides, the nature of the cocatalyst, the position of the corresponding metal in the Periodic System, and in essence (and evidently primarily) the acidity of the catalytic system. In particular, a relation has been traced between the acid–base properties of metal chloride complexes (taking into account the electronic configuration of the metal atom and also its position in the Periodic System) and their effectiveness and the selectivity of their action as catalysts for electrophilic processes. This can be seen in relation to the polymerisation reactions of isobutene from the C_4 hydrocarbon fractions[7,21,24] (Table 2), the degradation of hydrocarbons[3–5,36–49] (Table 3), the alkylation of phenols by polyalkenes[69,70] (Table 10), hydrogenolysis,[56–61] etc. Fig. 4 demonstrates to a first approximation the conventional boundary between the acid (electrophilicity and basic (nucleophilicity) properties of individual metal chlorides (straight line *AB*).

The metal chlorides located above the *AB* line or directly on it ($MgCl_2$, $BaCl_2$, $CaCl_2$, $SrCl_2$, $MnCl_2$, $CoCl_2$, $ZnCl_2$, $InCl_3$, $BiCl_3$, $SnCl_2$, $FeCl_2$) are characterised by a lower acidity than $AlCl_3$, $TiCl_4$, $SnCl_4$, and $FeCl_3$ and hence by a relatively mild catalytic activity. This is responsible for their fairly high activity and selectivity as catalysts of electrophilic processes. The metal chlorides located underneath the *AB* line, including $AlCl_3$, $SnCl_4$, $FeCl_3$, $TiCl_4$, etc., are 'hard' (strong) or 'superstrong' Lewis acids. Therefore their employment as catalysts for certain electrophilic reactions (for example, selective alkene polymerisation processes, degradation of polyalkenes and polydienes, desulfurisation of organosulfur compounds, alkylation of phenols and aminophenols by alkenes, polyalkenes, and polydienes, etc.) is not always effective, since undesirable side reactions may occur.

The results of theoretical calculations of the charges on the hydrogen atoms of the proton donors q_{H^+} in metal chloride-based complexes and other electrophilic compounds of the type of Brønsted acids[16] and also of the universal acidity index pK_a[14,15] in combination with experimental data on the relation between the acidity parameters of chemical compounds and the activity and selectivity of electrophilic catalysts in relation to the cationic polymerisation of alkenes[6–11] have led to a similar conclusion. An alternative measure of the acid strength of electrophilic catalysts is the relative acidity index [RAI/mequiv. (g. cat.)$^{-1}$, see

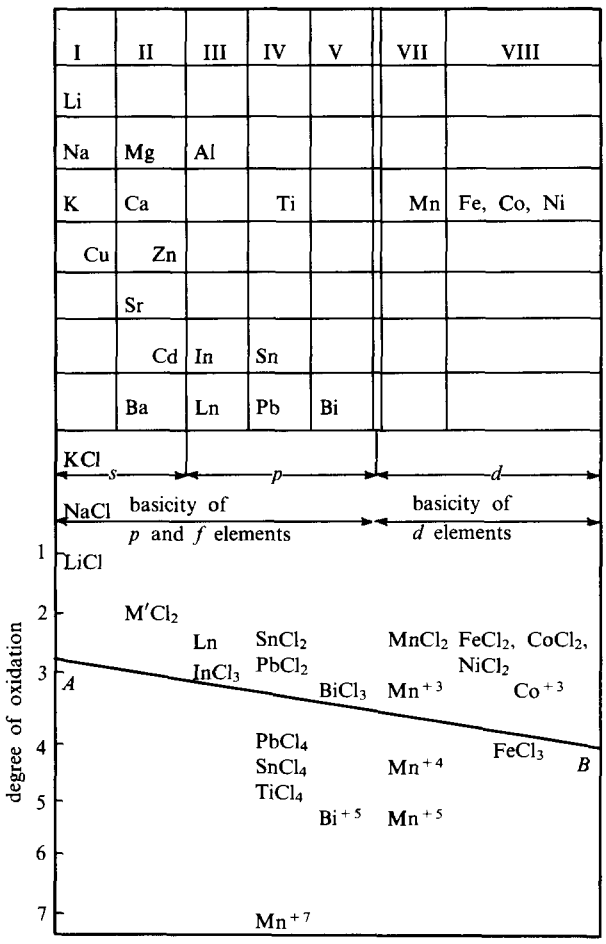


Figure 4. Variation of the acid–base properties of MCl_n as a function of the position of the metal in the Periodic System. M′ = Ba, Sr, Ca, Cd, Mg, or Zn.

Table 1],[13] which can be readily determined experimentally by differential nonaqueous titration [acetophenone (solvent)] and which does not require cumbersome theoretical calculations.

The data presented in Table 1 and also theoretical calculations,[6–11,14,15,21] have led to the discovery of a clear linear relation between the calculated (q_{H^+}, pK_a) and experimentally estimated (RAI) parameters of the acidity of the metal chloride-based complexes (in the form of Brønsted acids) (Fig. 5):

$$pK_a = 27.3 - 109.2\ q_{H^+},$$

(with a correlation coefficient of 0.98 and a standard error of 0.19);

$$RAI = 2.3 - 0.122\ pK_a,$$

and

$$RAI = 13.33\ q_{H^+} - 1.03,$$

(with a correlation coefficient of 0.99 and standard error of 0.085). The correlations between q_{H^+}, pK_a, and RAI are valid for an extremely large number of electrophilic catalytic systems based on metal chlorides and alkyl(aryl)metal chlorides involving Group IIA–VA and IIB–VIIIB metals, as well as relatively new catalytic systems based on metal chlorides and alkyl(aryl)metal chlorides involving Group IIIA metals with Group IA and IIA,B metal chlorides. Similar correlations have been observed for the complexes of boron fluorides and alkyl(aryl)boron fluorides with proton-donating compounds (H_2O, HF, ROH),[6–11] which in all probability makes it possible to reach a conclusion concerning the general

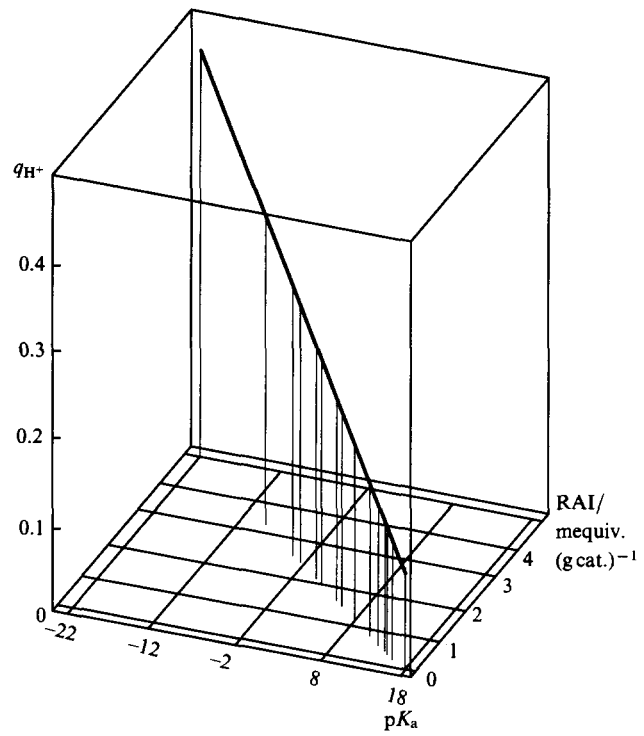


Figure 5. Relation between the parameters characterising the acidity of electrophilic catalysts (pK_a, RAI, q_{H^+}) (according to the data in Table 1).

character of both the methods for the estimation of the parameters of the acid strength of electrophilic chemical compounds and of the rather simple relation between them.

Analysis of the literature data and the results obtained[1-13, 17, 21, 25, 37, 40-49, 56-61, 69, 70] (Tables 1-4, 9, and 10) shows that the numerical values of the parameters characterising the acidity of electrophilic catalysts based on metal chloride complexes (q_{H^+}, pK_a, RAI) are a measure of their effectiveness and activity and of the selectivity of their action in various types of reactions occurring with participation of carbonium ions. The following rule is fairly strictly obeyed: the higher the relative acidity of the electrophilic systems formed in the interaction of Lewis acids with proton donors, the higher the activity but the lower the selectivity of the catalyst for processes occurring with participation of carbonium ions. Under these conditions (Fig. 6), there exist both an upper limit (the catalyst is extremely active, the contribution of side and secondary reactions is large) and a lower limit (extremely low activity of the catalyst) to the effectiveness of the action of catalytic systems (Fig. 6):

(a) $pK_a \gg 11$ [RAI $\leqslant$ 0.9 mequiv. (g cat.)$^{-1}$]—low acidity parameters; such catalytic systems are inactive in many electrophilic processes or their activity is low {ROH, H_2O, $H[R_3AlOH]$, $H[R_3AlOR]$, etc.};

(b) $-10 \ll pK_a \ll +11$ [RAI in the range from 0.9 to 3.0 mequiv. (g cat.)$^{-1}$]—optimum acidity parameters: the catalytic systems exhibit a fairly high activity and selectivity:

(c) $pK_a \leqslant -10$ [RAI $\geqslant$ 3.0 mequiv. (g cat.)$^{-1}$]—high acidity parameters. In this case an extremely high activity but as a rule a low selectivity are characteristic of the catalytic systems {$H[AlCl_3OH]$, $H[BF_4]$, etc.}.

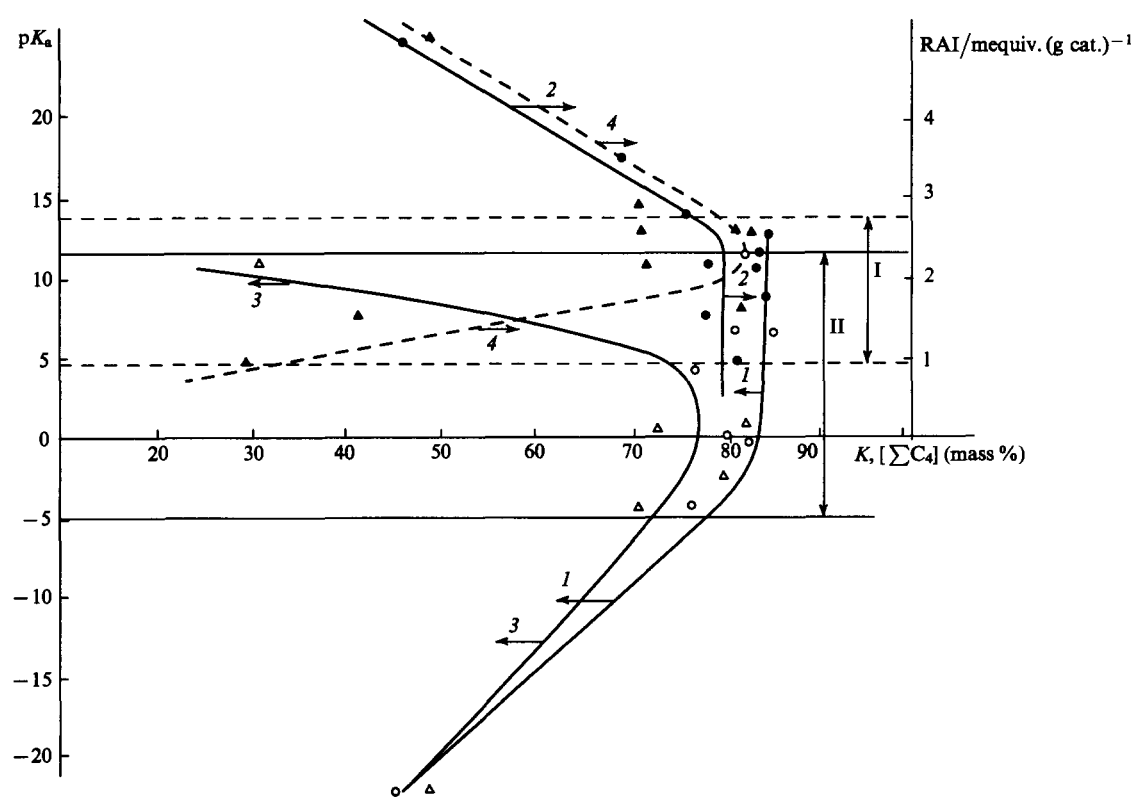


Figure 6. Conventional regions of the optimum values of pK_a (continuous lines) and RAI (dashed line) corresponding to the activity indices [K (mass %)] and selectivity indices {[$\sum C_4$], (mass %)} of the electrophilic catalysts $MCl_n \cdot H_2O$ and $[M'MCl_n] \cdot H_2O$ in relation to the thermocatalytic degradation of high pressure polyethylene ($\overline{M}_n = 22\,000$), [Cat] = 1 × 10^{-3} mol g^{-1}; T = 623 K, 1 h. Curves: (*1*) [$\sum C_4$] = $f(pK_a)$; (*2*) [$\sum C_4$] = f(RAI); (*3*) K = $f(pK_a)$; (*4*) K = f(RAI).

We may note, however, that in all probability the boundary values of the acidity parameters quoted may shift in the general case in one direction or another depending on the nature of the chemical process, the molecular structure, the solvent employed, etc. evidently mainly in view of the change in situ of the parameters of the acid strength of the electrophilic catalytic system employed.

The acidity of the classical catalysts for electrophilic processes, in particular $AlCl_3$ and BF_3, can be reduced by combining them with moderately basic chlorides of *s* or *d* elements. The class of the relatively new electrophilic catalysts, formed as a result of the interaction of halogen-containing compounds of aluminium with alkali or alkaline earth metal chlorides having the general formula $H[MAlR_nCl_mOH]$, where $n = 0$ or 1 and $m = 4$ or 3 for Na, Li, and K and 5 or 4 for Ca, Ba, Mg, Sr, Zn, Co. etc., is of interest in this connection.

VIII. Conclusion

The Brønsted acids comprising the complexes of Group II – VIII metal chlorides, which have a reduced acidity compared with $AlCl_3$ and are formed, in particular, as a result of the interaction of aluminium chlorides with Group I and II metal chlorides in the presence of proton-donating compounds (H_2O, ROH, etc.), are promising polyfunctional catalysts for many electrophilic reactions, in particular cationic polymerisation processes, the depolymerisation of oligo- and poly-alkenes, the degradation of macromolecules, the alkylation, hydrogenation and dehydrogenation of unsaturated hydrocarbons, the dehydrogenation of alkanes and alicyclic compounds, the desulfurisation (hydrogenolysis) of organosulfur compounds, etc. In the presence of such systems, such reactions proceed fairly selectively with a relatively high degree of conversion and under extremely mild experimental conditions (atmospheric pressure, $T = 270 - 650$ K).

An important factor is that the acidity of the chemical compounds may serve as the criterion determining the electrophilic activity of the catalysts and the selectivity of their action, i.e. their effectiveness. In all probability, by estimating the acidity indices of the catalysts of electrophilic processes, one may predict to a first approximation their effectiveness. The construction of characteristic relations (Figs. 5 and 6) for the series of electrophilic reactions occurring via the carbonium ion mechanism is of extremely great interest in this connection. The observed relations make it possible to estimate the postulated catalytic activity and selectivity of the action of potential electrophilic catalysts, to predict the direction of the changes in the activity and selectivity of the electrophilic catalysts, and to seek on this basis new catalysts for specific electrophilic chemical processes.

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Advances in the synthesis of polyoxometalates and in the study of heteropolyacids

G M Maksimov

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Abstract. The review surveys data on the known structures of polyoxometalates. The changes in this field which have occurred in the last ten years are traced. Heteropolyacids are considered in detail as a special case of polyoxometalates: their composition and structure, methods of synthesis, stability, and acidity. The bibliography includes 309 references.

I. Introduction

Polyoxometalates are an extensive class of polyoxoanions formed by Group V and VI metals.[1-3] They can be represented by the general formulae $(M_mO_y)^{x-}$ [isopolyanions (IPA)] and $(X_nM_mO_y)^{x-}$ [heteropolyanions (HPA)], where M = Mo, W, and V and, more rarely, Nb, Ta, or a mixture of these elements in the highest oxidation states, while X is a heteroatom. Iso- and hetero-polyanions are historic terms assigned at the time to families of typical representatives of these classes. As the chemistry of these compounds developed (particularly vigorously during the last 25 years), the boundary between IPA and HPA began to blur, which led to a more general name — polyoxometalates.[1] It has recently been suggested[2] that a still more general name be employed — metal–oxygen clusters. However, careful examination shows that IPA and HPA constitute merely an island (although a substantial one) in the vast sea of metal–oxygen clusters. We shall therefore employ for the time being the term polyoxometalates or polyoxoanions. The term heteropolyanions has been firmly retained for the special case involving the presence of one or several heteroatoms X within the ligand sphere of a polyoxometalate with X–O bonds. This applies also to the free protic acids corresponding to the HPA — they are unambiguously referred to as heteropolyacids (HPAC).

The set of elements M incorporated in polyoxometalates is restricted to atoms having a suitable combination of ionic radius and charge and capable of forming element — oxygen $d\pi-p\pi$ bonds. For the heteroatoms X, there is no such limitation. Bearing in mind that the heteroatoms can exist not only within but also outside the polyoxometalate sphere, it is clear that virtually all the elements of the Periodic System can serve as the heteroatoms X with the exception of the noble gas subgroup. The diversity of the X and M atoms and of their proportions is responsible for the existence of an enormous number of polyoxometalates.

The range of applications of these compounds is fairly wide and includes fields such as catalysis, analytical chemistry, medicine, electronics, protective coatings, and many others. The continuously growing interest of investigators in HPA and IPA is indicated by the extensive review literature. During the 10 years which have elapsed since the publication of Pope's monograph in 1983,[1] about 100 reviews have been published in English, German, Russian, Japanese, Chinese, Polish, Czech, and Spanish on the synthesis, structure, properties, and applications of HPA and IPA. We shall mention some of the most complete and interesting reviews. Thus the structures of polyoxometalates have been examined in Refs 2 and 4–7, and their spectra in Refs 8 and 9. The application of polyoxometalates in catalysis,[10-14] in analytical chemistry,[15-19] for the preparation of photochromic coatings,[20] and in pharmacology[17] has been described in fair detail. There are reviews on the use of polyoxometalates in electrocatalysis[21] and photocatalysis.[22] More than half of all the reviews are devoted to the use of polyoxometalates in catalysis, which indicates their effectiveness as catalysts. One may say that to a large extent the studies on IPA and HPA (especially HPA and HPAC) have been associated with their use in catalysis. The frequency of the publication of reviews concerning the structure, chemistry, and applications of polyoxometalates in catalysis and analytical chemistry is sufficient to trace the rapid changes in these branches of knowledge. At the same time, for a long time (20 years) there have been no reviews on the chemistry of defective HPA and their complexes, whilst a detailed review on the chemistry of HPAC[3] was published more than 30 years ago.

The elaborate chemistry of IPA and HPA has led to the existence of an enormous amount of spectroscopic data, the reviews and catalogues of which are extremely useful but their number is small. A review on nontraditional applications of IPA and HPA, including nontraditional catalytic reactions, has also been useful.

The question of the industrial application of polyoxometalates has been dealt with to a very slight extent indeed. Apart from the wide scale general application of HPA for analytical purposes on an industrial scale and in research laboratories, only the employment of HPA and HPAC as catalysts has been described.[11,20,23-25]

The aims of the present review are as follows: to trace the changes in the structural chemistry of polyoxometalates which have taken place after the publication of Pope's monograph[1] and to represent their entire diversity. Particular emphasis is laid on

G M Maksimov Catalysis by Metal Complex Laboratory, Boreskov Institute of Catalysis, Siberian Division of the Russian Academy of Sciences, prosp. Akademika Lavrent'eva 5, 630090 Novosibirsk, Russian Federation. Fax (7-383) 235 57 56.
Tel. (7-383) 35 02 84.

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the study of the present state of the chemistry of HPAC in connection with properties which are important for their employment in acid catalysis.

II. Polyoxometalates with known structures

After the publication of Pope's classical work,[1] an enormous number of communications concerning the determination of the structures of polyoxometalates by X-ray diffraction (XRD) appeared. In the course of only ten years, the number of new structures trebled. The extensive introduction of high-resolution NMR spectroscopy into practical research made it possible also to obtain in many instances data the information content of which was close to that of XRD results. This contributed significantly to progress in the chemistry of polyoxometalates. It is nowadays impossible to make any kind of reliable judgments about the structure of a new polyoxoanion without resorting to XRD or NMR spectroscopic data.

The principles governing the construction of polyoxometalates have been examined in detail[1,2,4,5] and we shall therefore not deal with this question. The empirical formulae of all the known IPA and HPA, which exist in solution in the form of discrete anions, polymeric anions, and anions detected only in the solid state and whose structures have been established,[26-93] are presented below. Their common feature is their synthesis in solution or from solution. The structures, differing in the construction of the inorganic framework of the anion, are indicated for organic IPA and HPA derivatives. The inorganic framework is understood as a three-dimensional lattice consisting mainly of Mo, W, V, and Nb (sometimes Ta and Cr) atoms to which the atoms of any elements other than C, N, and H are attached. The criteria for the differentiation of the structures are as follows: the number of atoms in the inorganic framework, the disposition of the atoms relative to one another without taking into account the type of atoms, the way in which the atoms are joined together, and isomerism. The structural distortions associated with changes in the type of atoms (for example, when W is replaced by Mo, P by As, etc.) are not taken into account and the fine details in the secondary structure (the disposition of the anions and countercations in the crystal lattice) are also disregarded, apart from the instances where the cations are linked directly to the framework of the anion (for example, in lanthanum decavanadate). When a homologous series exists, the general structural formula is indicated (R is the organic residue). If a single representative of the given structure is known, the complete composition of its anion is indicated.

For each structure, the literature references are given to one source (for an homologous series, as a rule the first source) in which the structure has been adequately described or to the only source available (so far as possible, references are given to reviews in which the structures are described). The IPA and HPA whose structures have been determined by X-ray diffraction are listed.

$M_5O_{12}(NO)_2R_4^{2-}$ [26]
$M_7O_{24}^{6-}$ [1]
$M_{10}O_{28}^{x-}$ (possibly with R) [1]
$(V_3O_8^-)_n$ [1]
$V_4O_8XR_4^{2-}$ [6]
$H_6As_6V_4O_{30}^{4-}$ [1]
$V_5O_{14}^{3-}$ [6]
$V_5O_{22}R_2(PR)_5^-$ [28]
$V_6O_{10}(AsR)_6^{2-}$ [29]
$(RX)_4V_6O_{19}$ [31]
$V_{10}O_{26}^{4-}$ [1]
$V_{10}O_{24}(ASR)_3^{4-}$ [29]
$H_4V_{10}O_{14}(PO_4)_7^{5-}$ [34]
$H_3V_{12}As_4O_{43}^{7-}$ [2]
$H_3Mn_3V_{12}O_{40}^{5-}$ [35]
$XV_{13}O_{38}^{7-}$ [1]
$V_{14}As_8O_{42}X^{x-}$ [2]
$M_6O_{19}^{x-}$ (possibly with R)[1,6]
$M_{10}O_{32}^{4}$ (possibly with R)[1,6]
$Nb_8O_{10}R_{20}$ [27]
$V_4O_{12}^{3-}$ [1]
$V_4O_8R_4^{4-}$ [6]
$(V_5O_{14}^{3-})_n$ [1]
$V_5O_9XR_4^{2-}$ [6]
$V_6O_{10}R_9$ [6]
$V_6O_8R_6^{2-}$ [30]
$V_9O_{16}R_4^{7-}$ [6]
$La_2V_{10}O_{28}$ [32]
$Se_4V_{10}O_{37}^{8-}$ [33]
$V_{12}O_{32}R^{4-}$ [6]
$XV_{12}As_8O_{40}^{x-}$ [2]
$V_{13}O_{34}^{3-}$ [36]
$XV_{14}O_{40}^{9-}$ [1]
$H_4V_{14}O_{50}(PR)_8^{6-}$ [37]
$XV_{15}O_{36}^{6-}$ [6]
$XV_{18}O_{42}^{x-}$ [1]
$HV_{19}O_{49}^{8-}$ [1]
$Mn_2V_{22}O_{64}^{10-}$ [35]
$(Se_2MoO_8^{2-})_n$ [41]
$Mo_4O_{11}R'NOR^{2-}$ [26]
$HXMo_4O_{15}R^{x-}$ [1]
$H_2As_6Mo_4O_{22}^{4-}$ [42]
$Mo_5O_{10}(O_2)_8^{6-}$ [44]
$Mo_5O_{17}R_4NO^{3-}$ [26]
$Mo_5O_{17}R'_4NO(RhR)_2$ [26]
$Mo_6O_{10}R_{12}$ [6]
$RAsMo_6O_{21}^{2-}$ [1]
$AsCoMo_6O_{30}^{4-}$ [46]
$(H_9NaP_4Mo_6O_{31}^{2-})_n$ [48]
$Mo_8O_yR_n^{x-}$ (7 isomers) [1,6]
$(Cu_2Mo_8O_{28}^{4-})_n$ [50]
$(Mo_8P_6O_{36})_n$ [52]
$M_{10}O_{34}^{8-}$ [1]
$Na_2Mo_{10}N_2O_{28}R_5^{4-}$ [53]
$Mo_{10}O_{29}R_9(NO)_3^{2-}$ [26]
$Te_6Mo_{12}O_{60}^{12-}$ [55]
$(H_{14}Fe_2Mo_{12}P_8O_{62}^{4-})_n$ [57]
$NaMo_{12}O_{54}(PR)_4^{9-}$ [59]
$Mo_{13}O_{40}(XR)_8^{2+}$ [60]
$H_6As_{10}Mo_{24}O_{90}^{8-}$ [62]
$Ce_4Mo_{29}O_{100}^{14-}$ [64]
$Mo_{36}O_{110}(NO)_4$ [65]
$X_8Mo_{58}O_{200}^{28-}$ [67]
$H_3W_6O_{22}^{5-}$ [68]
$H_2W_{12}O_{42}^{10-}$ (paratungstate)[1]
$Mn(Nb_6O_{19})_2^{12-}$ [1]
$(RX)_2(Nb_2W_4O_{19})_2^{x-}$ (2 isomers)[31]
$RX(M_6O_{19})_2^{5-}$ [31]
$V_5Mo_8O_{40}^{7-}$ [1]
$XM_4O_{24}^{3-}$ [71]
$XM_6O_{24}^{x-}$ (Anderson)[1]
$HS_2W_8O_{31}^{7-}$ [73]
β-A – $XM_9O_{34}^{x-}$ [1]
$Mg_8SiW_9O_{37}^{*}$ (2 isomers) [75]
$XW_{10}O_{36}^{x-}$ [1]
β-$XM_{11}O_{39}^{x-}$ [76]
α-$XM_{12}O_{40}^{x-}$ (Keggin, possibly with R) [1]
$PV_{14}O_{42}^{9-}$ [1]
$Cu_2Si_2Mo_{18}O_{66}^{12-}$ [1]
$P_4W_{14}O_{58}^{12-}$ [80]
$P_6W_{18}O_{79}^{20-}$ [80]
$KP_2W_{20}O_{72}^{13-}$ [82]
$As_2W_{21}O_{69}^{6-}$ [1]
$P_8W_{48}O_{184}^{40-}$ [85]
$XH_4NaW_{17}O_{56}F_6^{x-}$ [87]
$H_2SbW_{18}O_{60}^{7-}$ [74]
α$_2$-$P_2W_{18}O_{62}^{6-}$ [88]
α-A – $Ge_2Ti_6W_{18}O_{77}^{14-}$ [89]
$X_4X'_2W_{18}O_{64}^{x-}$ [1]
$H_2Sb_2W_{22}O_{76}^{12-}$ [74]
$H_5P_5Co_9W_{27}O_{116}^{16-}$ [91]
cis-$X(X'_2W_{17}O_{61})_2^{x-}$ [1]
$Na_2Sb_8W_{36}O_{132}^{22-}$ [74]
$XAs_4Co_2W_{40}O_{140}^{23-}$ [1]
$X_2X'Mo_{12}O_{42}^{x-}$ [1]
$(XX'Mo_{12}O_{42}^{x-})_n$ [1]
$H_2V_{15}As_6O_{42}^{6-}$ [2]
$V_{18}O_{44}R^{x-}$ [38]
$V_{22}O_{54}X^{x-}$ [39]
$V_{34}O_{82}^{10-}$ [40]
$(Mo_3O_{10}^{2-})_n$ (2 isomers) [1]
$Mo_4O_yR_n^{x-}$ (10 isomers) [6]
$H_4As_4Mo_4O_{26}^{4-}$ [1]
$(Mo_4P_2O_{16}^{2-})_n$ [43]
$Mo_5O_{16}R^{3-}$ [6]
$Mo_5O_{17}R'_4NORhR^-$ [26]
$(HMo_5O_{16}^-)_n$ [1]
$(RX)_2Mo_6O_{24}^{4-}$) (2 isomers)[1]
$SeS_3Mo_6O_{33}^{8-}$ [45]
$(Nd_2TeMo_6O_{24})_n$ [47]
$Mo_6O_{17}(P_2R)_2^{6-}$ [49]
$Mg_2Mo_8O_{22}R_{10}^{2-}$ [6]
$H_2TeMo_8O_{31}^{4-}$ [51]
$Mo_{10}O_{28}R_4^{4-}$ [6]
$H_4Co_2Mo_{10}O_{38}^{6-}$ [1]
$NiMo_{10}P_4O_{46}^{8-}$ [54]
$Mo_{12}O_{36}R_4^{4-}$ [6]
$As_2Mo_{12}O_{42}^{6-}$ [56]
$H_4As_4Mo_{12}O_{50}^{4-}$ [1]
$(H_{14}X_3P_8Mo_{12}O_{62}^{4-})_n$ [58]
$Mo_{14}O_{46}^{10-}$ [61]
$H_{31}Na_{14}Mo_{24}P_{17}O_{128}^{6-}$ [63]
$Mo_{36}O_{112}^{8-}$ [1]
$NaH_{15}Mo_{42}O_{109}R_7^{7-}$ [66]
$W_4O_{16}^{4-}$ [1]
$H_4W_{11}O_{38}^{6-}$ [69]
$RXM_6O_{19}^{x-}$ [31]
$(RU)_2(TiW_5O_{19})_2^{4-}$ [31]
$(RX)_5(Nb_2W_4O_{19})_2^{3-}$ [31]
$V_8Mo_4O_{36}^{8-}$ [1]
$X_6Mo_{57}O_{183}(NO)_6^{6-}$ [70]
$X_2M_5O_{21-23}^{x-}$ [1]
$H_2S_2W_6O_{31}^{4-}$ [72]
α-A – $XM_9O_{34}^{x-}$ [1]
α-B – $XW_9O_{33}^{9-}$ [74]
$XM_9O_{32}^{6-}$ [1]
α-$ZM_{11}O_{39}^{x-}$ [1]
$PW_{10}Ni_3O_{39}^{7-}$ [77]
β-$XM_{12}O_{40}^{x-}$ [1]
γ-$PV_2W_{10}O_{40}^{5-}$ [78]
$PMo_4V_9O_{41}^{8-}$ [79]
$P_4W_8O_{40}^{12-}$ [1]
$H_3P_5W_{18}O_{78}^{20-}$ [80]
$P_2W_{19}O_{69}^{14-}$ [81]
$X_2W_{21}O_{71}^{6-}$ [83]
$XP_5W_{30}O_{110}^{x-}$ [84]
α-$P_2W_{17}O_{61}^{10-}$ [86]
$H_2XW_{18}O_{60}^{7-}$ [1]
α-$X_2M_{18}O_{62}^{6-}$ (Dawson) [1]
β$_2$-$As_2W_{18}O_{62}^{6-}$ [88]
β-A – $Si_2X_6W_{18}O_{77}^{x-}$ [90]
$XSb_9W_{21}O_{86}^{18-}$ [1]
$X(\alpha\text{-}X'M_{11}O_{39})_2^{x-}$ [1]
$X_4P_4W_{30}O_{112}^{x-}$ [1]
$(RuClP_2W_{17}O_{61})_2O^{16-}$ [92]
$XMo_{12}O_{42}^{8-}$ (Dexter – Silverton) [1]
$XCr_4O_{16}^{3-}$ [93]

Compounds whose structures are postulated on the basis of spectroscopic data:

$H_7W_{11}O_{40}^{7-}$ [94]
$HMo_8V_2O_{32}^{5-}$ [95]
$(RX)_3(Nb_2W_4O_{19})_2^{5-}$ [31]
$Mo_4V_5O_{27}^{5-}$ [95]
$(Nb_2W_4O_{18})_2O^{6-}$ [96]
$P_2W_{12}O_{47}^{12-}$ [1]

β-B$-XW_9O_{34}^{x-}$ [97]
$X(HSiW_9O_{34})_2^{15-}$ [98]
$X(\alpha\text{-}X'W_{11}O_{39})_2^{x-}$ [99]
$X(\beta_i\text{-}SiW_{11}O_{39})_{62}^{x-}$ [101]
$XW_{11}X'(RX'')O_{39}^{x-}$ [1]
$\alpha_1\text{-}P_2W_{17}O_{61}^{10-}$ [1]
$\beta_1\text{-}As_2W_{18}O_{62}^{6-}$ (γ-[1]) [102]
$X_2W_{15}O_{56}^{12-}$ [1,103]
$X_2W_{16}O_{59}^{12-}$ [1,103]
$As_2W_{20}O_{68}^{10-}$ [1]
$X_4P_2W_{18}O_{64}^{x-}$ [105]
$X(\alpha_1\text{-}P_2W_{17}O_{61})_2^{17-}$ [106]
$NaSb_9W_{21}X_6O_y^{x-}$ [1]
$XAs_4W_{40}O_{140}^{x-}$ [1]
$RXP_2W_{15}Nb_3O_{62}^{x-}$ [109]
β-$XM_{11}O_{39}^{x-}$ (2 isomers) [1]
$(XX'W_{11}O_{39})_2O^{x-}$ [1]
$X(\alpha,\beta_2\text{-}SiW_{11}O_{39})_2^{x-}$ [100]
$SiW_{11}(Si_2R_2O)O_{39}^{4-}$ [1]
$[(XW_{11}X'O_{39})_2X'']_n^{x-}$ [1]
$\beta\text{-}P_2W_{17}O_{61}^{10-}$ [1]
$(\alpha,\beta)_1\text{-}X_2W_{18}O_{62}^{6-}$ (β-[1]) [102]
$As_2W_{19}O_{67}^{14-}$ [1]
$X_2W_{20}O_{70}^{10-}$ [104]
trans-$X(\alpha_2\text{-}X_2'W_{17}O_{61})_2^{x-}$ [1]
$NaSb_9W_{21}X_3O_{86}^{x-}$ [107]
$X_2X_2'As_4W_{40}O_y^{x-}$ [1]
$P_4W_{30}Nb_6O_{123}^{16-}$ [109]
$RXX'W_9Nb_3O_{40}^{x-}$ [108]

The $Mg_8SiW_9O_{37}$ isomers have been described insufficiently clearly[75] which gives rise to doubts concerning their genuine existence.

Polyoxometalates with a degree of condensation of the atoms M in the polyanion not less than 4 are listed above. One cannot fail to recognise that such subdivision appears somewhat artificial because species with degrees of condensation of 2 and 3 actually belong to the class of polyoxoanions. Pope[1] began his consideration of polyoxometalates with the lowest polyoxoanions (with a degree of condensation of 2 but without organic derivatives), while Chen and Zubieta [6] considered polyoxoanions with a degree of condensation of 3. The remaining reviews on IPA and HPA are frequently restricted to the description of the structures of polyoxoanions beginning with degrees of condensation of 5 or 6 without an explanation of such restriction. Thus by the time the present review was written, the structures of 176 polyoxometalates had been determined by X-ray diffraction. The existence of a further 36 structures has been postulated on the basis of some kind of spectroscopic data. In addition, there exist polyoxometalates (several tens) the structural formulas of which are based solely on the results of elemental analysis.

III. Polyoxometalates known in the form of protic acids

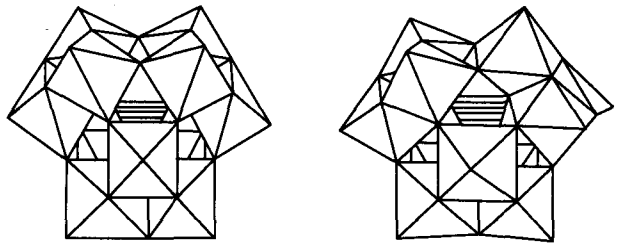
As already mentioned above, the interest in HPAC and their salts has been induced to a large extent by their use in catalysis and in the first place in acid catalysis. A large number of a wide variety of HPAC are known, but only some of them are used in laboratory practice, such as $H_3PMo_{12}O_{40}$, $H_3PW_{12}O_{40}$, $H_4SiW_{12}O_{40}$ and, much more rarely, $H_6P_2Mo_{18}O_{62}$ and $H_6P_2W_{18}O_{62}$. In our view, this is a consequence of the insufficient amount of information as to which HPAC exist. Experience gained in the use of HPAC in acid catalysis has shown that the effect of the HPAC does not always reduce solely to their action as strong acids. The properties of HPAC (including catalytic properties) differ significantly and sometimes also fundamentally depending on their structure and composition. In this sense, there still remains much to be done by investigators. In contrast to polyoxometalates as a whole, the number of new HPAC obtained during the last ten years has changed little. Only a few new HPAC with the Keggin structure and one HPAC of a new structural type have been synthesised. Apparently, the main types of HPAC have already been dis-covered, but the possibilities for the variation of the composition within the structural types are still great.

This section presents data on HPAC which exist in the solid state or at least in the form of a concentrated (not less than 0.1 M) solution. The properties of HPAC important for their employment in acid catalysis are listed briefly below: composition and structure, stability, acidity, and availability.

For the sake of brevity, henceforth abbreviated designations of HPAC will be used in the text (without H and O atoms), indicating the composition of the inorganic framework.

1. Heteropolyacids with the Keggin structure

In terms of a number of known compounds, HPAC with the Keggin structure constitute the most extensive and important class of polyoxometalates. It has been named after Keggin, the English investigator who first determined accurately the structure of the HPA anion of this class (Fig. 1).[1] Table 1 presents the compositions and temperatures of the onset of decomposition of the known HPAC with the Keggin structure, the existence of which is not open to doubt.



a *b*

Figure 1. The structures of the α- (*a*) and β-isomers (*b*) of Keggin HPAC: 12 MO_6 octahedra surround the XO_4 tetrahedron.

There is no doubt about the existence of the following HPAC with the Keggin structure:

$\alpha\text{-}H_3PW_{12}O_{40-n}(O_2)_n$, $n=1-4$ (not isolated in the solid state) [113]
$\beta\text{-}H_4SiW_{12}O_{40}$ [114]; $\beta\text{-}H_4GeW_{12}O_{40}$ [114]
$\alpha\text{-}H_6CoW_{12}O_{40}$ [3,123–125]
$\alpha\text{-}H_{6-n}H_2W_{12}F_nO_{40-n}$, $n=1-3$ [126]
$\beta\text{-}H_3PMo_{12}O_{40}$ [127]; $\beta\text{-}H_4SiMo_{12}O_{40}$ [110,129]
$\alpha\text{-}H_4GeMo_{12}O_{40}$ [3,129]; $\beta\text{-}H_4GeMo_{12}O_{40}$ [129]
$\alpha\text{-}H_4TiMo_{12}O_{40}$ [3,130,131]; $\alpha\text{-}H_3AsMo_{12}O_{40}$ [1,132]
$\beta\text{-}H_8AsMo_{12}O_{40}$ [1]; $H_7PV_{12}O_{36}$ [133]
$H_{3+n}PV_nW_{3-n}Mo_9O_{40}$, $n=1-3$ [136]
$H_5PV_2W_{10-n}Mo_nO_{40}$ [3]; $H_5PNb_2W_nMo_{10-n}O_{40}$ [137,138]
$\alpha\text{-}H_4PW_{11}NbO_{40}$ [141,142]; $H_4VW_{11}VO_{40}$ [144]
$H_5PW_{10}Nb_2O_{40}$ [142]
$H_5VW_{10}V_2O_{40}$ (not isolated in the solid state) [144]
$H_6SiW_{10}Nb_2O_{40}$ [147]; $H_7BW_{10}V_2O_{40}$ [3,148]
$H_{4+n}SiW_{12-n}V_nO_{40}$ ($n=2-4$) [3,146]
$H_4SiMo_nW_{12-n}O_{40}$ [3,145]; $H_6GeW_{10}V_2O_{40}$ [3]
$H_5BW_6Mo_6O_{40}$ [148]; $H_5GeW_{11}VO_{40}$ [150]
$H_4PMo_{11}NbO_{40}$ [152,153]; $H_5PMo_{10}Nb_2O_{40}$ [110]
$H_5SiMo_{11}NbO_{40}$ [157]; $H_6GeMo_{10}V_2O_{40}$ [3]
$H_7H_2W_{11}CrO_{39}$ (not isolated in the solid state) [158,159]

The existence of the following HPAC requires further confirmation (the temperatures of the onset of decomposition in the solid state in °C are given in brackets):

$H_6H_2W_{11}MnO_{39}$ [159]; $H_6CuW_{12}O_{40}$ [160]
$H_5AsW_{10}V_2O_{40}$ [161]; $H_5AsMo_{10}V_2O_{40}$ [161]
$H_6AsMo_9V_3O_{40}$ [161]; $H_7AsMo_8V_4O_{40}$ [162]
$H_3SbMo_{12}O_{40}$ [163]; $H_4CW_{12}O_{33}(O_2)_7$ [164]
$H_6H_2W_{12}O_{33}(O_2)_7$ [164]; $H_4SiW_{11}CrO_{40}$ (~300) [165]
$H_4SiW_{11}AlO_{39}$ [166]; $H_5GeW_{11}SnCo(CO)_3^-$
$P(C_6H_5)_3O_{39}$ [167]

The following are the heteropolyanions the existence of which is not open to doubt:

$H_4ZrW_{12}O_{40}$ [168]; $H_4TeW_{12}O_{40}$ (200) [169,170]
$H_4SeW_{12}O_{40}$ (47) [168,171]; $H_8SeW_8V_4O_{40}$ (187) [171]
$H_6SeW_{10}V_2O_{40}$ [172]; $H_7TeW_9V_3O_{40}$ [173]
$H_8TeW_8V_4O_{40}$ (~300) [173,174]; $H_8SiMo_{10}Sn_2O_{40}$ [177]
$H_{3+n}PMo_{12-n}V_nO_{40}$, $n=4-7$ [175,176]

Table 1. The known HPAC with the Keggin structure.

HPAC	T/°C[a]	Ref.
α-$H_3PW_{12}O_{40}$	400	3, 110–112
α-$H_4SiW_{12}O_{40}$	370	3, 110, 112
α-$H_4SiW_{12}O_{40}$	370	3, 110, 112
α-$H_6H_2W_{12}O_{40}$	20	3, 110
α-$H_5BW_{12}O_{40}$	240	3, 110, 112
α-$H_4GeW_{12}O_{40}$	~453	3, 115
α-$H_5GaW_{12}O_{40}$	380	116, 117
α-$H_4CW_{12}O_{40}$	280	118, 119
α-$H_5AlW_{12}O_{40}$	~400	120–122
α-$H_6ZnW_{12}O_{40}$	320	3, 112, 121, 123
$\alpha H_5FeW_{12}O_{40}$	~390	122, 123
α-$H_5CoW_{12}O_{40}$	~370	3, 123, 124
α-$H_3PMo_{12}O_{40}$	300	3, 110, 112
α-$H_4SiMo_{12}O_{40}$	200	3, 110
	300	112
	370[b]	128
α-$H_6SiMo_{12}O_{40}$	390[b]	128
α-$H_8SiMo_{12}O_{40}$	445[b]	128
$H_3PW_{12-n}Mo_nO_{40}$, $n = 1-11$	~490 for $n = 6$	3, 110, 134, 135
$H_{3+n}PV_nW_{12-n}O_{40}$ $n = 1-4$	~300 for $n = 1$	110, 139, 140
α-$H_5PW_{11}TiO_{40}$	450	143
α-$H_5PW_{11}ZrO_{40}$	450	143
α-$H_5PW_{11}CeO_{40}$	150	143
$H_6ZnW_6Mo_6O_{40}$	~300	149
$H_4PMo_{11}VO_{40}$	442	110, 151
	400	140
$H_5PMo_{10}V_2O_{40}$	~412	110, 151
$H_6PMo_9V_3O_{40}$	~396	110, 151
$H_5SiMo_{11}VO_{40}$	110	154, 155
$H_6SiMo_{10}V_2O_{40}$	200	3, 155, 156

[a] The temperature of the onset of decomposition in the solid state.
[b] At a heating rate of 300 K per hour.

The diversity of the HPAC is due to the variation of the central heteroatom X and of the composition of the ligand sphere. The available information about certain HPC, listed above (mainly with different X), has not been confirmed by reliable spectroscopic data and is based solely on the results of chemical analysis. The existence of these compounds requires further confirmation. For example, As^{5+} tends to form HPA of the type As_2W_{21} and As_2Mo_{18}, while HPA of the Keggin type are not characteristic of this anion. However, the introduction of vanadium into the ligand sphere sometimes stabilises the particular HPA structure (instances of stabilisation for $X = V^{5+}$ or S^{6+} have been accurately established) and the formation of stable HPAC having the composition $H_{3+n}As.(W, Mo)_{12-n}V_nO_{40}$ is therefore possible.

The existence of zirconium-containing HPAC is doubtful because Zr^{4+} is too large to be accommodated in the central cavity of the Keggin HPA. Furthermore, it does not form compounds with a coordination number of 4. ZrW_{12} was synthesised from the fluoride complex. Bearing in mind that fluorine forms a very stable complex with Zr^{4+},[168] one can postulate that this compound is in fact a fluorine-containing HPAC with an unknown structure.

As stated correctly by Pope,[1] in the study of HPAC with $X = Se^{4+}$, Te^{4+}, or As^{3+} 'one cannot ignore the influence of the lone pair of the heteroatom'. The compounds $PMo_{12-n}V_n$ are stable for $n = 1-3$.[179] In the synthesis of compounds with $n > 3$ by known methods, the latter undergo partial decomposition with loss of vanadium, the loss being greater the higher the value of n. HPAC with $n > 3$ can be scarcely obtained in a pure form.[142,146,179] It has been shown by spectroscopic methods that, on decomposition of $PMo_{12-n}V_n$, a certain amount of vanadium passes to the cationic component with simultaneous ejection of the excess phosphorus in the form of H_3PO_4.[179,180] The chemical composition of the mixture does not then change, or the change is much less than the extent of the synthesis of HPAC. For this reason, the postulated HPAC with $n = 4-7$ are most probably a mixture of HPAC with $n = 1-3$, H_3PO_4, and VO_2^+.

HPAC known not to exist (the corresponding HPA are stable in nearly neutral media) are sometimes mentioned in patents devoted to the application of HPAC in catalysis. Such non-existent HPAC include $H_nPW_9X_{3-n}Z_xO_{37}$ ($n = 6-7$; $x = 0, 1$; $X^{3+} = Fe^{3+}$, Cr^{3+}, $Z^{2+} = Co^{2+}$, Mn^{2+}, Zn^{2+}, Ni^{2+}),[181] $H_6P_2Mo_5O_{23}$, $H_9CoW_6O_{24}$, $H_7AsMo_{11}O_{39}$, $H_9PMo_9O_{34}$,[182] etc. In such cases, it is more correct to speak of catalysts having the corresponding composition and not of the individual HPAC. This also applies to $SiMo_{10}Sn_2$.

A whole series of HPAC with the Keggin structure have been obtained by cation exchange—for example, $H_2W_{11}Mo$,[183] $TlMo_{12}$,[184] $InMo_{12}$,[185] and the complex HPAC having the composition $X(Mo \text{ or } W)_{11}Z$.[1,186–193] They exist in the form of dilute solutions. Virtually nothing is known about the possibility of their existence in the solid state or in the form of concentrated solutions.

The replacement of W or Mo in the ligand sphere of the HPAC by V has an unambiguous effect on the stability of the HPAC. In terms of their stability in aqueous solutions, HPAC can be arranged in the following sequences:

$$PMo_{11}V > PMo_{12} > PMo_{10}V_2 > PMo_9V_3$$ [194]

$$SiMo_{12} > SiMo_{11}V > SiMo_{10}V_2$$ [195]

$$PW_{12},\ PW_{11}V,\ PW_{10}V_2 > PW_9V_3 > PW_9V_4$$ [139]

$$VW_{10}V_2 > VW_{11}V > VW_{12}\ \text{(hypothetical)}.$$[144]

All the vanadium-containing HPAC are in fact mixtures of HPAC with different values of n.[139,144,179,195] Only $PMo_{11}V$ and $PW_{11}V$ have been synthesised relatively easily.

$PMo_{12-n}W_n$,[179] $PW_{12-n}Nb_n$,[142] and apparently all the remaining mixed-ligand HPAC with $n > 1$ are also mixtures.

The stabilities of various HPAC in aqueous solution have been investigated by ^{17}O NMR methods (based on the rate of isotope exchange with $H_2^{17}O$) and by observing the formation of deposits in concentrated solutions (Table 2). The following HPAC stability series have been constructed on the basis of these data:

$$SiW_{12} > PW_{12} \gg PMo_{12} > SiMo_{12} > GeMo_{12}\ .$$

Hence it is seen that the composition of the ligand sphere has a greater influence on the stability of HPAC than X: HPAC with W are much more stable than those with Mo. The products of the hydrolysis of these HPAC have also been investigated. On hydrolysis of $SiMo_{12}$ and $GeMo_{12}$, deposits of MoO_3, SiO_2, and GeO_2 were precipitated from the solutions. $MoO_3(H_2MoO_4)$ was also precipitated from the PMo_{12} solution, the compound P_2Mo_{18} accumulating in the solution in accordance with the postulated reaction

$$PMo_{12} \longrightarrow PMo_9 \longrightarrow P_2Mo_{18}\ .$$

PW_{12} is apparently hydrolysed via a different mechanism:

$$PW_{12} \longrightarrow PW_{11} + WO_4^{2-}\ .$$

The hydrolysis of PW_{11} does not proceed any further.[196] A series of various tungsten-containing HPAC in terms of their resistance to acid hydrolysis in concentrated aqueous solutions has been

Table 2. Hydrolytic properties of HPAC in aqueous solutions.

HPAC	Temperature/ °C				
	70	110	200	250	270
$SiMo_{12}$	x	x	–	–	–
PMo_{12}	o	x	–	–	–
PW_{12}	o	o	o	+	+
P_2W_{18}	o	o	o	o	o
SiW_{12}	o	o	o	o	o
P_2Mo_{18}	o	o	x	–	–

Note. The solutions were kept in sealed tubes for 24 h (c_{HPAC} = 0.45 M (Keggin) and 0.225 M (Dawson).[196] Here and henceforth the following designations have been adopted: o — compound stable (no deposit); + — compound partly stable (solution turbid but a deposit is not precipitated); x — compound unstable (appreciable deposit); * compound almost stable.

constructed on the basis of experiments on ether extraction in the presence of inorganic acids:

$$PW_{12},\ P_2W_{21},\ P_2W_{18} > PW_{11}Ti > (PW_{11})_2Ce^{4+} > PW_{11}Ce^{4+},\ PW_{11}Cr^{3+} > PW_{11}Zr,\ PW_{11}Bi.$$

In these experiments, the compound $PW_{11}Cr^{3+}$ was obtained as a relatively unstable component in a mixture with PW_{12} and P_2W_{21}.[143] In organic and aqueous organic media, the HPAC are most stable than in water.[110]

The hydrolytic transformations in dilute solutions have been investigated only in relation to PMo_{12}. At a concentration of 0.01 M and below, PMo_{12} decomposes in water, affording unsaturated HPA of the type PMo_{11} and PMo_9 apparently via a mechanism involving alkaline hydrolysis as a result of the decrease in the acidity of the solution. At a concentration of 0.001 M, there is virtually no initial HPAC in the solution.[197] On the basis of general data indicating a decrease in the degree of polymerisation of tungsten and molybdenum following dilution of solutions,[198] it is reasonable to suggest that all the HPAC should hydrolyse in dilute solutions although to different extents and at different rates. One should apparently treat with extreme caution all data concerning dilute (less than 0.01 M) solutions of the HPAC.

Numerous published data on the thermal stabilities of HPAC (see above) should also be treated with care. The assignment of the position of the exothermic peak on the differential thermal analysis curve to the HPAC decomposition temperature is a source of numerous errors.[110] Under these conditions, factors such as the dependence of the rate of decomposition of the HPAC on the heating rate and the possibility of structural changes initiated by the supply of heat are frequently ignored. Thus, decomposition temperatures which are clearly too high have been indicated for HPAC such as (the decomposition temperatures are indicated in brackets in °C) PW_{12} (620), SiW_{12} (530), BW_{12} (420), etc.[199] In this connection, the study[112] where the measurements were accompanied by monitoring involving the ^1H NMR method appears accurate. It was stated in the corresponding communication that not all the HPAC can be obtained in the anhydrous state. Thus H_2W_{12}, BW_{12}, $SiMo_{12}$, and $GeMo_{12}$ decompose during dehydration.

Tsigdinos[110] suggested that the thermal stability be estimated by the method involving a check of the solubility of the HPAC after heat treatment under isothermal conditions. This method demonstrated that the HPAC with molybdenum decompose slowly even at room temperature, the decomposition accelerating above a certain temperature (350 °C for PMo_{12} and 200 °C for $SiMo_{12}$). This method was applied also to other HPAC (Table 3). A HPAC thermal stability series was constructed:

$$PW_{12} > PMo_{12} \gg SiW_{12} > GeMo_{12} > SiMo_{12}.$$

Table 3. Thermal stabilities of HPAC estimated by the Tsigdinos method (2 g of the HPAC was heated for 3 h in air and then stirred in 50 ml of water for 30 min).[196]

HPAC	Isothermal heat-treatment temperature/°C						
	180	250	300	350	370	390	400
$SiMo_{12}$	+	x	x	–	–	–	–
$GeMo_{12}$	o	o	+	–	–	–	x
SiW_{12}	o	o	*	*	*	+	x
PMo_{12}	o	o	o	o	o	+	x
PW_{12}	o	o	o	o	o	o	o

It did not agree with the hydrolytic stability series.[196] The Tsigdinos method makes it possible to estimate to some extent the thermal stability of the HPAC but does not take into account the possibility of solid-phase transformations.

The thermal transformations have been investigated in detail in relation to the following compounds: $SiMo_{12-n}V_n$, $PMo_{12-n}V_n$, PW_{12}, $PW_{11}Z$, and PMo_{12}. It has been shown with the aid of the NMR method that a mixture of $SiMo_{11}V$ and $SiMo_{10}V_2$ decomposes smoothly in the temperature range between 110 and 400 °C.[155] $SiMo_{11}V$ decomposes fully at 300 °C,[200] while $SiMo_{10}V_2$ is relatively stable up to 200 °C and its complete decomposition takes place in the temperature range 300 to 400 °C.[156] No structural rearrangements occur under these conditions.

The heteropolyacids $PMo_{12-n}V_n$, (n = 1 – 3) become insoluble after heat treatment at 200 – 400 °C,[201] their thermal stability diminishing with increase in n. The data on the decomposition temperatures, determined with the aid of derivatographic measurements and vibrational spectroscopy, are different in the studies of different authors (Table 4). The observed tendency[151,203] appears correct, but, bearing in mind the decrease in solubility,[201] the values obtained appear too high. Complete dehydration takes place in the temperature range between 380 and 410 °C.[202] The mechanism of the thermal decomposition of the vanadium-containing HPAC has been investigated. It was found that during heat treatment vanadium and phosphorus are ejected, compounds with a smaller vanadium content being stabilised under these conditions.[204]

After heat treatment for 2 – 5 h at 110 – 400 °C, the acid PW_{12} fully retains its solubility and the ^{31}P NMR spectrum also remains unchanged under these conditions (– 15.0 ppm). After heat treatment at 500 °C, the HPAC becomes partly soluble and new lines appear in the ^{31}P NMR spectrum at – 12.5 and – 13 ppm. Above 600 °C, the PW_{12} is fully insoluble.[205] It has been established by X-ray diffraction that the HPAC begins to change at 400 °C.[111] Salt-forming protons begin to be removed at 420 °C without the formation of the WO_3 phase.[206,207] Different investigators apply the same term (anhydride) to the phase formed at 420 °C, but they attribute different structures to it: $PW_{12}O_{38.5}$[208] or $PW_{12}-O-PW_{12}$.[207] The problem of the real structure of PW_{12} in the temperature range 400 – 500 °C remains obscure.

Table 4. Decomposition temperatures of HPAC of the type $PMo_{12-n}V_n$.

HPAC	n	T_{decomp}/°C	Ref.
PMo_{12}	0	433	203
$PMo_{11}V$	1	442	151
$PMo_{10}V_2$	2	412	151
PMo_9V_3	3	396	151
PMo_8V_4	4	293	203
$PMo_{12-n}V_n$	0 – 3	460	202

The thermal stability of complex HPAC of the type $PW_{11}Z$ (Z = Ti, Zr, Bi, Ce) has been investigated by IR and ^{31}P NMR spectroscopy after heat treatment under isothermal conditions. It was found that $PW_{11}Ti$ and $PW_{11}Zr$ are stable up to 450 °C (the decomposition to oxide phases takes place in the temperature range 450–500 °C), while $PW_{11}Bi$ decomposes partially at temperatures above 150 °C and fully at temperatures above 300 °C with formation of the bismuth salt of PW_{12}. The complex $PW_{11}Ce^{4+}$ begins to be converted into $(PW_{11})_2Ce^{4+}$ even at 150 °C and disappears from the thermolysis products in the temperature range 300–400 °C depending on the heat treatment time. After heat treatment, the specimens dissolve incompletely owing to the formation of Ce^{3+} salts. Owing to the subsequent decomposition of $(PW_{11})_2Ce^{4+}$, PW_{12}, H_3PO_4, and $PW_{11}Ce^{3+}$ appear in the thermolysis products. In terms of their thermal stabilities, cerium-containing HPAC can be arranged in the following sequence:[143]

$$PW_{11}Ce^{3+} > (PW_{11})_2Ce^{4+} > PW_{11}Ce^{4+}.$$

Numerous studies have been devoted to the problem of the thermal stability of PMo_{12}. Most information has been obtained by means of a combination of the methods of thermal analysis, X-ray diffraction, and ^{31}P NMR spectroscopy.[197,209] The PMo_{12} specimens retain their complete solubility after heating to 350 °C. At 385 °C, the specimens still dissolve almost completely but more slowly. After heat treatment at 400 °C and above, the specimens dissolve only partially, the Mo : P ratio in the solutions differing from 12 : 1.[197] The following scheme has been proposed for the thermal transformation on the basis of the results:[209]

$$H_3PMo_{12}O_{40}\cdot n\,H_2O \underset{n\,H_2O}{\overset{200-350\,^\circ C}{\rightleftharpoons}} H_3PMo_{12}O_{40} \underset{\sim 1.5\,H_2O}{\overset{385\,^\circ C}{\rightleftharpoons}}$$

$$\rightleftharpoons H_xPMo_{12}O_{38.5+0.5x} \xrightarrow{> 400\,^\circ C}$$

$$\longrightarrow (PMo_{12}O_{38.5})_n + MoO_3 + (MoO_2)_2P_2O_7 \xrightarrow[50\%]{450\,^\circ C}$$

$$\longrightarrow MoO_3 + (MoO_2)_2P_2O_7$$

$x \sim 0.1$

The phase with $x = 0.1 - 1.0$ is readily soluble in air with a humidity of 80%–90% and is converted into PMo_{12} in 2–4 days. It has been suggested[197] that the $(PMo_{12}O_{38.5})_n$ phase is the cationic-anionic complex $[PMo_{12}O_{39}^{-}][PMo_{12}O_{38}]^{+}$. The anionic part of the complex readily interacts with water, while the cationic component reacts with difficulty but also with regeneration of the initial HPAC.

The formation of the anhydride (or anhydride phases) is apparently a common feature of those HPAC which can exist in the anhydrous state. A partial loss (5%–10%) of protons occurs even on simple dehydration of the HPAC.[112] A gradual loss of protons in the temperature range 300–450 °C has also been noted for ZnW_6Mo_6.[149]

The decomposition temperatures of the mixed HPAC $SiMo_{12-n}W_n$ depend directly on n and have intermediate values between those for $SiMo_{12}$ and SiW_{12}.[210]

The Keggin heteropolyanions are capable of combining with electrons reversibly.[1] The corresponding HPAC also retain this property. Thus it has been possible to reduce PW_{12},[1] SiW_{12}, BW_{12}, H_2W_{12}[211] (by the addition of 6 $\bar{e}$), $SiMo_{12}$,[128] and PMo_{12}[212] (by the addition of 4 $\bar{e}$), fluorine-containing metatungstic acids[213] (by the addition of 6–24 $\bar{e}$), and many other HPAC (by the addition of 1–2 $\bar{e}$). The reduction has different effects on the properties of the HPAC. Thus the compound $AsMo_{10}V_2$ (provided that it exists) loses vanadium after the addition of two electrons.[161] The tungsten-containing compounds do not undergo a change in composition and structure on reduction (at least after the addition of 6 $\bar{e}$). The molybdenum-containing HPAC frequently undergo the isomerisation $\alpha \rightarrow \beta$.[1,110,212] For example, the following reactions take place on reduction in solution:

$$\alpha\text{-}PMo_{12} \xrightarrow{2^-} \alpha\text{-}PMo_{12}(2^-) \longrightarrow$$

$$\longrightarrow \beta\text{-}PMo_{12}(2^-) \longrightarrow \beta\text{-}PMo_{12}(4^-) + \beta\text{-}PMo_{12}$$

$$\downarrow 2^-$$

$$\beta\text{-}PMo_{12}(4^-)$$

The stable form β-PMo_{12} (4 $\bar{e}$) is rapidly reconverted into α-PMo_{12} on oxidation in water. In aqueous dioxane, this process is slower.[212] It is believed that α-$SiMo_{12}$ behaves similarly.[1,110] However, it has been found by X-ray diffraction that the reduced $SiMo_{12}$ (4 $\bar{e}$) has the structure of the α-isomer.[214]

The thermal stability of the reduced HPAC has been investigated in relation to $SiMo_{12}$. It was found that the specimens of the reduced HPAC are more stable than the initial $SiMo_{12}$. The reduced HPAC β-PMo_{12} (4 $\bar{e}$) is stable in aqueous solution up to 180 °C and is much superior in this respect to α-PMo_{12}.[215]

A high acidity is a most important property of the HPAC, which makes it possible to devise effective acid catalysts based on

Table 5. Acid dissociation constants of the HPAC in various solvents at 25 °C.[217]

HPAC	Acetone			Ethanol			Acetic acid
	pK_1	pK_2	pK_3	pK_1	pK_2	pK_3	pK_1
H_3PW_{12}	1.6	3.0	3.98	1.6	3.0	4.1	4.77
$H_4PW_{11}V$	1.8	3.2	4.37	–	–	–	4.74
$H_5PW_{10}V_2$	–	–	–	–	–	–	4.78
H_4SiW_{12}	2.0	3.61	5.3	2.0	3.96	6.3	4.97
H_3PMo_{12}	2.0	3.62	5.3	1.8	3.41	5.1	4.70
H_4PMo_{12} (1 $\bar{e}$)	2.1	3.69	5.5	1.9	3.77	5.9	
$H_4PMo_{11}V$	2.1	3.73	5.6	1.9	3.74	5.8	4.68
H_4SiMo_{12}	2.1	3.90	5.9	–	–	–	4.78
H_4GeW_{12}	–	–	–	–	–	–	4.25
$H_5GeW_{11}V$	–	–	–	–	–	–	4.65
$H_6GeW_{10}V_2$	–	–	–	–	–	–	4.60
$HClO_4$	–	–	–	–	–	–	4.87
HBr	–	–	–	–	–	–	5.6
H_2SO_4	–	–	–	–	–	–	7.0
HCl	4.0	–	–	–	–	–	8.4
HNO_3	–	–	–	3.57	–	–	10.1

them. A lot of space is always devoted to this property in reviews concerning the applications of the HPAC. The acidity of the Keggin HPAC has been investigated by various methods, which include the indicator method, the measurement of the diffusion coefficients and ionic conductivities, ion exchange, thermal desorption of bases, ^1H NMR spectroscopy,[20] kinetic methods,[10,13,125,216] and measurement of dissociation constants in solutions (Table 5).

It has been shown that all the HPAC investigated are strong multibasic Brønsted acids. In solutions, they are stronger than inorganic acids such as H_2SO_4, HBr, HCl, HNO_3, and even $HClO_4$. This is due to the large size of the HPA (diameter 10–12 Å) combined with a relatively low charge. In water, the Keggin HPAC are fully dissociated and it is impossible to determine the first three dissociation constants. However, this can be done in polar organic solvents (see Table 5). The weak dependence of the strength of the HPAC on their composition is striking, although here too one can differentiate certain characteristic features: (1) the tungsten-containing HPAC are stronger than the molybdenum-containing HPAC; (2) with increase in the basicity of the HPAC, their acidity diminishes; (3) the acidity of the HPAC diminishes after reduction.

Some doubts about the measurements of the dissociation constants arise from the fact that they were made for highly dilute solutions ($\sim 10^{-5}$ M) and the individuality of the HPAC in them had not been confirmed. However, there are grounds for the assumption that the correction for the hydrolysis of the HPA may influence at the same time the dissociation constants of the HPAC without affecting the general trends observed.

After the introduction of vanadium atoms into the HPAC, their basicity increases whilst their acidity falls. At the same time, HPAC such as PMo_9V_3 and PW_9V_3 are protonated even in their solutions.[218,219] Not all the protons are equivalent in the pentabasic GaW_{12}.[220] The reduced PMo_{12} and $SiMo_{12}$ (4 $\bar{e}$) contain protons bound to the heteropolyanion, but they are all equally strong acids as regards the first 3–4 protons.[221,222] Even the highly reduced $H_2W_{12}F$ (12 $\bar{e}$) affords an amorphous brown powder, having the general composition $H_{19}W_{12}O_{39}F$, which retains its acid character.[213]

The acidity of concentrated solutions of HPAC in water is greater than the acidity of solutions of sulfuric and perchloric acids at the same concentration by 1–1.5 units of the Hammett acidity function H_0.[13,217] The acidity of concentrated solutions of HPAC diminishes in the sequence

$$SiMo_{12} > PMo_{12} > SiW_{12} \sim PW_{12} .$$

This sequence does not agree with that of the dissociation constants possibly owing to the salt effects or the influence of hydrolysis.

The acidities of HPAC in nitrobenzene have been estimated from the formation constants of complexes with chloral hydrate. The following series was obtained:[13]

$$PW_{12} > PMo_{12} > SiW_{12} \approx GeW_{12} > SiMo_{12} > GeMo_{12} .$$

It follows from the data presented that the acidities of different HPAC in solutions vary in different ways with concentration and the solvent.

The mixed HPAC of the type $XMo_{12-n}W_n$ also exhibit a high acidity in solution, the latter increasing with increase in n.[135,223] A high acidity is apparently a common feature of all the Keggin type HPAC.

It has been shown by conductimetric, IR spectroscopic, and thermal desorption methods that the HPAC retain a high acidity also in the solid state (higher than that of aluminosilicate). In anhydrous HPAC, the protons are localised, but their mobility increases at temperatures above 150 °C for PW_{12} and SiW_{12} and above 250 °C for PMo_{12} and $SiMo_{12}$. The catalytic activities of the solid HPAC in acid-catalysed reactions usually decrease in the sequence

$$PW_{12} > SiW_{12} \approx PMo_{12} > SiMo_{12} ,$$

which agrees fully with the acidity series in solutions.[13]

According to adsorption calorimetric data, the proton centres of PW_{12} are fairly uniform and have strengths similar to those in H-mordenite; PW_{12}, which is believed to be the strongest acid among the HPAC, has acid centres with $H_0 < -8.2$.[20] Superacids with $H_0 = -14.52$ and even less can be obtained by combining the HPAC with $SbCl_5$.[224]

The distribution of the acid centres of PW_{12} and SiW_{12} in terms of strength has been investigated in detail by the indicator method combined with titration by n-butylamine (Fig. 2). The largest number of strong acid centres with $H_0 \leqslant -5.6$ have been observed in the HPAC after heat treatment in the temperature range 300–400 °C, their number diminishing sharply above 400 °C. The compound PW_{12} has a larger number of acid centres than SiW_{12}.[225] Such behaviour of the HPAC agrees well with their thermal stability data.

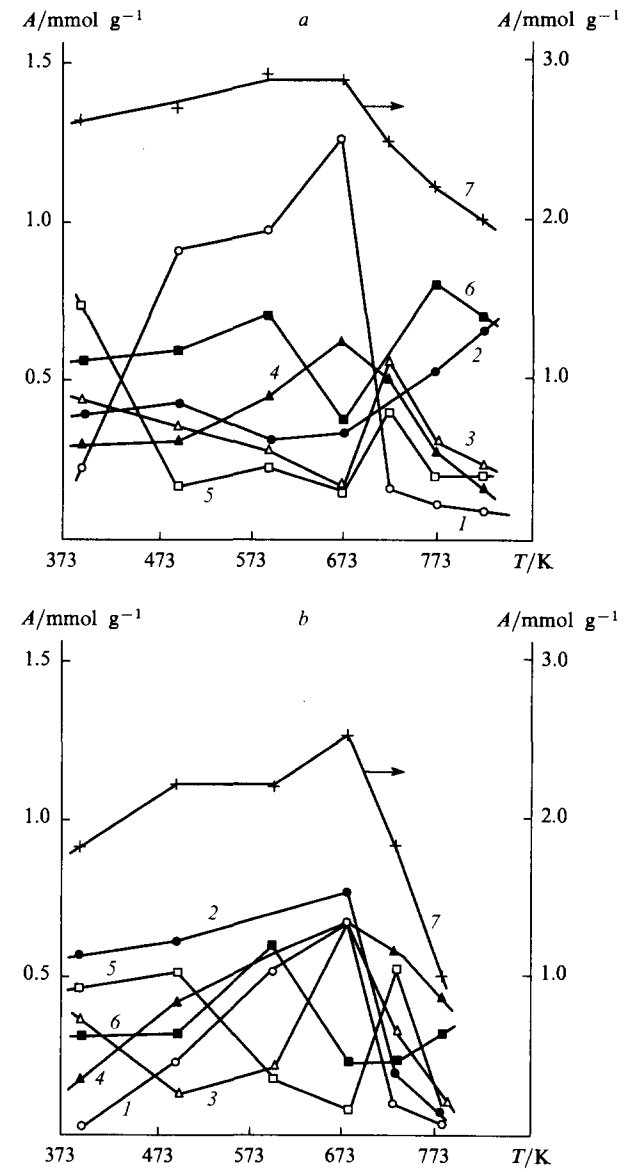


Figure 2. Distribution of the acid centres (A) in PW_{12} (a) and SiW_{12} (b) as a function of temperature.[225] Theoretical numbers of proton centres: 1.04 for PW_{12} and 1.39 for SiW_{12}. Hammett acidity functions: (*1*) $H_0 \leqslant -5.6$; (*2*) $-5.6 < H_0 < -3.0$; (*3*) $-3.0 < H_0 < 1.5$; (*4*) $1.5 < H_0 < 3.3$; (*5*) $3.3 < H_0 < 5.0$; (*6*) $5.0 < H_0 < 6.8$; (*7*) $H_0 \leqslant 6.8$.

The acidity of the HPAC $PMo_{12-n}V_n$ ($n = 0 - 3$) has been investigated by the method involving the thermal desorption of bases. After the introduction of vanadium into the PMo_{12} molecule, the acid centres become nonuniform and their strength and number decrease with increase in n.[226] After evacuation at 350 °C, such HPAC acquire the Mo^{5+} and V^{4+} centres and the Lewis acidity associated with them.[227]

HPAC with $X = P^{5+}$, in particular PW_{12}, PMo_{12}, and $PMo_{12-n}V_n$, are most important in practice because of their relatively high stability and availability. It is not fortuitous that all the examples of the industrial use of HPAC as catalysts known hitherto are based on the application of precisely these HPAC. The HPAC PW_{12} became exceptionally important for acid catalysis, since it has the highest thermal stability and acidity and the methods for its synthesis have been developed in fair detail. In Russia, PMo_{12} is cheaper but has poorer technological properties (lower resistance to hydrolysis and to the reduction of the anion by the organic medium).

2. Heteropolyacids with the Dawson structure

The structure of compounds of this type was first determined by Dawson in 1953 (Fig. 3). The compositions of the known HPAC with the Dawson structure are presented below (the temperatures of the onset of decomposition in the solid state are indicated in brackets):

α-$H_6P_2W_{18}O_{62}$ (210) [1,3,110,228]	α-$H_6As_2W_{18}O_{62}$ [1,3,110]
α-$H_6P_2Mo_{18}O_{62}$ (>120) [1,3,110,229]	α-$H_6As_2Mo_{18}O_{62}$ [1,3,110]
α-$H_6P_2W_{13}Mo_5O_{62}$ [3]	α-$H_6P_2W_{14}Mo_4O_{62}$ [3]
α_1-$H_6P_2W_{17}MoO_{62}$ [230]	α_2-$H_6P_2W_{17}MoO_{62}$ [230]

The existence of certain HPAC with the Dawson structure requires confirmation. These include $H_6PAsW_{18}O_{62}$[231] and $H_{6+n}P_2Mo_{18-n}V_nO_{62}$.[232] There are comparatively few compounds of this type. There is also little information about them.

Investigators have not been very active in the synthesis and study of the HPAC with the Dawson structure. Apart from those indicated above, $X_2W_{17}Z$, where $X = As^{5+}$ or P^{5+} and $Z = Sn^{4+}$, Ge^{4+}, Mn^{3+}, Co^{3+}, Fe^{3+}, or Cr^{3+}, have been obtained by cation exchange in the form of dilute aqueous solutions.[190,233-235] Nothing is known about the possibility of their existence in the solid state or in the form of concentrated solutions. The heteropolyacid $P_2W_{17}Ce^{4+}$ has not been obtained, while $P_2W_{17}Ti$ exists in a concentrated solution (with a content of 43%) only in a mixture with other HPAC.[142] Dawson β-heteropolyacids have not been obtained. The synthesis of β-P_2W_{18} in a concentrated solution has been reported,[231] but it was subsequently found that, when the solution of the salt is acidified, the HPAC decomposes to PW_{12} and α-P_2W_{18}.[142]

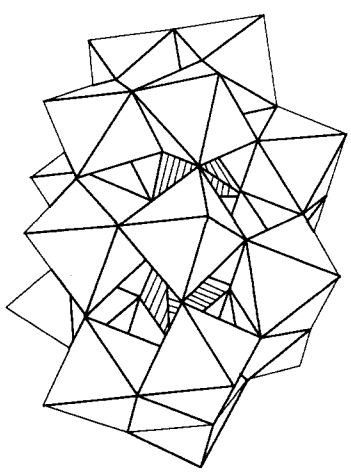


Figure 3. The structure of the Dawson HPAC (α-isomer). The two XM_9 fragments of the Keggin HPA are joined together to form a dimer.

In highly acid solutions, the HPAC α-P_2W_{18}, α-As_2W_{18}, and α-P_2Mo_{18} are entirely stable and are actually more stable than the corresponding Keggin HPAC (α-P_2W_{18} is very stable on hydrolysis in water, although α-P_2Mo_{18} is less stable) (Table 2). In contrast to these compounds, α-As_2Mo_{18} decomposes slowly in the presence of strong acids.[110]

The thermal stability of α-P_2W_{18} has been studied in relative detail. It has been found by differential thermal analysis at a heating rate of 2.5 K min^{-1} that α-P_2W_{18} is dehydrated at 350 °C. Although the DTA curve did not show a distinct exothermic peak, which is usually identified as the HPAC decomposition point, it was concluded that α-P_2W_{18} decomposes at 640 °C.[236] Other workers[207] noted that the behaviour of α-P_2W_{18} on heating is different from that of PW_{12}. They did not detect the anhydride and postulated (without any evidence) that this HPAC decomposes immediately to WO_3, but it was not clear what was the decomposition temperature. It was noted that, after heat treatment at 400 °C for 2 h, the HPAC ceased to dissolve. Subsequently, the same workers[237] recorded the ^{31}P NMR spectra of the heat-treated specimen but these did not throw light on the situation either.

In the most thorough investigation,[228] the thermal transformations of α-P_2W_{18} were investigated by a set of methods: differential thermal analysis (DTA) (heating rate 2.5 K min^{-1}), ^1H NMR, and IR spectroscopy. It was shown that the anhydrous HPAC cannot be obtained and that the last phase retaining the structure of the initial HPAC is $H_6P_2W_{18}O_{62}.2.6H_2O$ and all the protons in this phase are nonhydrated. The phase is formed in the temperature range from 225 to 250 °C and on further increase of temperature the protons are gradually eliminated. The crystallisation of $18WO_3.P_2O_5$ begins at a temperature of about 610 °C (at the selected heating rate), but the deformation of the structure of the initial HPAC was already noted at 210 °C. It remained obscure which phases exist in the temperature range 210-610 °C.

The thermal transformations of α-P_2Mo_{18} were also investigated combining the DTA and IR and ^1H NMR spectroscopic methods. Four endothermic effects due to the dehydration and partial decomposition of the HPAC were observed in the temperature range 120-300 °C. It was discovered that the phase $H_6P_2Mo_{18}O_{62}.3H_2O$ with non-hydrated protons was formed at 270 °C. On further heating, a change in the HPAC structure was observed and the oxide phase crystallised at 530 °C.[229] On thermolysis, α-P_2W_{18} and α-P_2Mo_{18} behave similarly.

The Dawson heteropolyacids can also be reduced without change in structure, at least on addition of 6 $\bar{e}$,[238] the reduction occurring more readily than that of the corresponding Keggin HPAC.[110] It has been found[238] that stable Dawson HPAC have been reduced by the addition of an odd number of electrons.

The direct determination of the acid salts of Dawson HPAC by the indicator method is difficult owing to their colour. It has only been possible to demonstrate[239] that H_0 for P_2W_{18} is less than −3.0. However, according to certain indirect data, it is possible to infer a high acidity of the Dawson HPAC. Thus all the protons of P_2Mo_{18} (2 $\bar{e}$) and P_2Mo_{18} (4 $\bar{e}$) are titrated (8 and 10 respectively), and only in P_2Mo_{18} (6 $\bar{e}$) the last two protons are not titrated.[238] The reduced P_2W_{18} (2 $\bar{e}$) is also a strong acid, all eight of its protons being titrated.[240] It has been noted that the reduced tungsten HPAC are stronger acids than the reduced molybdenum HPAC.[238] In the acid-catalysed conversion of methanol, P_2W_{18} is almost as active as PW_{12} even after preliminary reduction with hydrogen.[239] On the other hand, in the synthesis of *tert*-butyl methyl ether, the Dawson HPAC proved actually more active than the Keggin acids,[13] which indicates not only their very high acidity but also the specificity of their catalytic action. In the decomposition of isobutyl

propionate, P_2W_{18} is less active than the Keggin HPAC,[125] but these data require confirmation, since the question of the thermal stability of α-P_2W_{18} is not clear — the HPAC may change with the conditions of their preparation (evacuation for 8 h at 150 °C).[125]

The methods of synthesis of the Dawson HPAC have been less thoroughly developed and are more difficult than for the Keggin HPAC. This in fact accounts also for the small number of studies in which the HPAC were used as catalysts. Conditions for the synthesis of α-P_2W_{18} and α-P_2Mo_{18} by electrodialysis in almost quantitative yields have been discovered recently.[142] Only the ammonium salt of P_2W_{18} is manufactured in Russia, whilst other Dawson HPAC or their salts are not.

No examples of the practical use of the Dawson HPAC are known. One may mention only a Japanese patent[241] in which it is stated that P_2Mo_{18} may be employed in the industrial hydration of isobutene instead of the unstable PMo_{12}.

3. Other heteropolyacids and isopolyacids

The compositions of other isopolyacids and heteropolyacids, different from the Keggin and Dawson HPAC, the existence of which has been reliably established are presented below (the temperatures of the onset of decomposition in the solid state are indicated in brackets in °C):

$H_6As_2W_{21}O_{69}$ [1,142]
$H_8TeMo_6O_{24}$ (Anderson) [243]
$H_9CrMo_6O_{24}$ [3,110,142,245]
$H_5IMo_6O_{24}$ [3,110]
$H_8ThMo_{12}O_{42}$ (125) [110,246]
$H_8UMo_{12}O_{42}$ (120) [110,247]
$H_2Ln_2XMo_{12}O_{42}$ [249]
$H_9NaF_6W_{18}O_{56}$ [251]
β-$H_4Mo_8O_{26}$ [252]
$H_6P_2W_{21}O_{71}$ (150) [242]
$H_9FeMo_6O_{24}$ [3,110,244,245]
$H_9CoMo_6O_{24}$ [3,110,142,245]
$H_8CeMo_{12}O_{42}$ (Dexter–Silverston) [3,110]
$H_8NpMo_{12}O_{42}$ [248]
$H_6MnMo_9O_{32}$ [110,250]
$H_{10}(PW_{11}O_{39})_2Ce$ (300) [143]
$H_8Mo_{36}O_{112}$ [253].

The existence of certain HPAC requires confirmation:

$H_9AlMo_6O_{24}$ (270) [110,254]
$H_{11}(SiW_{11}SnO_{39})_2Co(CO)_3$ [167]
$H_9GaMo_6V_6O_{24}$ (270) [110,254]
$H_9(PW_{11}SnO_{39})_2PdC_3H_5$ [167].

The structures of many HPAC are unknown:

h-$H_5BW_{12}O_{40}$ [1]
$H_{16}S_2W_{16}V_4O_{72}$ [144]
$H_8VMo_6O_{24}$ [257]
$H_2W_{10}VO_{33}$ [259]
$H_4SW_8V_2O_{34}$ (225–300) [260]
$H_6As_2Mo_2O_{12}$ [3]
$V_2O_5 \cdot I_2O_5$ [3]
$WO_3 \cdot nH_2O_2$ ($n = 0.4-0.7$) [262]
$Te^{4+}W_{18}$ [263]
$Te^{4+}W_8V_4$ (300) [173,174]
$Se^{4+}W_{12}$ (47) [168,171]
$Se^{4+}W_8V_4$ (187) [171]
$Se^{4+}W_7V_3$ [265]
$Sb^{3+}-W$ [266]
$H_{10}NiW_{17}F_4O_{55}$ [255]
$H_6V_2Mo_{12}O_{44}$ [256]
$H_4V_2W_8O_{31}$ [258]
$H_{18}W_{24}VO_{83}$ [259]
$10\,WO_3 \cdot V_2O_5$ [261]
$H_3AsMo_3O_{13}$ [3]
BeW_9 [110]
$Te^{4+}W_{12}$ (200) [169,170]
$Te^{4+}W_9V_3$ [173]
$W:Te^{6+} = 4-18$ [264]
$Se^{4+}W_{10}V_2$ [172]
$Se^{4+}W_8V_3$ [265]
$Se^{4+}W_6V_3$ [265]
$As^{5+}-W$ [266]
M–F–W (M = Nb, V, Fe, Al) [267]
M–F–Mo (M = V, Ti) [267]
$As^{3+}-W$ [268]

Heteropolyacids the existence of which is open to doubt:

$H_8CeMo_{10}O_{36}$ [269]
$H_8CeW_{12}O_{42}$ [270]
$H_4CeW_8O_{28}$ [270,271]
$H_6ThUW_{18}O_{61}$ [272]
$H_8CeMo_8O_{30}$ [269]
$H_6CeW_{10}O_{35}$ [270]
$H_5CeW_8O_{28}$ [271]
$H_8SiW_{11}O_{39}$ [273]

The heteropolyacids β-$H_4Mo_8O_{26}$, $H_8Mo_{26}O_{112}$, BeW_9, $H_{10}NiW_{17}F_4O_{55}$, $H_8CeMo_{10}O_{36}$, $H_8CeMo_8O_{30}$, $H_5CeW_8O_{28}$, and $H_6ThUW_{18}O_{61}$ have not been isolated in the solid state. The HPAC belonging to the series with the Anderson structure are most numerous (Fig. 4). Dilute solutions of GaW_6[274] and $NiMo_{6-n}W_n$ ($n = 0-6$)[275] have been obtained by cation exchange, but nothing is known about the stability of these HPAC.

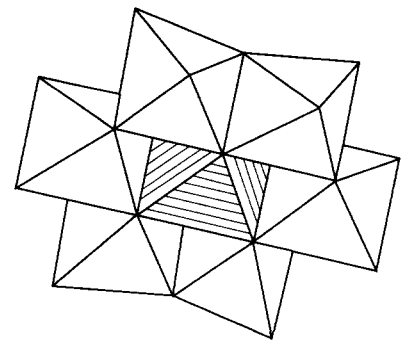


Figure 4. The structure of the Anderson HPAC. Six MO_6 octahedra surround the central XO_6 octahedron.

As a rule, the Anderson HPAC (except the HPAC with $X = I^{7+}$) are tribasic–tetrabasic, whereas the remaining protons are rigidly bound to the HPA. The stability of such HPAC is low. Thus $FeMo_6$ and $CoMo_6$ are stable in aqueous solutions for several weeks,[245] but in the solid state all the Anderson HPAC can be isolated only by evaporation at a low temperature. The strength of their acid centres is unknown. One can only postulate that the titratable protons are fairly weakly bound to the HPA. Examples of the use of such HPAC are also unknown.

The structure of the molybdenum HPAC with heteroatoms having high coordination numbers was first described correctly by Dexter and Silverton in 1968 (Fig. 5).[1] The stability of such HPAC is low. In aqueous solutions, they decompose gradually, but their hydrates can be stored for some time.[246,247] On heating, UMo_{12} loses part of the water of crystallisation in the temperature range from 40 to 120 °C and subsequently the compound begins to decompose. Its analogues behave similarly.[247] The minimum degree of hydration of $ThMo_{12}$ corresponds to ten water molecules. The compound $ThO_2 \cdot 12MoO_3 \cdot 4H_2O$ undergoes rapid dehydration on heating to 200 °C. It dissolves in water, but is not the initial HPAC. Slow heating to 125 °C leads to the same compound, but it has now lost its solubility. In aqueous solutions, these HPAC decompose slowly to complexes of the type X_nMo_{12} ($n = 2-3$).[246] As a result, it becomes possible to obtain HPAC with a ratio $Mo:X < 12$, which are in fact mixtures of the initial HPAC and their complexes. The structure of one of these complexes, namely $H_2Nd_2(H_2O)_{12}UMo_{12}O_{42} \cdot 12H_2O$, has been determined (Fig. 6). This compound is not a salt of a HPAC, since the neodymium atom is bound covalently to the HPA. This is a dibasic

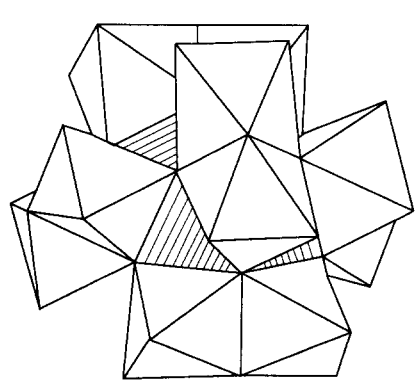


Figure 5. The structure of the Dexter–Silverton HPAC: 12 MoO_6 octahedra surround the central XO_{12} icosahedron.

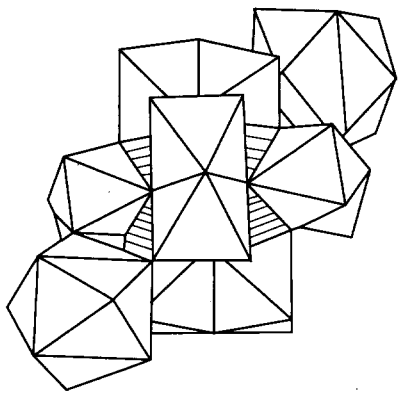


Figure 6. The structure of the HPAC $H_2Ln_2XMoO_{12}O_{42}$: two tri-capped trigonal Ln^{3+} prisms are joined to the Dexter–Silverton anion.

complex HPAC — a strong acid with respect to both protons. It is almost insoluble in water (7×10^{-4} M)[249,276] and is therefore of interest for heterogeneous acid catalysis as the only example of an insoluble HPAC.

Among other similar complex HPAC, dilute aqueous solutions of acids having the compositions $CeMo_{12}Nb$ and $CeMo_{12}Nb_2$ have been obtained. Their structures have not so far been established.[269]

The Dexter–Silverton heteropolyacids are strong acids. Thus five of the eight protons in $NpMo_{12}$ form H_3O^+ ions,[248] while $CeMo_{12}$ is also active in the acid-catalysed synthesis of *tert*-butyl methyl ether, like PMo_{12}.[277] The synthesis of the ether is the only known attempt to employ HPAC of a similar type as a catalyst, probably in view of their low availability and low stability.

The HPAC of the type P_2W_{21} has been investigated in relatively high detail (Fig. 7). It is entirely stable on storage in solution and in the solid state. In their study of the thermal stability of P_2W_{21} by the DTA method alone, French investigators[207] concluded that P_2W_{21} is also stable, like PW_{12}. Later they found[237] that nevertheless P_2W_{21} and PW_{12} behave differently on heating. It was found with the aid of IR and ^{31}P NMR spectroscopy that, on heating in the temperature range 150–300 °C, P_2W_{21} is converted into PW_{12} both in solution and in the solid state. Measurements of the Hammett acidity functions H_0 of concentrated aqueous solutions showed that,

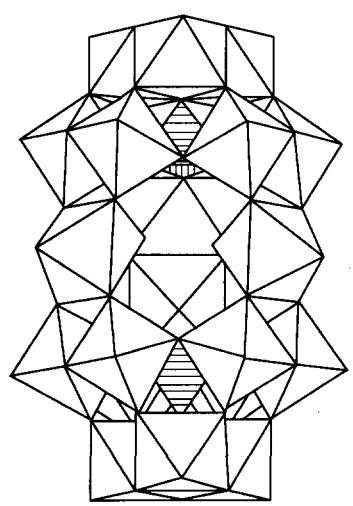


Figure 7. The structure of the HPAC $H_6P_2W_{21}O_{71}$: three $WO_5(H_2O)$ octahedra connect two PW_9 fragments of the Keggin HPA.

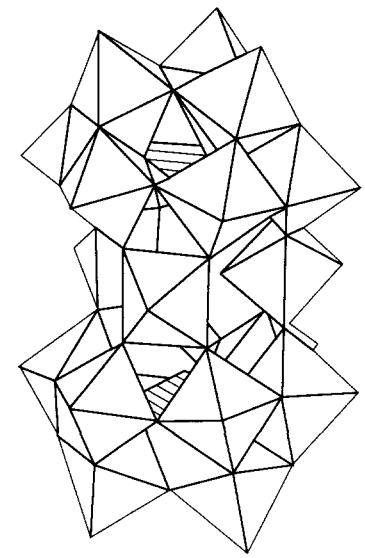


Figure 8. The structure of the HPAC $H_6As_2W_{21}O_{69}$: the $WO_5(H_2O)$ octahedron and two WO_5 pyramids connect two AsW_9 fragments in which the WO_6 octahedra surround the AsO_3 pyramids.

at equal concentrations, P_2W_{21} is actually a stronger acid than PW_{12}, although their acidities are approximately the same when calculated per proton.[242] Examples of the use of P_2W_{21} are unknown. It has been suggested that the HPAC $As_2^{5+}W_{21}$ exists, but it has not been isolated. The HPAC $As_2^{3+}W_{21}$ has a similar structure (Fig. 8) but its properties have not been studied.

NaF_6W_{18} is extremely resistant to the action of acids and alkalis (Fig. 9).[251,278] Apparently complex HPAC based on it exist.[251,255] The properties of similar HPAC have also not been investigated; their study is probably held back by the inconvenient methods of synthesis.

The heteropolyacid $(PW_{11})_2Ce^{4+}$ (Fig. 10) is entirely stable in the solid state at moderate temperatures. Above 300 °C, the following transformations take place:

$$(PW_{11})_2Ce^{4+} \longrightarrow PW_{12} + PW_{11}Ce^{3+} + H_3PO_4.$$

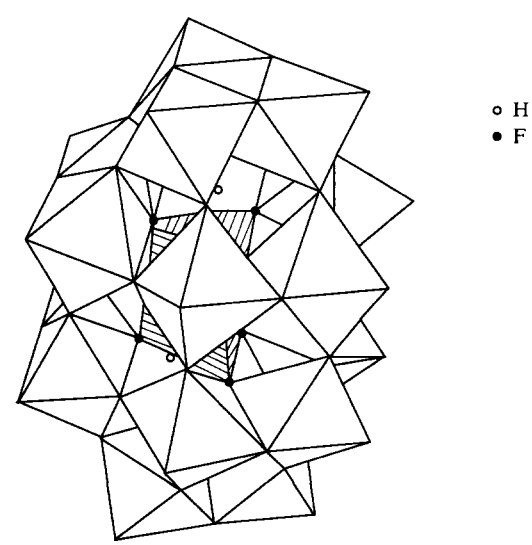


Figure 9. The structure of the HPAC $H_7H_2NaF_6W_{18}O_{56}$: the trigonal Na^+ prism and two protons occupy the central cavity of the HPA having a structure close to that of the Dawson HPA.

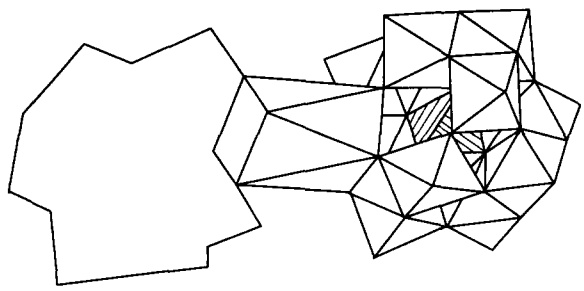


Figure 10. The structure of the HPAC $H_{10}(PW_{11}O_{39})_2Ce$: the square CeO_8 antiprism connects two PW_{11} fragments of the Keggin HPA.

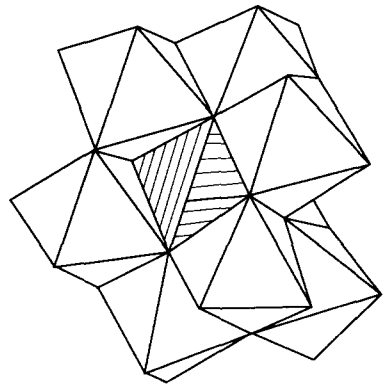


Figure 11. The structure of the HPAC $H_6XMo_9O_{32}$: nine MoO_6 octahedra surround the central XO_6 octahedron.

The mixtures of thermolysis products always contain also the initial HPAC. The decomposition to oxide phases is observed in the temperature range 450–500 °C.[143] Probably other complex HPAC with lanthanide and actinide ions exist.

The heteropolyacid $Mn^{4+}Mo_9$ (Fig. 11) can be obtained in the solid state, but its solutions are relatively unstable.[110,250] The stability of the acid $H_8As_4Mo_{12}O_{50}$, obtained by cation exchange in the form of a dilute aqueous solution, is also low. It is a strong acid: the first four hydrogen atoms dissociate fully and a further four dissociate partially.[279]

Electrodialysis of a solution containing $NaAsO_2$ and Na_2WO_4 in molar proportions of 1:11 afforded a concentrated solution in which 50% of the tungsten was in the form of $H_7AsH_2W_{18}O_{60}$. However, this HPAC was not isolated in the solid state and its properties were not investigated.[142]

The heteropolyanions $XP_5W_{30}O_{110}^{x-}$ are stable in strongly acid (6 M HCl) aqueous solutions,[280] which suggests the existence of the corresponding HPAC. However, such HPAC were not specially isolated and investigated.

As already mentioned above, there are a series of HPAC about which it is only known that they exist. As regards the type of their behaviour, one may postulate that these mixed Mo–V and W–V HPAC have the Keggin structure. However, another structure of these acids is also possible. It has been suggested (but not demonstrated) that the S–W–V HPAC has a structure analogous to that of P_2W_{20}.[144] According to ^1H NMR data, all its protons are hydrated,[260] i.e. it is a fairly strong acid.

Heteropolyacids containing an X heteroatom with a lone pair (Se^{4+}, Te^{4+}, Sb^{3+}, As^{3+}) cannot have the Keggin structure (attributed to them previously) by virtue of the coordination structure of the XO_n polyhedron (usually a trigonal pyramid). HPA with the following structures are known for them: $X_2W_{21}O_{69}^{6-}$, $H_2XW_{18}O_{60}^{7-}$, $X_4W_{40}O_{140}^{29-}$, and $X_9W_{21}O_{86}^{19-}$. Probably the HPAC synthesised with such heteroatoms have one of the structures presented above or they are mixtures of HPAC with similar structures. All these HPAC are strong acids[173,263,281] with moderate thermal stability (up to 200 °C), but some of their protons are retained up to 500 °C.[170]

HPAC containing Te^{6+} are strong acids.[264]

The structures of the corresponding Keggin HPAC have been attributed to the acids synthesised in the presence of HF.[267] However, experience gained in a number of investigations[126,251,255] has shown that it is impossible to ignore the influence of F^- on the structure of the HPA and to reduce the effect of HF to the simple effect of an acid. Two versions of the synthesis of such HPAC are known: from the metatungstate[126] or from NaF_6W_{18}.[251] In terms of the conditions in their synthesis,[267] the second version is more probable, but this naturally requires confirmation.

The existence of certain HPAC, indicated in the literature, may be questioned. Thus the HPAC with a Mo : Ce ratio less than 12 were already mentioned. It is known that the Ce^{4+} ion does not form with tungsten HPA having the Dexter–Silverton structure,[1] so that there is also no corresponding CeW_{12} HPAC. The HPAC containing W^{6+} and Ce^{3+} or Ce^{4+} do not exist in a strongly acid medium.[1,142] This can also be said about the HPAC $UThW_{18}$. The heteropolyanion SiW_{11} is a precursor of the acid SiW_{12} and does not exist in the form of a free acid.[1]

Among the isopolyacids, only the Mo^{6+} acids are known in solutions. When the solutions are acidified, cation exchange or electrodialysis affords solutions which are stable for 24 h.[142] It has been suggested that molybdenum is present in these acids in the form of β-Mo_8[252] or Mo_{36}.[253] Such solutions are suitable for the synthesis of MoO_3 or deposited MoO_3/SiO_2 catalysts.[252]

4. Methods of synthesis of heteropolyacids

Several methods of synthesis of HPAC are known. The most general of these involves the acidification of a solution of a mixture of the initial reactants.[1,3,110,139,250]

$$Na_2WO_4 + H_3PO_4 \xrightarrow{H^+} H_3PW_{12}O_{40}$$

$$Na_2WO_4 \xrightarrow{HF} H_{6-n}H_2W_{12}O_{40-n}F_n$$

$$Na_2MoO_4 + Cr(NO_3)_3 \xrightarrow{H^+} H_9CrMo_6O_{24}$$

$$Na_2MoO_4 + NaVO_3 + H_3PO_4 \xrightarrow{H^+} H_{3+n}PMo_{12-n}V_nO_{40}$$

The reaction by no means takes place smoothly in all cases and in conformity with the stoichiometry. Sometimes an excess of the heteroatom is needed (for example, $X = B^{3+}$ or Si^{4+} in the synthesis of XW_{12} or $X = P^{5+}$ or As^{5+} in the synthesis of X_2W_{18}), or the appropriate temperature must be maintained (low for relatively unstable HPAC or actual refluxing for X_2W_{18}), or a definite order of mixing of the reactants is required. If the component containing X is sparingly soluble, special measures must be adopted to transfer it to the solution.[267]

Acidification can be achieved in several ways. The commonest way involves the use of an inorganic acid (usually HCl or H_2SO_4), after which the HPAC is isolated from the solution of the salts by extraction with ether.[1,3,110,250] However, this method of isolation has numerous disadvantages: a narrow range of extractable HPAC (Keggin and Dawson HPAC and HPAC of the type X_2W_{21} and NaF_6W_{18}), among which compounds with low stabilities may decompose during extraction as a result of the very high acidity of the solution, the nonquantitative yield of the HPAC (for example, not more than 80% for PW_{12}[282] and in reality the yield is even less), fire risk, the need to employ an extraneous reagent, a large amount of waste water produced, corrosion of the equipment, and contamination of the products by the inorganic acid. There is also an advantage: the possibility of removing from the HPAC the impurities which are not

extractable by ether (for example unsaturated HPAC) or of separating mixtures of HPAC extractable under the conditions of different acidities. Despite the disadvantages, the method has been used hitherto in industry to synthesise PW_{12} and SiW_{12} and also in laboratory practice.

In another procedure, acidification is carried out by cation-exchange resins.[3,110,250] Almost all the known HPAC can be obtained with its aid. This method can be regarded as the most universal among all those known. It also has its disadvantages and advantages. The former include the need to regenerate the resins, which leads to waste water, and the need to concentrate dilute solutions of the HPAC; the latter include the absence of corrosion, a very high yield of the HPAC (100% with respect to W or Mo), universality, the 'softness' of the acidification, and a high degree of purification as regards cations. The Dexter–Silverton heteropolyacids can be obtained only in this way, since ion exchange makes it possible to remove the cations even from sparingly soluble HPAC salts. After the cation exchange, dilute solutions of the HPAC are obtained, from which the product is isolated either by evaporation or by salting out with an acid.[283] A combination of two methods is also possible — acidification by an acid and ion-exchange resins.[284,285]

The third acidification procedure, the most progressive one, is electrochemical acidification. It consists in the electrochemical removal of the cations from the initial solution and compensating for them with protons. The process is carried out in flow-type electrodialysers (when all the components are in solution) or dialysers of the nonflow type (solutions with precipitates, as in the synthesis of SiW_{12}).[286] The anodic compartment contains a solution of the initial components, while the cathodic compartment contains a solution of alkali. The compartments are separated by a membrane based on a cation-exchange resin. When a current is passed through the apparatus, the cations pass through the membrane into the cathodic compartment and the anolyte is acidified.

Compounds containing tungsten, molybdenum, and heteroanions are incapable of passing through the membrane. On acidification of the anolyte, they interact, forming the HPAC. The alkali accumulates in the catholyte and can be used again to prepare the initial solution. The only side products of the synthesis are gaseous H_2 and O_2, formed as a result of the decomposition of water at the electrodes. The advantages of this method include a high yield of the HPAC (100% with respect to W and Mo), the absence of solid and liquid waste, and the possibility of doing without extraneous reagents. The disadvantages are the use of special equipment, including dangerous equipment (powerful current sources), the need for the additional removal of impurities from the HPAC (for example the excess of X or impurity HPAC), and the need to follow the concentration of the cation in the anolyte. However, the principal advantages of the method — the high yield of the HPAC and the absence of waste — make up for the above disadvantages and therefore the method is being developed actively at the present time.

Almost all the known most important HPAC such as SiW_{12},[286,287] BW_{12} (with additional purification by extraction with ether),[288] PW_{12},[282,289] P_2W_{21},[242] P_2Mo_{18}, α-P_2W_{18}, PMo_6W_6, $CoMo_6$, $PMo_{12-n}V_n$, $PW_{12-n}V_n$, and $PW_{12-n}Nb_n$ ($n = 1, 2$),[142] as well as new HPAC such as $PW_{11}Ti$, $PW_{11}Zr$, $PW_{11}Bi$, $PW_{11}Ce$, and $(PW_{11})_2Ce$[143] have been obtained by the electrodialysis method. A mixture of HPAC, 90% of which comprised $As_2^{3+}W_{21}$ and $H_2As^{3+}W_{18}$, has been obtained in a system containing As^{3+} and W^{6+}. Assessment of the possibilities of electrodialysis led to the conclusion that this method is suitable for the synthesis of HPAC stable in the form of concentrated aqueous solutions. On the basis of this principle, it proved impossible to obtain HPAC of the type β-P_2W_{18}, NaP_5W_{30}, and many others. The limitations of the methods have also been noted. Thus, owing to the chemical processes on slow electrochemical acidification, it is impossible to obtain PMo_{12}. Solutions of certain HPAC (for example, those containing Cr^{3+}) have a high electrical resistance, which prevents cation exchange through the membrane.[142]

Apart from the synthesis of HPAC, electrodialysis is used to obtain H_2WO_4 with an increased purity[290] and metatungstate salts.[291–295] The creation of an industrial electrodialyser with an output of 50–70 tonnes of tungsten per year and an overall membrane area of 2.5 m^2 has been reported.[297]

We may mention yet another (obsolete) acidification method — the method involving the decomposition of salts,[3,110] for example in accordance with the reactions[3]

$$Ba_3H_2W_{12}O_{40} + 3\,H_2SO_4 \longrightarrow 3\,BaSO_4 + H_6H_2W_{12}O_{40},$$

$$Hg_5BW_{12}O_{40} + 5\,HCl \longrightarrow 5\,HgCl + H_5BW_{12}O_{40}.$$

The initial HPAC salts were obtained in their turn with the aid of inorganic acids. Thus this procedure is a modification of the method involving the acidification of the initial solutions by inorganic acids. Previously this method has a preparative value, but nowadays it has lost it.

The method of synthesis of HPAC next in importance involves the interaction of simple oxides (oxides or acids). Thus phosphomolybdic acids can be obtained from H_3PO_4 and $MoO_3(H_2MoO_4)$.

$$MoO_3 + H_3PO_4 \longrightarrow PMo_{12} \text{ (or } P_2Mo_{18})$$

The composition of the product depends on the reaction conditions: reactant ratio, temperature, and reaction time. For the molar ratio Mo : P = 12, approximately 70% of the molybdenum dissolves in the form of PMo_{12} after refluxing for 3–5 h. After evaporation, the product is isolated in the solid state, but it has to be recrystallised in order to remove the excess H_3PO_4. The best version of the synthesis of PMo_{12} involves the use of a fourfold excess of molybdenum. In this case, the pure acid PMo_{12} is formed immediately, while the excess molybdenum is used for the succeeding cycles of the synthesis. After refluxing with an excess of H_3PO_4 (the optimum ratio is Mo : P = 3) and allowing the mixture to stand for 15–17 days at 20 °C, P_2Mo_{18} is formed. It is best to use MoO_3, since H_2MoO_4 is usually contaminated by ammonia.[3] For the ratio Mo : P = 12, it is possible to attain the complete dissolution of MoO_3 with formation of pure PMo_{12}, provided that one adds to the solution an organic solvent (for example *tert*-butyl alcohol) or a reductant until the attainment of the degree of reduction corresponding to PMo_{12} (4 $\bar{e}$) with subsequent reoxidation.[296] For the ratio Mo : P < 12, mixtures of the HPAC P_2Mo_{18}, PMo_{12}, PMo_{11}, and PMo_9 are obtained[3,197] and the attempt to increase the yield of PMo_{12} by employing an excess of H_3PO_4 (75%–100%) in the synthesis[297] must therefore be recognised as unsuccessful. If the MoO_3 is subjected to preliminary mechanochemical activation, the time required for its dissolution is shortened to several minutes even without using an excess of H_3PO_4 (as happens, for example, in the synthesis of P_2Mo_{18}).[298]

For catalytic purposes it is not always important which of the P–Mo HPAC is present in the solution, since they are all strong acids. Simple dissolution of MoO_3 in a solution with H_3PO_4 (this is achieved using the ratio Mo : Po $\approx$ 6) is sometimes sufficient to obtain an active catalyst.[293,300]

Certain vanadium-containing HPAC can be obtained in the same way. Thus $PMo_{11}V$ is synthesised in a quantitative yield by refluxing a suspension of MoO_3 and V_2O_5 in H_3PO_4 solution with stoichiometric reactant ratios for 5–6 h.[301,302] The heteropolyacid $PMo_{10}V_2$ is more difficult to synthesise: an excess of V_2O_5 and a time of the order of 20 days are required. If hydrothermal conditions are employed, the process is accelerated and in this case it is actually possible to introduce

tungsten into the HPAC.[302] The duration of the synthesis of $PMo_{12-n}V_n$ ($n = 1-6$) is reduced to 1–2 days if V_2O_5 is dissolved beforehand in a dilute solution of H_2O_2 at a low temperature and with the molar ratio $H_2O_2 : V_2O_5 = 1.5-40$.[303]

After a suspension of MoO_3 has been refluxed in a Na_3AsO_4 solution, a solution of the sodium salt of As_2Mo_{18} is formed, from which the HPAC can be isolated by extraction with ether or by cation exchange.[3,250] The heteropolyacids $H_3AsMo_3O_{13}$ and $V_2O_5.I_2O_5$ with hitherto unknown structures have been synthesised by interaction in solutions of oxides or acids.[3]

In the synthesis of tungsten-containing HPAC, the method considered involves considerable difficulties. The reactivities of the initial reactants H_2WO_4 and WO_3 are very low and these compounds hardly dissolve in acid solutions. Only H_2WO_4 freshly precipitated at a temperature below 50 °C reacts with H_3PO_4, affording a yield of the HPAC up to 92%.[3] Apart from PW_{12}, other P–W HPAC are formed under these conditions. These as well as other impurities have to be removed by extraction with ether.[304] The method of synthesis via molybdenum or tungsten halides is a variety of this method. The halides hydrolyse rapidly with formation of molybdenum and tungsten oxy-acids, which immediately react with the heteroatom.[268]

Thus the method of synthesis of HPAC from the initial acids and oxides has limitations associated with the low solubilities or reactivities of the initial compounds. Realistically, one can obtain with its aid only certain HPAC containing molybdenum and vanadium, whereas for the purposes of acid catalysis tungsten-containing HPAC are of greatest interest. In order to facilitate the synthesis or reduce the amount of waste, it is possible to use a combination of methods. For example, WO_3, MoO_3, and V_2O_5 may be dissolved in solutions of Na_2WO_4, Na_2MoO_4, or $NaVO_3$ and the latter can then be acidified by some method.[142] Another application of this procedure involves the synthesis of HPAC/carrier catalysts by forming the HPAC directly on the surface of the carrier.[305,306]

The third method of synthesis of the HPAC, which can be regarded as general, involves their preparation via other HPA or IPA.[1] This method is almost always used in the synthesis of complex HPAC, where the starting materials are unsaturated HPA.[1,142,143]

$$SiW_{11} + Z^{x+} \xrightarrow{H^+} SiW_{11}Z$$

$$PW_{11} + Z^{x+} \xrightarrow{H^+} (PW_{11})_2Z$$

$$P_2W_{17} + Z^{x+} \xrightarrow{H^+} P_2W_{17}Z$$

Bearing in mind the enormous diversity of the ions Z, the unsaturated HPA, and their combinations, there is no doubt that a multiplicity of new HPAC can be obtained by this procedure.

The unsaturated heteropolyanion PW_{11} serves as a source for the synthesis of the acid P_2W_{21}.[242,289] Vanadium-containing HPAC can be conveniently obtained from a simpler HPAC.[307]

$$PMo_{12} + V_2O_5 + H_3PO_4 \longrightarrow H_{3+n}PMo_{12-n}V_nO_{40}$$

$n = 1-3$

Keggin β-heteropolyacids can be readily obtained by reducing (4 $\bar{e}$) Keggin α-HPAC in solutions.[1,110,130,212] HPAC with a definite composition and definite positions of other atoms in the structure can be conveniently constructed from polyunsaturated HPA of the type of PMo_9.[136]

Various HPAC are frequently synthesised from tungsten, molybdenum, and niobium isopolyanions. Almost all the HPAC with Anderson, Dexter–Silverton, and Keggin structures, in which a transition metal ion serves as the heteroatom, have been obtained in this way. In the synthesis, this ion must be retained in solution and, in order to achieve this, the latter must be acid. In such cases, the IPA is the most suitable source of ligands.

$$Mo_4O_{24}^{6-} + Cr^{3+} \xrightarrow{H^+} H_9CrMo_6O_{24}$$

$$H_2W_{12}O_{42}^{10-} + Zn^{2+} \xrightarrow{H^+} H_6ZnW_{12}O_{40}$$

$$H_2W_{12}O_{40}^{6-} + Ga^{3+} \xrightarrow{H^+} H_5GaW_{12}O_{40}$$

Under these conditions, it is also possible to employ isopolyacids as such.[266] In some cases, the use of IPA is particularly preferable. Thus, in order to avoid the formation of P_2W_{21} in the synthesis of PW_{12} by electrodialysis, the PO_4^{3-} anion should be added to the acidified solution only after the complete conversion of the WO_4^{2-} ion into the IPA.[289] The compound $K_7HNb_6O_{19}$ is the only convenient source of niobium in the synthesis of niobium-containing HPAC. The acids $H_2Ln_2XMo_{12}O_{42}$ are obtained from Dexter–Silverton HPAC as such.[249]

Finally, mention should be made of a specific method of synthesis of the HPAC CW_{12} and of its peroxo-analogue by dissolving WC_2 in H_2O_2.[118,119,164]

A method of synthesis of HPAC by the heat treatment of their ammonium or tetraalkylammonium salts may be encountered in certain patents.[181,308,309] However, on thermal elimination of the ammonium cations, the structure of the HPA is disrupted. Such methods may be regarded as methods of synthesis of catalysts whose compositions correspond to those of the initial HPA salts but not the HPAC.

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Adsorption of mixtures of polymers from dilute and semidilute solutions

Yu S Lipatov, T T Todosiichuk, V N Chornaya

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Abstract. Recent studies of adsorption from solutions of mixtures of polymers have been examined. The experimental results reveal an interrelation between the adsorption of polymers from a mixture, the thermodynamic compatibility of the components in solution, the change in the thermodynamic quality of the 'mixed solvent' (polymer + solvent), and the critical crossover concentration for each component (on the one hand) and the averaged critical concentration for the mixture. The influence of the aggregation of macromolecules in solutions of mixtures on the adsorption in the concentration regions above and below the critical concentration for the overlapping of macromolecular globules has been demonstrated. The bibliography includes 30 references.

I. Introduction

According to current views on the properties of solutions of polymers these solutions can be divided into dilute and semidilute.[1] In a dilute solution the macromolecular globules are separated in space, but when the critical concentration c^* (and therefore the critical volume fraction of polymer φ) is reached the globules begin to come into contact and they overlap. The concentration region in which the globules overlap (the cross-over region) corresponds to the local concentration within the globule, giving a solution concentration $\varphi^* < \varphi < 1$. The overlapping is accompanied by a compression of the globules and by a decrease in their size. The critical concentration c^* is determined by the molecular mass of the polymer and by the thermodynamic quality of the solvent. Various theoretical models have been proposed to determine the concentration c^*: according to them this quantity is inversely proportional to the characteristic viscosity $[\eta]$, and the proportionality coefficient depends on the model chosen for the interaction of the globules.[2–6]

Many published data show that macromolecular associations or aggregates with a long average lifetime can be formed in solutions of polymers, depending on their concentration and on the thermodynamic quality of the solvent.[7,8] The size of the aggregates is also determined by the molecular mass and by the nature of the solvent. In solutions of any concentration we find a mobile equilibrium between the aggregated and the free macromolecules. From the standpoint of classifying the solutions into dilute and semidilute it is evident that the aggregation processes should begin in a dilute solution and stop at the transition to a semidilute solution, where all the macromolecules overlap and create a network.

In a series of studies in our laboratory[7,9] the conditions for the formation of aggregates, their size, and number per unit volume have been determined. Comparing these data with the results of adsorption studies (from solutions) led to the formulation of the concept of aggregative adsorption.[10,11] Essentially this concept states that in an appropriate concentration region of the solution, in which macromolecular aggregates are formed, both aggregated and nonaggregated macromolecules are simultaneously transferred to the adsorbent surface during adsorption, but the transfer of the molecular aggregates is energetically more favourable. As a result there are almost no aggregates in the solution over the adsorbent after the adsorption equilibrium has been established, but after some time their equilibrium concentration in the solution is re-established.

The aggregative adsorption mechanism has provided an explanation for several experimental data which did not fit the traditional description of adsorption from dilute solutions,[12,13] such as large adsorptions, well in excess of the calculated monolayer value, with a relatively small proportion of segments bound to the surface, an inversion of the effect of the thermodynamic quality of the solvent on the adsorption following changes in concentration, a dependence of the adsorption on the adsorbent : solution ratio, etc.[7] In the aggregative adsorption mechanism the large difference between the adsorption of polymers and the adsorption of species of low molecular mass is stressed.[10] In the adsorption of polymeric molecules not only the conformation of the adsorbed molecules but also the size and number of the macromolecular aggregates depend on the concentration of the solution, so that at different points of the adsorption isotherm we are dealing with different ratios of these species in the solution. From this point of view it is interesting to consider the adsorption of mixtures of polymers from dilute and from semidilute solutions, in which the aggregation conditions of polymer molecules of each kind should be different. It may be assumed that the adsorption of a mixture of polymers from a common solvent is affected by their thermodynamic compatibility (or noncompatibility) in the solution, defined by the thermodynamic polymer–polymer interaction parameter.

Yu S Lipatov, T T Todosiichuk, V N Chornaya Institute for the Chemistry of High-molecular-mass Compounds, National Academy of Sciences of the Ukraine, Khar'kovskoe shosse 48, 253160 Kiev, Ukraine. Fax (7-044)552 40 60

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A large group of experimental data on the adsorption of mixtures of polymers is now available.[14-19] In most cases a marked selectivity of the adsorption of one of the components is observed in the adsorption from a mixture. When this effect was first reported[14-16] it seemed reasonable to assume that a noncompatible pair of polymers in solution would also show a more marked segregation of identical macromolecules, i.e. a more marked aggregation. This effect should depend on the overall concentration of the components in solution, on the concentration ratios, and on the concentration of each component (with respect to the remoteness from or closeness to the crossover region for the given polymer).

An analysis of all the available data showed that the adsorption of polymers should be examined from the following standpoints. A solution of a mixture of two polymers in a common solvent can be described as a solution of the polymer A in a solution of the polymer B in the same solvent, and also as a solution of the polymer B in a solution of the polymer A. In this case the thermodynamic quality of the 'mixed' solvent (solvent + polymer) for each polymer will be different from the quality of the pure solvent. The adsorption of each polymer will depend on the influence of the other polymer on the thermodynamic quality of the 'mixed' solvent. Thus the adsorption of each component will be determined not only by the affinity of that component for the surface but also by the ratio of the components. However, this simple and self-evident conclusion introduces serious difficulties in the analysis of the adsorption of mixtures if the analysis is attempted in the classical approach to the determination of the adsorption isotherms.

In the experimental method originally used to study adsorption from mixtures the concentration of the solution was assumed to remain constant, the only variable being the ratio of the dissolved components.[14] This method can give information on the preferential adsorption of the various polymers as a function of the presence of the other. However, it is not a strict method, since each change in the ratio of the components in solution produces a change in the thermodynamic quality of the 'mixed' solvent for each component, i.e. the adsorption conditions were not identical for mixtures of different composition.

There is also a second experimental method in which the concentration of one component only is varied in the solution of the mixture, whereas the concentration of the other component is kept constant. In this case we can construct the adsorption isotherm for the component of variable concentration. This experimental scheme is simply equivalent to studying the adsorption of the given component from solvents of different thermodynamic quality, and therefore it does not readily detect the specific aspects of the adsorption of mixtures if the system displays specific adsorption.

The third method (a continuous increase in the concentration of the solution, as in the classical method of constructing the isotherm) involves adding to the solution the two components in constant relative amounts. However, even this method cannot be called strict, as in this case we have a simultaneous adsorption of the two components in different proportions (depending on their relative adsorbability), and under these conditions each component is adsorbed from a solvent of thermodnamic quality appropriate for that component.

We know of no other method of studying the adsorption of mixtures of polymers. The most important aspect of the adsorption of a mixture of polymers is that it cannot be studied in the classical variant of the construction of adsorption isotherms: the specific features of the adsorption of mixtures are in fact determined by the difference and variability of the thermodynamic quality of the solvent for each component. Thus it is impossible to formulate a 'pure' experiment on the selectivity of the adsorption, since it is impossible to ensure that the solvent has the same thermodynamic quality for each of the polymers. The only way to design a 'pure' experiment is to examine the adsorption of the components from a melt of the two polymers, in the absence of a solvent. We have attempted a study of this type,[20] but even this was not a strictly adsorption-determined experiment.

If the discussion of the adsorption of mixtures is approached from the standpoint of dilute and semidilute solutions it becomes obvious that the aggregation and adsorption conditions should depend on the critical concentration for the overlapping of the macromolecular globules in the mixture, i.e. on the concentration region in which the contact and the overlapping of the globules of different polymers sets in. Obviously, under these conditions we cannot use the c^* values for the different components in the solvent, since in a solution of the mixture the thermodynamic quality of the 'mixed' solvent differs from the quality of the pure solvent and depends on the concentration and on the concentration ratio of the components.

II. Critical concentrations for solutions of polymer mixtures

The theory of solutions of mixed polymers from the point of view of their hydrodynamic properties is still not fully developed. Two approaches to the calculation of the critical concentrations in mixtures are possible.

Table 1. Critical concentrations of polymers in solutions of mixtures, determined by the expression $c^* = 1/[\eta]$.

A. PS–PBMA–CCl_4 system.			B. PC–PCL–$CHCl_3$ system		
c/g (100 ml)$^{-1}$ [a]	$[\eta]$/100 ml g^{-1}	c^*/g (100 ml)$^{-1}$	c/g (100 ml)$^{-1}$ [a]	$[\eta]$/100 ml g^{-1}	c^*/g (100 ml)$^{-1}$
PBMA–'mixed' solvent (PS–CCl_4)			PC–'mixed' solvent (PCL–$CHCl_3$)		
0	0.95	1.05	0	0.45	2.20
0.5	0.60	1.66	1.0	0.45	2.20
1.0	0.50	2.00	2.0	0.35	2.86
1.5	0.44	2.27	3.0	0.27	3.70
2.0	0.34	2.94	4.0	0.19	4.50
3.0	0.30	3.33	6.0	0.20	5.00
PS–'mixed' solvent (PBMA–CCl_4)			PCL–'mixed' solvent (PC–$CHCl_3$)		
0	1.10	0.90	0	0.090	11.1
0.25	0.90	1.11	0.5	0.075	13.3
0.50	0.80	1.25	1.0	0.065	15.4
1.00	0.75	1.33	1.5	0.050	20.0
1.50	0.50	2.00	2.0	0.045	22.0
2.00	0.40	2.50	2.5	0.040	25.0

Notes. The following symbols are used: PS polystyrene; PBMA polybutylmethacrylate; PC polycarbonate; PCL polycaprolactone.
[a] Concentration of mixed solvent.

The first uses well known relationships for determining c^*, but the characteristic viscosity of one of the components of the mixture is calculated in the presence of the second polymer, taken in a known proportion. We carried out these calculations for a series of polymer pairs, using their adsorption data given below. The critical concentration for the overlapping of the macromolecular globules was determined by the expression $c^* = 1/[\eta]$, where the characteristic viscosity was found by the standard method using an Ubbelohde viscometer. The special feature of the determination of the critical concentration in a polymer mixture in this approach is the use of a 'mixed' solvent. As can be seen from the data in Table 1 an increase in the concentration of the 'mixed' solvent produces a fall in $[\eta]$, and therefore also an increase in c^* for the given polymer. These data also show a worsening of the thermodynamic quality of the 'mixed' solvent (as compared with the pure solvent) for both the polymers in solution. Therefore the c^* values for the pure solvents cannot be used to study the adsorption of the components of a mixture in the concentration regions below and above the crossover. In all the three experimental methods of determining the adsorption considered above the component ratio in solution is not constant, and therefore the critical concentration of each of the components in the presence of the other determined in this way is also not constant. We consider this approach to be unacceptable also because the c^* values are determined without allowing for the fact that the bulk of the solution is filled with globules of two kinds, and that each kind is 'unaware' of the other. The region of uniform filling of the bulk by globules of two kinds will be in a different concentration region, defined by the size of the globules of each of the components and by their concentration in the solution.

Therefore we shall use an 'averaged' critical concentration for the mixture, determined from the 'averaged' characteristic viscosity. In contrast to the approach previously developed[21,22] we propose the following expression for the 'averaged' characteristic viscosity:

$$[\eta]_m = [\eta]_A\varphi_A + [\eta]_B\varphi_B \ , \qquad (1)$$

where φ_A and φ_B are the volume fractions of the components in their mixture, with $\varphi_A + \varphi_B = 1$.

Thus, for a mixture of the macromolecules A and B (and irrespectively of their thermodynamic compatibility) the crossover region should be reached by each of the polymers at concentrations below c_A^* or c_B^* because the bulk of the solution is already occupied by globules of molecules of kind A and B. We assume that $c_m^* = 1/[\eta]_m$. In that case the averaged crossover concentration is a function of the concentration ratio of dissolved molecules of kinds A and B.

The critical concentrations and the characteristic viscosities for a range of pairs and for their constituent components in a common solvent are shown in Tables 2 and 3. We have studied the adsorption of these same pairs. The PS–PBMA and PS–polydimethylsiloxane (PDMS) system are thermodynamically incompatible in solution, whereas the PC–PCL pair is compatible in the solvents which we have chosen.

An analysis of the data in Tables 2 and 3 shows that in the PS–PBMA system with similar c^* values for the two components

Table 2. Critical concentration and critical viscosity in the polymer–solvent system.

System	$[\eta]$/100 ml g^{-1}	c^*/g (100 ml)$^{-1}$
PS–CCl_4	1.13	0.88
PBMA–CCl_4	0.96	1.04
PCL–$CHCl_3$	0.09	11.10
PC–$CHCl_3$	0.45	2.20
PC–$CH_3COOC_2H_5$	0.46	2.20
PDMS–$CH_3COOC_2H_5$	0.11	9.00

Table 3. Characteristic viscosities of the mixture $[\eta]$ (in 100 ml g^{-1}) and critical concentrations [in g (100 ml)$^{-1}$] of polymers in solutions of mixtures determined from the 'averaged' characteristic viscosity.

c_A^*	$[\eta]_m$	c_m^*	c_B^*	c_A^*	$[\eta]_m$	c_m^*	c_B^*
PS–PBMA–CCl_4 system							
0.5	0.99	1.01	2.5	2.0	1.07	0.93	1.0
1.0	1.02	0.98	2.0	2.5	1.10	0.90	0.5
1.5	1.05	0.95	1.5				
PCL–PC–$CHCl_3$ system							
1.0	0.41	2.4	9.0	6.0	0.22	4.5	4.0
2.0	0.38	2.7	8.0	7.0	0.19	5.3	3.0
3.0	0.34	2.9	7.0	8.0	0.16	6.2	2.0
4.0	0.31	3.2	6.0	9.0	0.13	7.7	1.0
5.0	0.27	3.7	5.0				
PS–PDMS–$CH_3COOC_2H_5$ system							
0.5	0.28	3.6	0.5	2.0	0.34	2.9	1.0
1.0	0.34	2.9	0.5	2.5	0.35	2.8	1.0
1.5	0.37	2.7	0.5	0.5	0.13	7.7	9.0
2.0	0.38	2.6	0.5	1.0	0.14	7.1	9.0
2.5	0.40	2.5	0.5	1.5	0.155	6.45	9.0
0.5	0.22	4.5	1.0	2.0	0.17	5.9	9.0
1.0	0.28	3.6	1.0	2.5	0.18	5.5	9.0
1.5	0.31	3.2	1.0				
PDMS–PS–$CH_3COOC_2H_5$ system							
2.0	0.175	5.7	0.5	14.0	0.132	7.6	1.0
6.0	0.13	7.5	0.5	18.0	0.130	7.8	1.0
10.0	0.125	7.9	0.5	2.0	0.30	3.4	2.5
14.0	0.12	8.3	0.5	6.0	0.21	4.8	2.5
18.0	0.119	8.4	0.5	10.0	0.18	5.7	2.5
2.0	0.220	4.5	1.0	14.0	0.16	6.2	2.5
6.0	0.160	6.4	1.0	18.0	0.15	6.7	2.5
10.0	0.139	7.2	1.0				

the parameter c_m^* is weakly dependent on the ratio of the components in solution. On the other hand for the PC–PCL system we observe a marked increase in c_m^* with increasing concentration of PCL, due mainly to the only moderately high molecular mass of PCL. In the PS–PDMS system with constant (but different) concentrations of PDMS the critical concentration of the mixture falls with increasing concentration of PS, but with a constant concentration of PS and a variable concentration of PDMS it increases. These results must be included in any analysis of the adsorption from mixtures in dilute and semidilute solutions.

III. Adsorption from solutions of mixtures

The experimental methods of determining the adsorption from mixtures used in our work have already been described.[18,19] In this section we present data on the adsorption on Aerosil of three pairs of polymers: PS–PBMA and PS–PDMS (incompatible in solution) and PC–PCL (compatible). The adsorption of PS–PBMA and PCL–PC mixtures was studied at constant concentrations of the mixture in solution and different component ratios, and the adsorption in the PS–PDMS system was studied at a constant concentration of one of the components and a variable concentration of the other.

1. The polydimethylsiloxane – polystyrene – ethyl acetate system

The dependence of the adsorption of PDMS from a mixture with PS in a common solvent at different constant concentrations of PS (above and below the c^* value for PS) is shown in Fig. 1 in A (adsorption) – c/c_m^* coordinates. As can be seen, in the crossover region and above c_m^* the adsorption decreases after going through a maximum, both in the adsorption of pure PDMS and in the adsorption from its mixtures containing different amounts of PS.

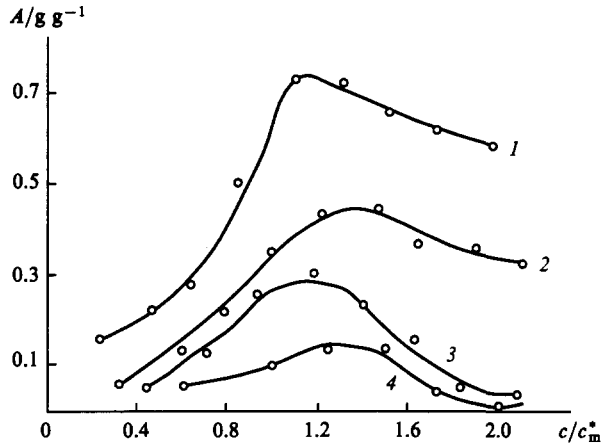


Figure 1. Dependence of the adsorption of PDMS from an individual solution (*1*) and from its mixtures with PS (*2–4*) in ethyl acetate on the concentration of PDMS for PS concentrations of 0.5 (*2*), 1.0 (*3*), and 2.5 (*4*) g(100 ml)$^{-1}$.

The absolute adsorption values are very large, suggesting aggregative adsorption. The same suggestion applies also to the decrease in adsorption at concentrations above c^*_m. As the concentration of PS in the solution is increased (thus worsening the thermodynamic quality of the 'mixed' solvent) the adsorption decreases but the maximum in the region of reduced concentrations greater than 1 is retained (above the crossover region). As has already been mentioned we ascribe this behaviour to the worsening of the quality of the solvent for PDMS, which by decreasing the size of the globules also decreases the size of the aggregates.

In Fig. 2 we show the corresponding data for PS, which indicate that in this case the effects discussed above are less marked (even though the aggregation of PS should be much greater because of its greater molecular mass, see below). The adsorption of PS is much lower, and almost independent of the concentration of PDMS, but an adsorption maximum is observed in the region of concentrations much lower than c^*_m. Obviously, in this case PDMS has a higher affinity for the adsorbent surface, and this produces a higher selectivity of the adsorption, promoted by noncompatibility with the PS.

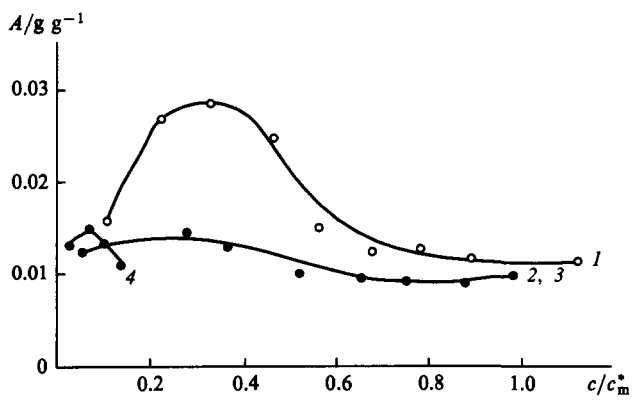


Figure 2. Dependence of the adsorption of PS from an individual solution (*1*) and from its mixtures with PDMS (*2–4*) in ethyl acetate on the concentration of PS for PDMS concentrations of 0.5 (*2*), 1.0 (*3*), and 9.0 (*4*) g (100 ml)$^{-1}$.

2. The polystyrene – polybutylmethacrylate – carbon tetrachloride system

The plots in Fig. 3 show that in the crossover region the adsorption of PS from a mixture with PBMA forms a broad maximum, whereas the adsorption of PBMA increases monotonically (Fig. 4). Under these conditions the adsorption of PS from the mixture is lower, and that of PBMA is higher than for the same adsorptions from a pure solvent. These results denote preferential adsorption from the mixture with PBMA. Evidently, in this case the noncompatibility of the components promotes the preferential adsorptions of one of the components under conditions in which the adsorption of the pure components from the common solvent are approximately equal.

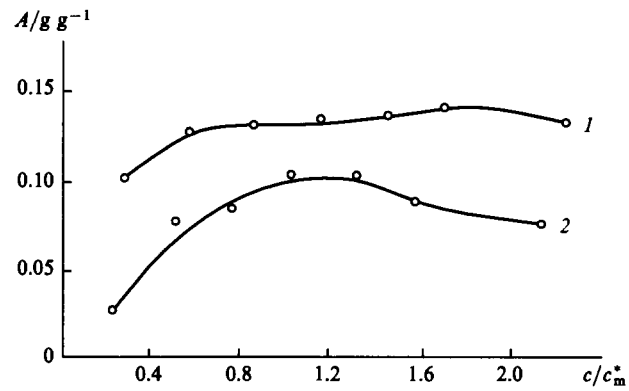


Figure 3. Dependence of the adsorption of PS from an individual solution (*1*) and of its mixture with PBMA (*2*) in carbon tetrachloride on the concentration of PS.

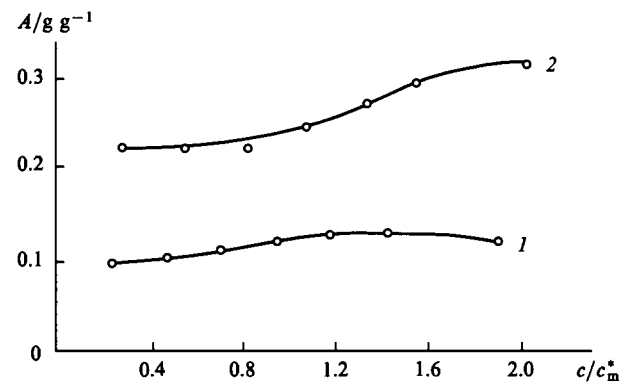


Figure 4. Dependence of the adsorption of PBMA from an individual solution (*1*) and from its mixture with PS (*2*) in carbon tetrachloride on the concentration of PBMA.

In Fig. 5 the data for this system are presented differently: in the form of a plot of the ratio of the adsorptions of the components against the concentration of the mixed solvent (the concentration of PBMA in solution is plotted horizontally) while keeping the overall concentration of the solution constant at 3 g (100 ml)$^{-1}$. It is clear from this figure that the PBMA is adsorbed preferentially at all component ratios in the solution. However, a minimum is found in the plot. A similar minimum occurs (Fig. 6) in the plot (obtained in our laboratory) of the second virial coefficient A_2 for the ternary PS – PBMA – solvent system. The concentration at which the minimum for this pair of polymers is seen coincides with the c^* value of each of the components (we note that these are not very different) and with c^*_m. After passing through c^*_m the ratio of the adsorptions increases again.

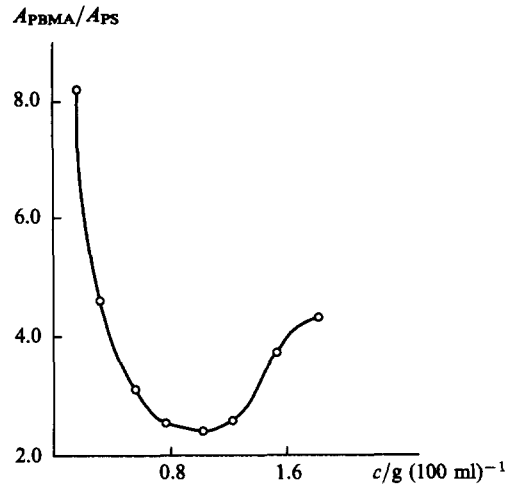


Figure 5. Dependence of the ratio of the adsorptions of PBMA and PS on the concentration of PBMA.

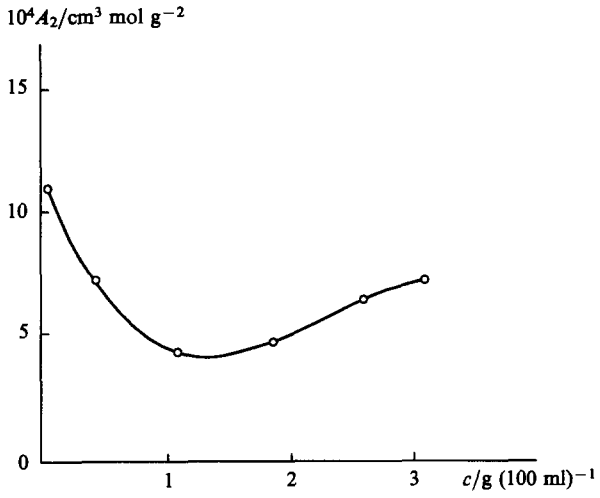


Figure 6. Dependence of the second virial coefficient A_2 on the concentration of the 'mixed' solvent for the PS–'mixed' solvent (PBMA–CCl_4) system.

Comparing Figs 5 and 6 shows the important role of the varying thermodynamic quality of the 'mixed' solvent in the adsorption from mixtures.

3. The polycaprolactone – polycarbonate – chloroform system

The adsorption of a compatible pair of polymers (polycaprolactone and polycarbonate) in a common solvent has been studied from a solution of constant concentration but variable composition. The dependence of the adsorption of PCL on c/c_m^* is shown in Fig. 7. For PCL we see a maximum in the crossover region. The adsorption of PCL is clearly predominant, in spite of its low molecular mass, and therefore the adsorption of PC begins only at high enough concentrations of this polymer in the mixture (Fig. 8), exceeding c^*. However, the adsorption of each of the components from the common solvent is higher than from the mixture: we attribute this effect to the thermodynamic compatibility of the components.

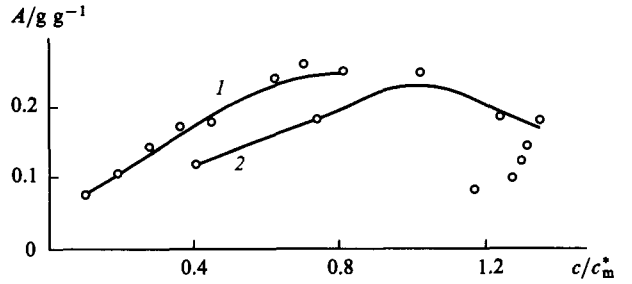


Figure 7. Dependence of the adsorption of PCL from an individual solution (*1*) and from its mixture with PS (*2*) in chloroform on the concentration of PCL.

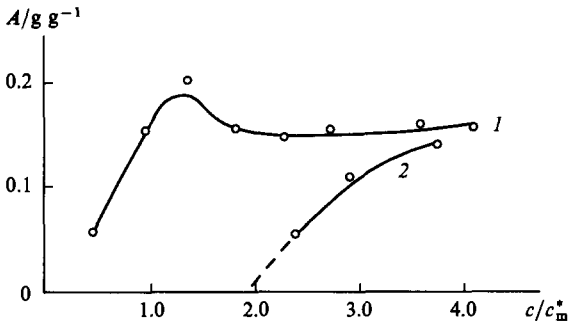


Figure 8. Dependence of the adsorption of PC from an individual solution (*1*) and from its mixture with PCL (*2*) in chloroform on the concentration of PC.

IV. Aggregation in solutions of macromolecules and in their mixtures

We shall now examine some experimental results on the formation of aggregates of these polymers in solution. In order to facilitate the comparison with the data on the adsorption of polymers discussed above these results were obtained by the turbidity spectrum method, which allows the size and number of aggregates to be determined from the spectral dependence of the intensity of light scattering in the visible region. The theoretical foundations of this method were laid by Heler and Pangonic[23] on the basis of the theory of Mie,[24] developed for isotropic spheres. We used a modification of this method.[25]

Data on the formation of aggregates in solutions of PS, PBMA, and PC are shown in Table 4 (see next page). Solutions of PDMS are transparent in the visible region of the spectrum. Aggregates of low-molcular PCL were also not detected, probably because of their small size (the turbidity spectrum method can be used to determine the size of aggregates above 200 Å).

An analysis of the results in Table 4 shows that in this polymer the formation of aggregates begins at concentrations below c^*, and also in the region above crossover. The size of the macromolecular aggregates usually increases with the concentration and depends on the temperature (but the temperature dependence of the adsorption has not been studied yet). However, the dependences on concentration and temperature are not unambiguous, because the quantities of interest are determined both by the change in the quality of the solvent with temperature and by the equilibrium constant of the reaction between aggregated and nonaggregated macromolecules, which is also temperature dependent. In different systems the size and number of the aggregates vary with temperature in different ways in the regions above and below c^*, and therefore it is difficult to identify any well defined trends in their changes.

Table 4. Size r (in Å) and number of macromolecular aggregates per unit volume N (in 10^{-9} cm^{-3}) as a function of the concentration of solution c [in g (100 ml)$^{-1}$] at 25 °C.

c	r	N	c	r	N
PS–CCl_4					
0.5	400	2.3	2.5	620	2.0
1.0	460	5.6	3.0	700	1.6
1.5	530	4.2	3.5	1400	0.1
2.0	590	2.6			
PBMA–CCl_4					
0.5	400	4.50	2.5	1900	0.08
1.0	700	1.30	3.0	2700	0.07
1.5	900	0.48	3.5	3300	0.01
2.0	1400	0.20			
PC–$CHCl_3$					
1.0	300	0.9	6.0	600	34.7
2.0	400	3.2	7.0	600	37.0
3.0	500	5.0	8.0	700	53.0
4.0	450	18.8	9.0	700	80.0
5.0	500	25.5	10.0	800	90.0
PS–$CH_3COOC_2H_5$					
0.25	1000	0.017	3.00	890	5.90
0.50	2000	0.08	5.00	890	6.88
1.00	3000	0.10	7.00	890	7.14
1.50	4000	0.27	8.00	900	7.64
2.00	800	4.40	10.00	890	7.90
2.50	850	5.04	12.00	700	9.80

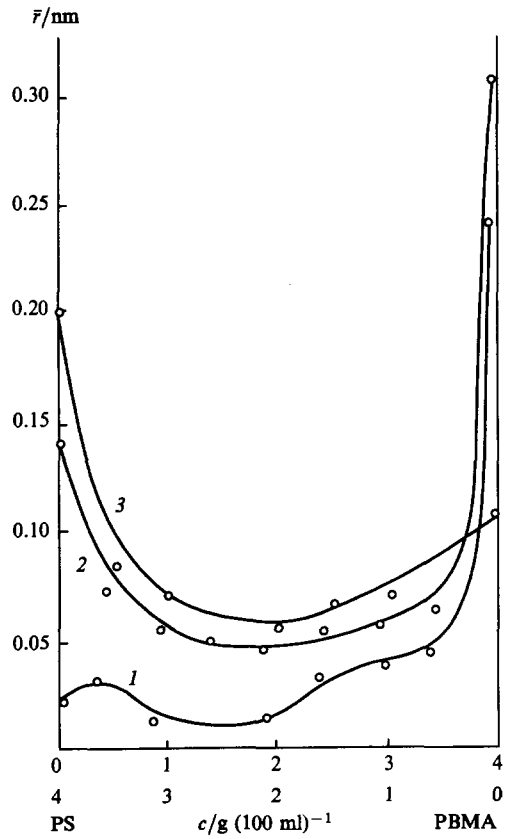


Figure 9. Dependence of the average size of the aggregates of macromolecules in a PS–PBMA–CCl_4 mixture on the composition of the 'mixed' solvent. T, °C: (*1*) 10; (*2*) 25; (*3*) 60.

However, it is obvious that aggregation processes take place also in solutions of mixtures, and that the trend towards aggregation of the molecules of each kind should be most marked when the thermodynamic compatibility of the components is low and the thermodynamic quality of the 'mixed' solvent is poor. In Fig. 9 we also show the averaged size of the aggregates of macromolecules in a PS–PBMA mixture as a function of the composition of the 'mixed' solvent [for an overall solution concentration of 3 g (100 ml)$^{-1}$]. As can be seen the presence of a 'second' polymer (incompatible with the 'first') leads to a marked decrease in the size of the aggregates as a result of the worsening of the thermodynamic quality of the solvent and of the possible collapse of the macromolecules.[26] This is consistent with the data on the characteristic viscosity of one of the components in the presence of the other. The decrease in size of the macromolecules may lead to a decrease in the average size of the aggregates in a solution of the mixture.

V. Conclusion

The experimental data quoted above show the existence of an interdependence between the adsorption of polymers from a mixture, the thermodynamic compatibility of the components in solution, the change in the thermodynamic quality of the 'mixed' solvent, and the critical crossover concentration for each component (on the one hand) and the mean critical concentration for the mixture. The influence of the aggregation of macromolecules in solutions of mixtures of polymers produced by the above factors on the adsorption in the concentration regions above and below c_m^* is also obvious. As a rule the adsorption decreases as the system goes through c_m^*: this may be due (among other reasons) to the fact that the size and number of the macromolecular aggregates which constitute the mixture of components also depend on c^* and are not identical in the regions below and above c^*. Since the formation of aggregates produces a change in the thermodynamic quality of the solvent it is obvious that the presence of a second component must alter the formation conditions of the aggregates by worsening the thermodynamic quality of the 'mixed' solvent (irrespectively of whether the given pair of polymers is compatible in solution).

The high adsorptions of both the individual components and their mixture can be explained only in terms of the aggregative adsorption mechanism: differences in the behaviour of the systems during adsorption in the region above or below the crossover can be attributed to changes in the aggregation conditions of macromolecules of different kind and different concentration regimes under conditions of continuously varying thermodynamic quality of the solvent. The passage through the crossover region produces changes in the structure of the solution as a result of the formation of a network of contacts and of the overlapping of the macromolecular globules. However, in reduced coordinates the passage through the crossover region often does not lead to significant changes in adsorption, i.e. the adsorption is not markedly affected by whether the system is close to or far from the crossover. Therefore the influence of regime of the mixed solution on the adsorption of its components can probably be identified from the dependence of A on c/c_m^*.

Thus the change in the thermodynamic quality of the solvent produced by the introduction of various quantities of a second polymer is mainly responsible for the behaviour of the adsorption from mixtures and for the selectivity of the adsorption of one of the components. Another factor which lack of space prevented us from discussing in the present review is the affinity of the components towards the adsorbent surface. This requires studies on different adsorbents. The simultaneous influence of various factors has so far prevented the development of a theory of adsorption from mixtures.

The theory of adsorption from mixtures is still in its first stage of development, in spite of the fact that the first papers on this topic were published 17 years ago. The number of

experimental data is small, and the number of variables to which the adsorption is sensitive is large: they include the molecular mass of the components,[27] the nature of the adsorbent,[29] and the interaction of the components in solution (the thermodynamic interaction parameter), and also the molecular mass distribution, the formation of aggregates in different regimes, the problems associated with their determination, etc.

However, since the structure of the adsorption layers of mixtures is determined by the conditions of adsorption from the mixtures, and since the adsorption layers play an important role in polymeric composite materials based on multicomponent polymer systems, the further study of the adsorption of mixtures and also the study of the structure of adsorption layers of mixtures[30] are of the greatest importance.

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'Smart' polymers in biotechnology and medicine

I Yu Galaev

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Abstract. **'Smart' water-soluble polymers and hydrogels are capable of responding reversibly to slight changes in the properties of the medium (pH, temperature, ionic strength, the presence of certain substances, illumination, electric field), the response of the system being readily seen with the naked eye (the formation of a new phase in a hitherto homogeneous solution, sudden swelling or contraction of the hydrogel). The properties of such polymers and hydrogels are examined. The use of 'smart' polymers and hydrogels for the concentration of protein solutions and the dehydration of suspensions, for the creation of membranes with a controllable permeability, for the isolation and purification of biomolecules, for the immobilisation of biocatalysts, and for the creation of sensor systems and systems for the controlled release of medicinal drugs is discussed. The bibliography includes 261 references.**

I. Introduction

In recent years, investigators have devoted much attention to the so called 'smart or intelligent materials'. Materials capable of responding to slight changes in the external medium in a preprogrammed manner are combined under this name.[1] A specialist journal has actually appeared, namely the *Journal of Intelligent Material Systems and Structures* (Technomic Publishing), in which data on this topic are published.

Among the water-soluble polymers and hydrogels, the term 'smart' may be applied to systems which respond reversibly to slight changes in the properties of the medium (pH, temperature, ionic strength, the presence of certain substances, illumination, electric field), the response of the system being readily visible with the naked eye (the formation of a new phase in a hitherto homogeneous solution, sudden swelling or contraction of the hydrogel).

Such systems are evidently attractive for biotechnology and medicine. They place in the hands of investigators a simple method for manipulating the system. Heating/cooling by several degrees or slight changes in the pH can be achieved rapidly and easily and this permits a reversible and repeated transition from a homogeneous to a heterogeneous system and an alteration by a factor of several tens of the degree of swelling of the hydrogels. Such systems have already found practical applications in the isolation and purification of biologically active substances and in the immobilisation of biocatalysts. They can be used for the controlled release of medicinal drugs, in biosensors, and for the modelling of regulation processes in the living cell associated with phase transitions in membranes.

All living organisms move by virtue of the isothermal conversion of chemical energy into mechanical work, expressed, for example, by the contraction of muscles and by the movement of the flagella or cilia of microorganisms. Hydrogels based on 'smart' polymers, capable of markedly swelling (expanding) or, conversely, contracting in response to external stimuli in the form of thermal, chemical, or electrical energy, may be used for the modelling of such systems. The history of the creation of the first systems of this kind in the 1950s is associated with names familiar in polymer chemistry such as those of Kuhn and Katchalsky.[2,3]

A micromotor or a flapping wing, a gel 'beetle' climbing an inclined slope, and a gel 'finger' bending and straightening out in air and not in solution as in most other cases, the motion of all of which was initiated by a gel, were demonstrated in the Section of Polymer Gels of the Congress of the Japanese Polymer Society held in December 1991 in Tsukuba.[4,5]

The aim of the present review was to draw the attention of chemists and biochemists to certain interesting and useful properties of 'smart' polymers and to stimulate, on the one hand, the use of such systems in biochemical and biotechnological research and, on the other, to stimulate the search for and synthesis of new homopolymers and copolymers with such properties.

II. 'Smart' polymers

For a polymer system to become 'smart', i.e. capable of responding strongly to slight changes in the external medium, a first-order phase transition, accompanied by a sharp decrease in the specific volume of the macromolecule, must occur in it. The theoretical foundations of such processes were laid by Flory.[6] One of the main conditions for the manifestation of critical phenomena in swollen polymer networks or linear macromolecules is the presence of a 'poor' solvent. In such a solvent, the forces of attraction between the segments of the polymer chain may overcome the repulsion forces associated with the excluded volume, which leads to the collapse of the polymer chain.

The three-dimensional structure of macromolecules is determined by four fundamental interactions: van der Waals forces, hydrophobic interactions, electrostatic interactions, and

I Yu Galaev Department of Biotechnology, The Chemical Centre, Lund University, P O Box 124, S-22 100 Lund, Sweden.
Fax (4-646) 10 47 13. Tel. (4-646) 10 82 56.
e-mail: Igor.Galaev@biotek.lu.se.

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hydrogen bonds. The electrostatic interactions between like charges of the polymer chain constitute the most effective repulsion forces. The osmotic pressure within a hydrogel, arising due to low-molecular-mass counterions, also promotes the swelling of hydrogels. Van der Waals forces, hydrophobic interactions, hydrogen bonds, and the interaction of ions of opposite sign constitute attraction forces and give rise to phase transitions in polymer solutions or to the collapse of hydrogels. The differences in the nature of the interactions inducing the phase transition are manifested to the greatest extent in the temperature dependence of the swelling or collapse of hydrogels.[7] If van der Waals forces (for example, the phase transition in a partly hydrolysed polyacrylamide gel in water–acetone mixtures)[8] or hydrogen bonds (for example, the phase transition in a gel consisting of interpenetrating networks of polyacrylamide and polyacrylic acid)[9] are responsible for the collapse of the hydrogel, then the hydrogel swells following an increase in temperature and contracts when it is reduced. On the other hand, if the collapse of the gel is induced by hydrophobic interactions (for example, the phase transition in the gel of the *N*-isopropylacrylamide–sodium acrylate copolymer)[10] or the interaction of ions of opposite sign [for example, the phase transition in the acrylamide–acrylate–(*N*-acryloyl-3-aminopropyl)trimethylammonium copolymer],[11] then the opposite temperature dependence is observed — the gel swells at a low temperature and contracts when the temperature is raised. In certain hydrophilic gels, for example in the acrylamide–sodium vinylsulfonate copolymer, there is a possibility of two phase transitions. In 65% acetone at low temperatures, the gel is in a state of collapse but begins to swell rapidly at temperatures above −10 °C. Up to 55 °C, the gel remains in its swollen state and then its collapse begins again.[12]

For highly hydrophilic ionogenic polymers, the solvent can become sufficiently poor as a result of the addition of an organic solvent to water. Critical phenomena (precipitation of the polymer from the solution or the collapse of the polymer gel) in the presence of 30%–70% acetone, 1-propanol, or ethanol have been observed for both synthetic polymers (copolymers comprising acrylamide and ionogenic comonomers)[11,13–16] and natural polymers (hyaluronic acid,[17] DNA,[18–20] gelatin,[20] agarose[20]).

For nonionogenic polymers, the solubility of which in water is determined by the formation of hydrogen bonds, water becomes a poorer solvent with increase in temperature. For example, when aqueous solutions of the homopolymers with ethylene oxide and its copolymers with propylene oxide are heated above the lower consolute temperature (LCT), the solution divides into two phases — the phase enriched in the polymer and the aqueous phase which contains hardly any polymers. On neutralisation of ionogenic groups, aqueous solutions of polyelectrolytes also divide into two layers on heating (for example, polymethacrylic acid at pH ~3 and temperatures > 50 °C).[21] As a rule, the LCT for such polymers is 60 °C and above (see, for example, Pandya et al.[22] and Louai et al.[23]), which is relatively unsuitable for biomolecules. However, such polymers can be used successfully to create reversibly soluble catalysts for homogeneous chemical reactions. Thus a homogeneous hydrogenation catalyst, which precipitates on heating to 50–60 °C, has been created on the basis of a block-copolymer of ethylene and propylene oxides (Pluronic) and a rhodium complex. After precipitation, the catalyst can be readily separated from the reaction mixture, dissolved at room temperature, and reused.[24]

For the appearance of critical phenomena in the systems described above, extreme conditions are necessary (a high concentration of the organic solvent, a high temperature, and low pH values), leading to the rapid denaturation of the biomolecules. For this reason, they have not so far found applications in biotechnology. However, the development of enzymology in nonaqueous media and of new methods for the immobilisation and stabilisation of biocatalysts may render such systems promising from the standpoint of biotechnology.

This review deals with polymers and hydrogels in which critical phenomena are observed in aqueous solutions at temperatures not exceeding 40–45 °C and at weakly acid or neutral pH values.

1. Polymers sensitive to changes in pH

Owing to the neutralisation of the charged macromolecule as a result of a change in the pH of the medium, water becomes a poor solvent for the neutral polymer molecule; a possibility of critical phenomena arises. As already mentioned above, for highly charged polyelectrolytes, such as polymethacrylic acid, critical phenomena occur at extreme pH values and temperatures. A decrease in the charge of the macromolecule and an increase in its hydrophobicity as a result of copolymerisation with hydrophobic comonomers make it possible to achieve critical phenomena within an acceptable pH range. For the copolymers of dimethylaminoethyl methacrylate with n-alkyl methacrylates, the collapse of the gels occurs at pH 6.0–6.5 at room temperature. With increase in the content of n-alkyl methacrylate in the gel, the difference between the volumes of the collapsed and swollen gels diminishes and the transition is observed at lower pH values. An increase in the length of the alkyl substituent in n-alkyl methacrylate also diminishes the difference between the volumes of the collapsed and swollen gels but does not exert a systematic influence on the pH of the transition.[25]

Aqueous solutions of methacrylic acid–methyl methacrylate copolymers and derivatives of cellulose which have been rendered hydrophobic [containing carboxy-groups (carboxymethylethylcellulose, cellulose acetate-phthalate, hydroxypropylmethylcellulose phthalate or acetate-succinate)], which are homogeneous at pH > 4 – 5.5, do not separate into aqueous and polymer phases on acidification[26] Such polymers are manufactured on an industrial scale and are widely used in the manufacture of medicinal drugs (Table 1). The shell surrounding a tablet comprising such polymers does not dissolve in the stomach at pH 1.4 and protects the drug against the harmful influence of the contents of the stomach. Having entered the intestine (pH 6.7–7.4), the shell of the tablet dissolves, which enables the drug to be rapidly assimilated into the blood. On the other hand, the copolymer of diethylaminoethyl methacrylate with methyl methacrylate and butyl methacrylate is insoluble at neutral pH values, but dissolves in an acid medium. The shell comprising this polymer protects the tablet against dissolution in the saliva and under these conditions the mouth is not affected by the unpleasant taste of bitter medicines.[27]

Table 2 presents the monomers used in pH-sensitive synthetic polymers and hydrogels. Monomers containing both weak acid or basic groups and strong acids or bases are used to create such systems. The pH-sensitive hydrogels are obtained by radical polymerisation in the presence of a cross-linking agent or by the chemical cross-linking of a water-soluble polymer with the aid of a bifunctional agent. By varying the composition of the monomers and the content of the cross-linking agent, it is possible to obtain hydrogels with various pH-sensitivities and degrees of swelling. The degree of swelling of a hydrogel, i.e. the response of the system to a change in the external conditions, depends mainly on the charge of the monomer, the pK of the ionogenic group, the degree of ionisation, the concentration of the ionic monomer in the polymer network, the degree of cross-linking of the hydrogel, and the pH and the ionic strength of the surrounding medium.[30]

Hydrogels containing acid groups swell in a weakly alkaline medium but collapse in an acid medium. On the other hand, hydrogels with basic groups swell in an acid medium but collapse on raising the pH. Polyampholytic hydrogels, obtained from comonomers one of which is soluble in an alkaline medium but insoluble in an acid medium (for example, methacrylic acid), while the other is actually soluble in an acid medium but insoluble in an alkaline medium [for example, 2-(*N*,*N*-dimethylamino)ethyl methacrylate], swell to the maximum extent at neutral pH values. When such gels are acidified or rendered alkaline, they undergo rapid dehydration.[34]

Table 1. Industrially manufactured polymers used in medicinal preparations.

Copolymer	Molecular mass	Ratio of carboxy- and ether groups	Trade name	Manufacturer	Country
Methacrylic acid–methyl methacrylate	135000	1:1	Eudragit L	Röhm Pharma GMBH	Germany
	135000	1:2	Eudragit S	Röhm Pharma GMBH	Germany
	–	–	MPM-05, MPM-06	Tanabe Seiyaku Co. Ltd	Japan
Carboxymethylethyl-cellulose	–	–	CMEC	Freund Sangyo Co. Ltd	Japan
Cellulose acetate-phthalate	–	–	CAP	Wako Pure Chemicals Ltd	Japan
Hydroxypropylmethyl-cellulose phthalate[28]	–	–	HP-50, HP-55	Shin-Etsu Chemical Co. Ltd	Japan
Hydroxypropylmethyl-cellulose acetate-succinate[28]	–	–	AS-M, AS-H	Shin-Etsu Chemical Co. Ltd	Japan
Diethylaminoethyl methacrylate–methyl methacrylate (or butyl methacrylate)	150000	–	Eudragit E	Röhm Pharma GMBH	Germany

Table 2. The monomers used in pH-sensitive 'smart' polymers and hydrogels.

Type of hydrogel	Monomer	pH-sensitive group	Ref.
Acid	Methacrylic acid	$-COOH$	27
	Acrylic acid		29
	Maleic acid		30
	N-Acryloyl-*p*-amino-benzoic acid		31
	Styrenesulfonate	$-SO_3Na$	32
	Sulfonyloxyethyl methacrylate	$-SO_3H$	32
Alkaline	Aminoethyl methacrylate	$-NH_2$	32
	N,*N*-Dimethylamino-ethyl methacrylate	$-NMe_2$	25
	N,*N*-Diethylamino-ethyl methacrylate	$-NEt_2$	33
	Vinylpyridine	$-NC_5H_4$	32
	Vinylbenzyltrimethyl-ammonium chloride	$-NMe_3^+Cl^-$	32

Physicochemical models of the swelling of hydrogels usually take into account the change in the free energy as a result of three factors: (1) the osmotic pressure of the mobile counterions within the gel (the Donnan theory); (2) the mixing of the polymer with the solvent (the Flory–Huggins theory); (3) the stretching of the macromolecules, increasing the free energy, which ultimately actually determines the limiting degree of swelling. Thus the increase in entropy as a result of the mixing of the polymer with an effective solvent increases the swelling of the gel. If the solvent is poor, then the entropy gain is inadequate and the gel does not swell. The extension of the macromolecules during the swelling of the polymer network is described by the elasticity theory, which postulates that the polymer network consists of cross-linked polymer chains in a free Gaussian conformation.[33]

The physicochemical models of the swelling describe satisfactorily only the swelling of weakly charged hydrogels with univalent counterions at high degrees of swelling.[16] For low degrees of swelling or for gels with a high charge density, the theory agrees poorly with experiment. Thus, for a high charge density in the gel, the activities of the ions are no longer equal to their concentrations. In a weakly swollen gel, the effective relative permittivity is lower than in the surrounding solution. This situation is energetically unfavourable for any ion and the latter tends to leave the gel. This tendency intensifies with increase in the hydration radius of the ion. For a low degree of swelling, an appreciable proportion of the water in the gel is in a state where it is bound to the polymer. The ability of such molecules to solvate counterions is much lower. In a highly charged gel at a high degree of swelling, it is no longer permissible to neglect the electrostatic interactions between the fixed charged groups and the mobile counterions, as is done in the Donnan theory. The electric potential in the gel ceases to be uniform, since the counterions tend to be localised in the vicinity of the charged groups. Furthermore, the Donnan theory does not take into account the specific ionic effects, for example, the cross-linking of the polymer chains by polyvalent counterions and complex formation.

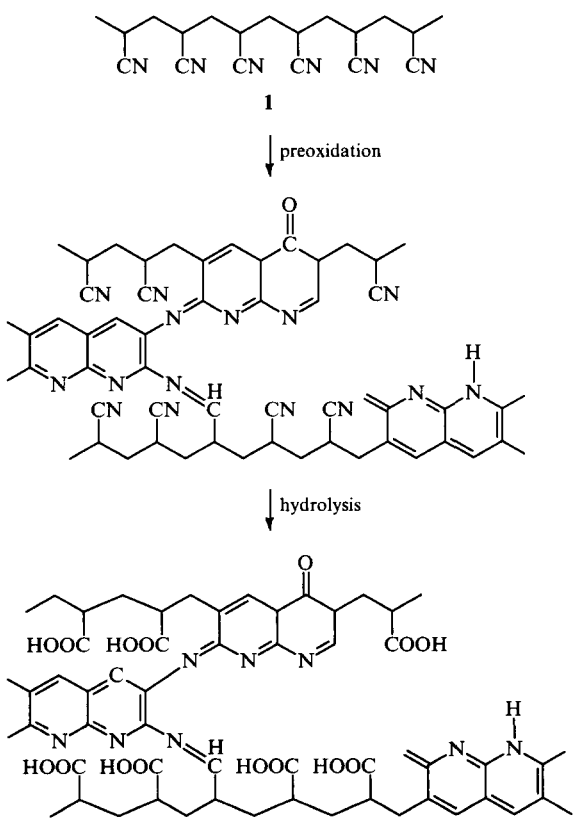
The factors listed above explain the absence of a satisfactory general theoretical model of the swelling of hydrogels.[33]

The change in pH near the electrode is used to create polymer systems responding to the electric potential.[35] Thus a column of a partially hydrolysed (20% of amide groups) polyacrylamide gel 3 cm long in 50% acetone shortens by a factor of 200 under the influence of a potential (> 1.15 V). In the electric field, the protons move to the cathode, while the negatively charged acrylic group of the polymer chain tends to move to the anode. A mechanical stress arises in the bulk of the gel, reaching a maximum in the vicinity of the anode and a minimum near the cathode, which under the conditions of a poor solvent leads ultimately to the collapse of the gel (in a purely aqueous solution, only a gradual decrease in the size of the gel without collapse takes place). The collapse of the gel is reversible and in the absence of an electric field the gel swells again. The response time in such a system is measured in hours. The response can be accelerated by decreasing the size of the gel and by increasing the

electric field strength. The 150–300 μm polyacrylate microparticles undergo a decrease in volume by 90% after 50 s in a 46 V electric field.[36] When the potential of a polypyrrole film is altered from −0.6 to 0.4 V, the pH in its vicinity changes from 4 to 10. The Gaussian polyacrylate gel microparticles on the surface of the film then dissolve in only 15 s. When the initial potential (−0.6 V) is restored, the microgel particles are reformed (in 10 s).[37]

A biodegradable gel, swelling reversibly when the pH is altered, has been obtained from the copolymer of *N,N*-dimethylacrylamide, *N*-*tert*-butylacrylamide, the *p*-nitrophenyl ester of *N*-methacryoylglycylglycine and acrylic acid cross-linked covalently with the aid of *N,N'*-(ω-aminocaproyl)-4,4'-diaminobenzene.[38]

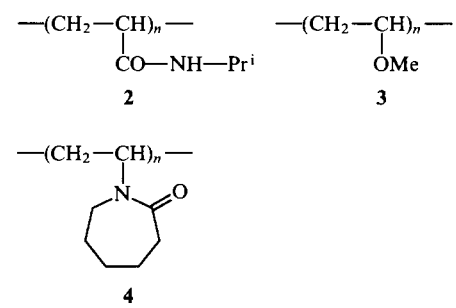
The critical phenomena in highly charged polyelectrolytes, occurring at extreme pH values, are of interest from the standpoint of the possibility of converting chemical energy into mechanical energy and of modelling biomechanical systems. Such systems are nowadays already capable of developing forces sufficient to lift by 0.5 cm a motor-car weighing 800 kg,[39] whilst a composite film consisting of the vinyl alcohol–acrylic acid and vinyl alcohol–acrylic acid–allylamine copolymers is capable of undergoing a change in size in response to a change in the solvent (the replacement of ethanol by 0.01 M NaOH) in only 40 s.[40] The artificial muscle model, created at the Tokyo Technological Institute, is even more striking.[41] Modification by partial oxidation and hydrolysis of the industrially manufactured polyacrylonitrile fibres **1** imparts to the latter the ability to swell strongly in an alkaline medium (1 M NaOH) and to contract in an acid medium (1 M HCl). The elongation reaches 80% in 2 s and the force developed under these conditions is 12 kgf cm^{-2}. For comparison, we may note that skeletal muscles are elongated by 30% in 10^{-2}–10^{-3} s, developing a force of 4–10 kgf cm^{-2}. Thus the effectiveness of artificial muscles almost approaches that of biological muscles.



The mechanical systems capable of converting various types of chemical energy into mechanical work have been examined in an extensive review by Osada,[39] whose coworkers carried out much successful work in this field.

2. Polymers sensitive to changes in temperature

Thermoresponsive polymers and hydrogels with a LCT below 40–45 °C are considered in this section. In their classical work,[42] Taylor and Ceranowski derived a rule according to which there exists a region where the polymer solution has a LCT. One of the most complete lists of polymers having a LCT in aqueous solutions is presented in the review by Galaev and Mattiasson.[43] Polymers with a wide variety of LCT have been synthesised.[44] The possibility of using some of them in biotechnology has been vigorously investigated at the present time. These are mainly poly-*N*-isopropylacrylamide **2** (poly-NIPAA) and other poly-*N*-alkylacrylamides as well as poly-(methyl vinyl ether) **3** (PMVE). Recently poly-*N*-vinylcaprolactam **4** (PVCL) and ethylene oxide–propylene oxide copolymers have attracted the attention of investigators.



The greatest number of publications have been devoted to NIPAA. The NIPAA homo- and copolymers are readily obtained by radical polymerisation in aqueous[45] or organic[46,47] solvents. Poly-NIPAA is soluble in acetone, chloroform, dioxane, tetrahydrofuran, lower alcohols, and cold water; it forms a separate phase at a temperature of about 32 °C, the LCT being almost independent of the molecular mass (*M*) of the polymer.[47] Poly-NIPAA cannot be fractionated into narrow molecular-mass fractions when an aqueous solution of the polymer separates into layers comprising different phases on heating. A carefully dried mixture of acetone and cyclohexane is used for the fractionation.[48]

Narrow molecular mass fractions of poly-*N,N*-diethylacrylamide with a very narrow distribution of molecular masses (polydispersity less than 1.2) have been obtained by polymerising the corresponding monomer with transfer of the group (live polymerisation) in dry tetrahydrofuran, the process being initiated by the methyl(trimethylsilyl)acetal of dimethylketene and catalysed by tetrabutylammonium acetate.[49] However, the molecular mass of the polymer synthesised is low and amounts to only 4700. The lower consolute temperature is 30 °C for the poly-*N,N*-diethylacrylamide synthesised by radical or live polymerisation and 40 °C for that synthesised by anionic polymerisation.[50,51]

The synthesis of copolymers of NIPAA with acryloyloxysuccinimide (used for the covalent immobilisation of proteins),[52] the modification of poly-NIPAA designed to obtain a porous glass[53] and polymer membranes,[44,54,55] and the preparation of block-copolymers of NIPAA with ethylene oxide,[56] the aqueous solutions of which do not separate into two phases on heating, in contrast to the poly-NIPAA homopolymer, but form a gel[57,58] have been described.

The properties of poly-NIPAA in aqueous solutions and the phase transition on heating have been investigated in detail by various methods: turbidimetric,[47,48] viscometric,[48,49] calorimetric,[48,60,61] light scattering,[60,61,63] fluorescence,[63–66] and EPR.[67] The influence of surfactants and of the inclusion of

hydrophobic or ionogenic comonomers on the LCT of poly-NIPAA has been investigated,[59,68-72] while the influence of the phase transition on the sorption of poly-NIPAA on aerosils with various hydrophobic properties has also been studied.[73]

The phase separation of aqueous solutions of poly-NIPAA on raising the temperature is caused by the conformational transition of the macromolecule from a loose globule to a compact coil. Such a transition is accompanied by a sharp decrease in the size of the macromolecule,[62] a decrease in the mobility of the fluorescent dansyl label bound covalently to the polymer,[64] and a fivefold increase in the nonradiative energy transfer between the pyrene and naphthalene labels bound covalently to the macromolecule.[65] The enthalpy of the transition is consistant with the loss of approximately one hydrogen bond per monomer unit.[45] The heat capacity of poly-NIPAA decreases with increase in temperature. The decrease in the heat capacity of poly-NIPAA reflects the collapse of the polymer chain on heating accompanied by a decrease in the number of contacts between the polymer molecule and water molecules similar to that occurring when a protein is renatured after being denatured by cooling.[61]

The formation of multimolecular micelles, consisting of a hydrophobic core surrounded by solvated poly-NIPAA chains, has been observed for the hydrophobically modified NIPAA copolymers at temperatures below the LCT.[63] The exchange of polymer molecules between the micelles is very slow.[66] At the LCT, the collapsed micelles aggregate and effective mixing of the copolymer molecules becomes possible.[63,66] The endothermic enthalpy of the phase separation of the ternary NIPAA–butyl methacrylate–X copolymers, where X is a hydrophilic, hydrophobic, cationic, or ionic comonomer, decreases linearly with increase in the LCT. Thus the hydrophobic interactions between the polymer side groups intensify with increase in temperature owing to the decrease in the structure formation in the water around these groups. It was concluded that the change in the LCT induced by the incorporation of other comonomers is determined by the overall change in the hydrophilicity of the copolymer and not by the direct influence of the hydrophilicity or charge of the comonomer on the water molecules in a structured arrangement around the hydrophobic groups.[71]

Since the hydrophobic interactions are the main driving force inducing the phase separation, the LCT of poly-NIPAA or of its copolymers may be regulated by influencing the effectiveness of these interactions. The introduction of hydrophobic and hydrophilic comonomers respectively decreases and increases the LCT of the polymer.[74] The LCT of poly-NIPAA diminishes with increase in the ionic strength of the solution and increases in the presence of ionic detergents forming stable complexes with the polymer.[57,68-70,75] Organic solvents miscible with water weaken the hydrophobic interactions of the side groups of poly-NIPAA and increase the LCT. However, in the presence of 40–60 vol% of certain solvents (methanol, tetrahydrofuran) the LCT of poly-NIPAA decreases to 0 °C and below.[76]

The gels of poly-NIPAA and other *N*-alkyl-substituted polyacrylamides are obtained by adding cross-linking agents (usually *N,N'*-methylenebisacrylamide) to the initial reaction mixture, by radiation-induced polymerisation,[77] or by cross-linking the copolymer with the aid of a bifunctional agent.[38] The introduction of ionogenic comonomers makes it possible to obtain hydrogels sensitive to changes in both temperature and pH.[78-80] Macroporous gels with high rates of swelling and dehydration have been synthesised at temperatures below the LCT of poly-NIPAA.[81] The poly-NIPAA gel in a granulated form can be obtained by emulsion or suspension polymerisation.[82-84] By employing different *N*-alkyl-substituted polyacrylamides, it is possible to synthesise thermoresponsive hydrogels (TH) with a LCT ranging from 5.5 °C for the poly-*N*-acryloylpiperidine gel to 72 °C for the poly-*N*-ethylacrylamide gel.[85]

The study of the phase transitions in hydrogels of poly-NIPAA[86-97] and other *N*-alkyl-substituted polyacrylamides[93,98-101] was initiated by Ilavsky et al.[98] and Tanaka and coworkers.[10] These investigations are continuing to develop vigorously also at the present time. The dependence of the time required for the phase transition on the size of the gel specimen makes it possible to describe the phase transition approximately as a collective diffusion process.[94] The formation of separate collapsed sections or of a thin film of the collapsed gel on the surface of the specimen plays an important role in this.

The influence of surfactants,[75,102,103] organic solvents,[76,101,104] salts,[105] and poly(ethylene glycols)[106] and of the inclusion of ionogenic comonomers[87,89,98,100,107] on the collapse and swelling of gels has been investigated. The nonradiative energy transfer[108] and mechanical stresses[109] arising on collapse of poly-NIPAA gels have been studied. It is of interest to note that sodium chloride at a concentration of ~1 M induces the collapse of the poly-NIPAA hydrogel at room temperature, whereas other salts exert a typical salting-out effect — the gel is gradually dehydrated with increase in the salt concentration.[105] The strong hydrophobic interaction of the isopropyl groups of poly-NIPAA with the alkyl group of sodium dodecyl sulfate results in the poly-NIPAA gel behaving in the presence of the detergent as a gel of the copolymer of NIPAA with the anionic monomer.[102,103]

A detailed theoretical discussion of the models of the phase transitions in poly-NIPAA gels may be found in recent reviews.[110,111]

Poly(methyl vinyl ether) **3** is obtained by the cationic polymerisation of methyl vinyl ether, this polymer being produced industrially.[85] The LCT for aqueous solutions of PMVE is 34–38 °C.[85,112] The PMVE gel is obtained by the γ-irradiation of polymer solutions.[85] Irradiation at temperatures above the LCT[113] or careful selection of the conditions (irradiation dose, polymer concentration)[114] make it possible to obtain gels with high rates of swelling and dehydration when the temperature is altered. The phase transitions in solutions[45,112,115] and in PMVE gels[85,86,113,116-118] have been studied much less than in poly-NIPAA.

As for poly-NIPAA, hydrophobic interactions apparently play the main role in the phase transition in PMVE.[112] The molar enthalpy of the phase transition is lower for PMVE than for poly-NIPAA,[86] but the phase transition in PMVE is also accompanied by the loss of one hydrogen bond per monomer unit,[118] as in poly-NIPAA.

Polyvinylcaprolactam **4** (PVCL) is obtained by the radical polymerisation of vinylcaprolactam in an organic solvent[120] or in bulk.[121,122] The thermodynamics of the phase transition in aqueous PVCL solutions have been investigated by Tager and coworkers.[123-126] The LCT for aqueous PVCL solutions depends on the molecular mass of the polymer and varies from 31 °C for the polymer with $M = 1\,250\,000$ to 40 °C for the polymer with $M = 15\,500$.[43] The Gibbs free energy, enthalpy, and entropy of mixing of PVCL with water are negative over the entire range of compositions. With increase in temperature, the mixing becomes less exothermic. It has been suggested that hydrophilic and hydrophobic hydration of the polymer takes place in aqueous PVCL solutions. In the ranges of temperatures and compositions close to the binodal curve, the hydrophobic hydration predominates, as a consequence of which the miscibility of the polymer with water diminishes and phase separation takes place.[123]

Cellulose derivatives, in particular hydroxypropylmethylcellulose and ethoxyethylcellulose, are also promising for use in biotechnology. They are distinguished by a high chemical stability and a satisfactory biological compatibility. The LCT for aqueous solutions of these polymers is 50–60 °C, but in the presence of salts and surfactants it diminishes to almost 0 °C.[127-129]

Among epoxyethane derivatives, nonionic detergents, especially Triton X-114 (*p-tert*-octylphenyl ether of polyoxyethylene with a degree of polymerisation of 7–8) have found extensive

application in biotechnology. The copolymers of ethylene and propylene oxides have also attracted the attention of investigators recently. Aqueous solutions of Triton X-114 have a LCT in the region of 18 °C. They are used to extract hydrophobic proteins into the polymer phase (the so called cloud point extraction). However, strictly speaking Triton X-114 ($M = 450 - 500$) and similar compounds are oligomers and not polymers, so that their study is outside the scope of the present review. The theoretical principles and practical aspects of the use of cloud point extraction of detergents have been examined in detail in a brilliant review by Hinze and Pramauro.[130]

The 50:50 ethylene oxide–propylene oxide copolymer with $M = 4000$ (manufactured by the Union Carbide Company under the trade name UCON 50-HB-5100) has an LCT of 55 °C. However, in the presence of a 0.2 M sodium sulfate solution the LCT diminishes to 40 °C.[131] A more hydrophobic copolymer containing 80 mol.% of propylene oxide ($M = 2000$) has a lower LCT (18 °C).[132]

The methacrylic acid–methacrylate copolymer described above (Eudragit S 100),[27] aqueous solutions of which separate into layers on acidification, forms a separate polymer phase in a neutral medium at 40 °C in the presence of 50 mM Ca^{2+}. The copolymer redissolves when the temperature is reduced.[133,134]

The first communication about reversible gel formation in an inorganic system has appeared recently. The aluminium polyphosphate hydrogel dissolves when the temperature is reduced and reforms at room temperature.[135]

The reversibly flocculating latexes are interesting systems. The minimum NaCl concentration inducing flocculation diminishes with increase in temperature and reaches a constant value at temperatures above the LCT. At a certain NaCl concentration, the latex begins to flocculate after the attainment of a certain temperature, but it can be redispersed on cooling. The formation of such latexes based on poly-NIPAA[136–140] and its copolymers,[77,84,141,142] *N*-acryloylpyrrolidine–*N*-acryloylpiperidine copolymers,[143,144] methacrylic acid esters, and ethylene oxide oligomers with degrees of polymerisation of 1,2,4–5, and 7–8 has been described.[145]

3. Polymeric complexes

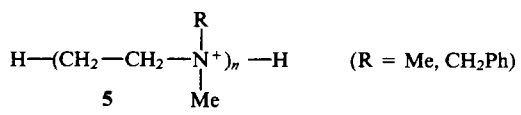
Polymeric complexes, i.e. complexes formed by two different polymers or a polymer and a low-molecular-mass compound, have recently attracted increasing attention by investigators.[146]

The formation of a polyelectrolyte complex is described in a general form by the following scheme:[147]

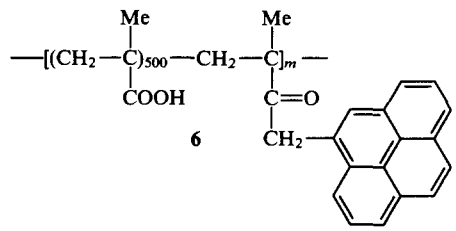
$$(A^-k^+)_n + (K^+a^-)_m \rightleftharpoons$$
$$\rightleftharpoons [(A^-K^+)_x(A^-k^+)_{n-x}(K^+a^-)_{m-x}] + xa^- + xK^+ ,$$

where A^- and K^+ are the anionic and cationic groups in the polymer and a^- and k^+ are their low-molecular-mass counterions. The degree of conversion Θ is defined as the ratio of the number of interionic bonds formed to its maximum possible value ($\Theta = x/m$ for $n \geqslant m$ or $\Theta = x/n$ for $m \geqslant n$). The solubility of polymeric complexes in water depends on the fraction of the charged ionic group z and on the relative length of the oppositely charged polyions and also on the pH and the ionic strength of the solution. The polymeric complexes formed by polymers with $z = 1$ have minimum solubility at $\Theta \to 1$. Nonstoichiometric polyelectrolyte complexes in which one of the polyions predominates can be represented as an unusual block copolymer consisting of a charged hydrophilic block containing one polymer chain and a neutral hydrophobic block containing two polymer chains.

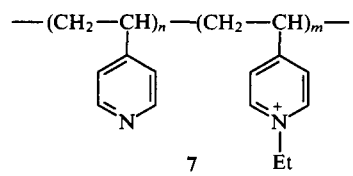
The cooperative nature of the interaction between the polyions makes such polymeric complexes exceptionally stable even for fairly low degrees of polymerisation of the polyions. For example, the dissociation constant of the polymeric complexes of polymethacrylic acid with quaternised oligoethyleneimines **5** becomes negligibly small even for the octamers.[147]



5



6



7

Despite the high stability of the polymeric complexes, they are capable of exchanging the polyions. The nature and length of the polyion are of fundamental importance in exchange reactions.[148] The polymethacrylate complex **6** (PMA) (degree of polymerisation 4100), containing a fluorescent label (1 label for each 500 monomer units), with partially quaternised poly-4-vinylpyridine **7** (P-4-VP) (degre of polymerisation 170) is capable of exchange with polyphosphates (PP) with different degrees of polymerisation (from 20 to 230):

$$\text{P-4-VP.PMA} + \text{PP} \rightleftharpoons \text{P-4-VP.PP} + \text{PMA} .$$

The equilibrium in this reaction in 0.3 M NaCl is fully displaced to the right for the long polyphosphates and to the left for the shortest polyphosphate. For a fixed degree of polymerisation of the polyphosphates ($n = 70$), the reaction equilibrium is fully displaced to the right in 0.3 M LiCl and to the left in 0.3 M KCl, the equilibrium remaining unchanged in 0.3 M NaCl. Such phenomena have no analogues in nonpolymeric systems and can serve as useful models for the regulation of processes in the living cell with the aid of biopolymers.[148]

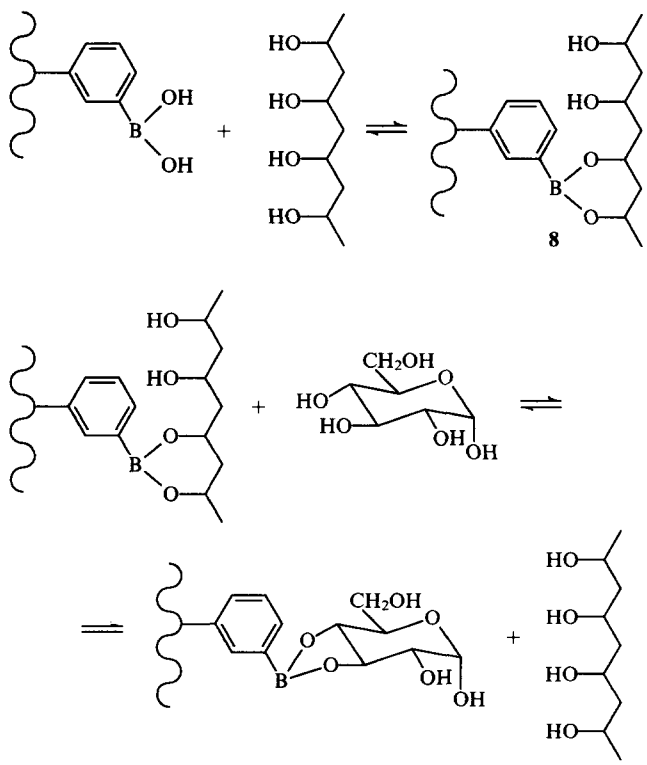
Systems capable of undergoing marked but reversible changes in their properties and of responding to slight changes in the medium may be included among 'smart' polymeric complexes. Nonstoichiometric polyelectrolyte complexes (NPC), formed in the interaction of a polycation (for example, poly-*N*-ethyl-4-vinylpyridinium bromide) and an excess of a polyanion (for example that of polymethacrylic acid) are systems promising for biotechnology.[149–151] The ability of such complexes to be precipitated quantitatively from solution when the pH of the latter is altered by only 0.3 of a unit is an attractive feature.[149]

Another interesting group comprises complexes between uncharged polymers, which are obtained as a result of numerous weak interactions, for example via hydrogen bonding between polyacrylic acid and polyacrylamide.[9] The strength of the hydrogen bonds increases with increase in temperature. Thus the gel formed by interpenetrating polyacrylic acid and polyacrylamide polymer networks collapses on cooling to ~20 °C and swells again on heating.[9]

Kabanov and coworkers[152,153] observed complex formation between polymethacrylic acid and polyoxyethylene (POE). Complexes between high-molecular-mass polymethacrylate (or polyacrylate) and POE are formed in this case when the molecular mass of the latter exceeds a certain critical value, which is 2000 for the complex with poly(methyl methacrylate) and 6000 for that with polyacrylate. The complex between POE and polymethacrylate is stabilised by hydrophobic interactions, its stability increasing with increase in temperature, while that of the complex between POE and polyacrylate depends little on temperature.

The important role of hydrophobic interactions (in which the α-methyl group of the polymethacrylate participates) in the stabilisation of the complex between POE and polymethacrylate has been observed also in the study of the influence of the nature of the solvent. Thus the critical molecular mass of POE, necessary for the formation of its complex with polymethacrylate, increases sharply on passing to more hydrophobic water–methanol mixtures, whereas for the polyacrylate complex it remains virtually constant.[154] The marked reversible temperature dependence of the complex formation reaction between polymethacrylate and POE in the range 25–45 °C renders such systems interesting for biotechnological use.[39,155,156]

Boric acid affords stable complexes with polyol compounds. The complex between poly(vinyl alcohol) and the *N*-vinylpyrrolidinone–*N*-acryloylamidophenylboronic acid copolymer is formed as a result of the interaction of boric acid with the hydroxy-groups of the polyol, but in the presence of an excess of another polyol (for example, glucose) the complex decomposes. The removal of glucose (for example, by dialysis) again leads to complex **8**,[157,158] so that the complex formation reaction depends reversibly on the presence of glucose, i.e. the given system can be used as a detector for the presence or absence of glucose.



Among the complexes between polymers and low-molecular-mass compounds investigated, mention should be made of the complex formed by the poly-2-acrylamido-2-methylpropanesulfonic acid with n-dodecylpyridinium chloride. This system responds to changes in the electric potential by a change in the form of the gel.[159]

III. Applications of 'smart' polymers

1. Concentration of protein solutions and dehydration of suspensions

When hydrogels collapse, their volume contracts by a factor of 1000.[86] Their ability to absorb up to several grams of water per gram of the gel and then to give up the absorbed water after a slight change in conditions is used in the dehydration of suspensions and in the concentration of protein solutions. Such processes are based on the cycle presented in Fig. 1.[160]

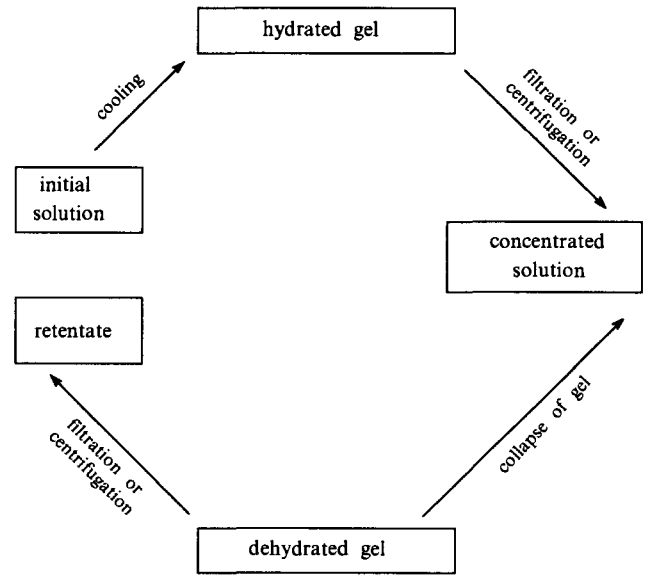


Figure 1. The removal of water from suspensions and concentration of protein solutions.[160]

The gel dehydrated beforehand swells in the initial solution, 'taking up' water. Low-molecular-mass substances, capable of permeating into the gel pores, diffuse within the gel. On the other hand, high-molecular-mass substances, which are incapable of permeating into the pores, remain in solution in a concentrated form. The swollen gel is separated from the solution and regenerated by inducing its collapse (it is heated above the critical temperature or the pH and the ionic strength of the solution are altered). The gel collapses and gives up the previously absorbed water together with the low-molecular-mass substances dissolved in it. After separation by filtration or centrifugation, the dehydrated gel is again ready to concentrate a fresh portion of the initial solution. By regulating the composition and degree of cross-linking of the gel, it is possible to alter its selectivity with respect to the molecular mass and charge of the sorbed solutes.[161–164] When collapsed gels are used for concentration and dehydration (swellex process or gel dewatering process), it is possible to combine the high productivity of liquid extraction with the selectivity of membrane methods.[162]

The idea of concentrating protein solutions by adsorbing water on solid particles had already appeared in the 1960s.[165] However, attention was concentrated only on the stage involving adsorption without the regeneration of the gel, i.e. on the left-hand part of the cycle presented in Fig. 1. Only after the appearance of 'smart' hydrogels has it become possible to carry out economically the entire cycle.

Solutions of casein and bovine serum albumin have been concentrated by a factor of 4.6–4.8 with the aid of a sulfonated polystyrene gel cross-linked by divinylbenzene (the gel was regenerated by means of a concentrated salt solution). The yield of the protein was then 95%–99%.[162]

The appearance of thermoresponsive hydrogels (TH), which collapse on heating, made this type of process even more attractive. The thermoresponsive NIPAA hydrogel has been used to concentrate cellulases from the *Trichoderma reesei* culture liquid.[162]

Cussler and coworkers[166] developed an industrial process for the preparation of soya protein by dehydrating the mother liquor with the aid of poly-NIPAA-TH (Fig. 2).

After the extraction of soya oil, the soya beans are ground up and the proteins are extracted with water at pH 8.5. The mother liquor is separated by centrifugation. In the traditional technology, the proteins are precipitated with acid. The most

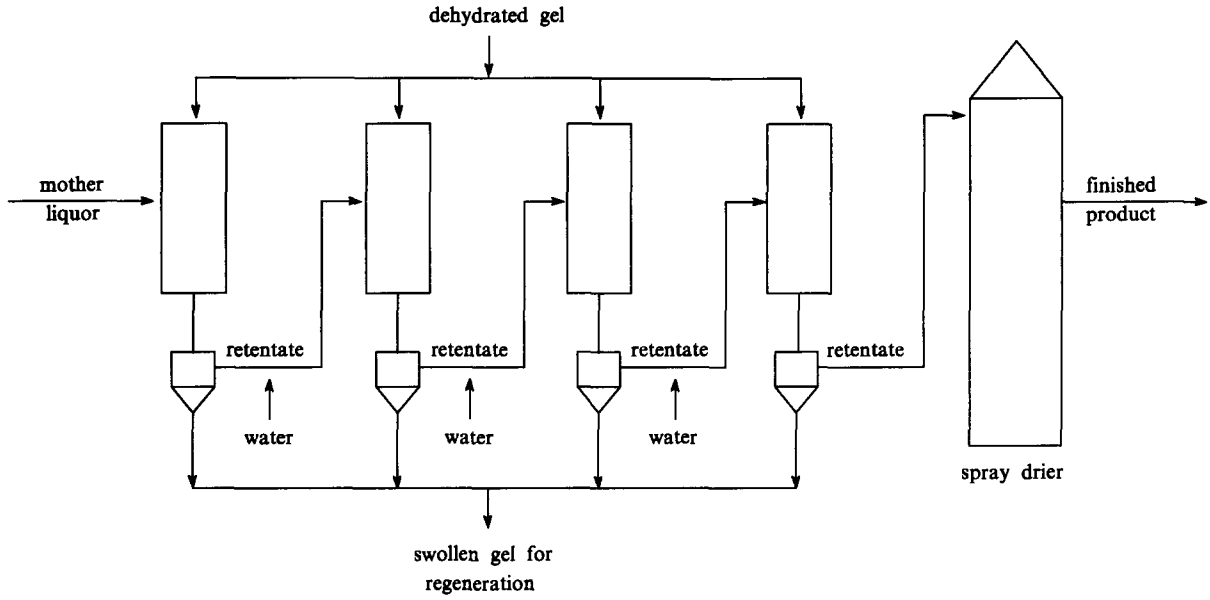


Figure 2. Industrial preparation of soya protein.[160]

valuable among them (the albumin-like proteins) are not precipitated under these conditions and are lost, while the toxic phytins are precipitated. The protein precipitate is dissolved at pH ~7 and dried on a spray dryer. From 100 kg of the initial raw material, 33 kg of the product is obtained.

In the proposed technology, the mother liquor is treated at 5 °C with the collapsed poly-NIPAA-TH, after which the gel swells, adsorbing 40% of water. The swollen gel is separated by centrifugation and the retentate is diluted with water and again treated with the collapsed gel (this procedure is repeated 2–4 times), which makes it possible to separate the protein from low-molecular-mass impurities. After this, the retentate, containing 15% of dry substances, is transferred to the spray dryer. From 100 kg of the initial raw material, one obtains 45 kg of the product. The yield with respect to the protein exceeds 80%.[166]

The new process is not free of disadvantages, one of which is the adsorption of the protein on the surface of the gel particles. However, it does have significant advantages: a high yield of the product as a result of the retention of albumin-like proteins, the absence of the precipitation stage with acidification, which makes it possible to retain a greater amount of the proteins in the native form, and better consumption qualities of the product because of the absence of toxic phytins and a higher protein content. Economic analysis, carried out on industrial apparatus, showed that the capital expenditure on the manufacture of the protein is recovered in 3.2 years.[160]

The PMVE-based thermoresponsive hydrogel is used to remove water from suspensions, in particular the culture liquids of microorganisms.[167,168] This type of process makes it possible to overcome a number of the disadvantages of the traditional filtration. Thus the filtration area may be readily increased by increasing the number of TH particles; the 'pie' comprising the microorganisms, formed on the surface of the particles, is continually disrupted as a result of the increase in the geometrical size of the TH particles on swelling; the path traversed by water from the bulk of the suspension to the filtering surface is greatly shortened.

Engineering calculations have shown that it is necessary to have 7–8 kg of dry PMVE-TH for the preparation of 1 kg of dry substances. In order to compete with the most productive strip filters, the TH particles must withstand at least 2000 cycles, so that an increase in the mechanical strength of the PMVE-TH particles is the primary condition for the successful introduction of the TH into practice.[168]

2. Membranes with a controllable permeability

The ability of 'smart' polymers to undergo a distinct transformation from an uncoiled globule into a compact coil has been used to create membranes with a controllable permeability. The principle of the operation of such a membrane is illustrated in Fig. 3. In the uncoiled conformation, the polymer molecules immobilised on the surface do not prevent the permeation of the solutes into the pores. In the compact conformation, the polymer molecules block or strongly hinder the entry of the solutes into the pores.

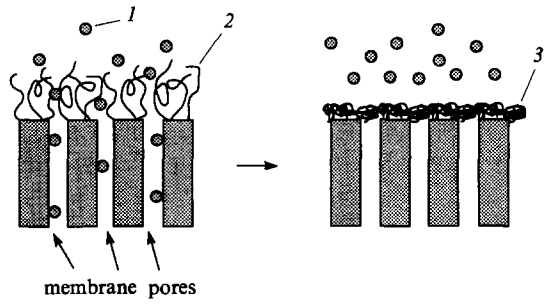


Figure 3. Controllable permeability of a membrane as a function of the conformation of the polymer. (*1*) Solute; (*2*) polymer in the uncoiled conformation; (*3*) polymer in the compact conformation.

Permeability controlled by varying the pH has been achieved when poly-4-vinylpyridine or polyacrylic or polymethacrylic acid were immobilised on the surfaces of the membranes of nylon capsules. In the first case, the permeability increases with decrease in the pH, while in the second it increases with increase in the pH.[169] When the pH is reduced from 6 to 3, the permeability of the polymethacrylate membrane to fluorescence-labelled dextran (M = 10000) changes by a factor of 85.[170]

The regulation of permeability by varying the temperature has been achieved in the immobilisation of poly-NIPAA or other poly-*N*-alkylacrylamides on the pore surface.[44,54,55,171] The change in the effective pore size due to the transition of the immobilised NIPAA molecules from the uncoiled conformation to the compact conformation makes it possible to regulate gel-permeation chromatography by varying the elution temperature.[53]

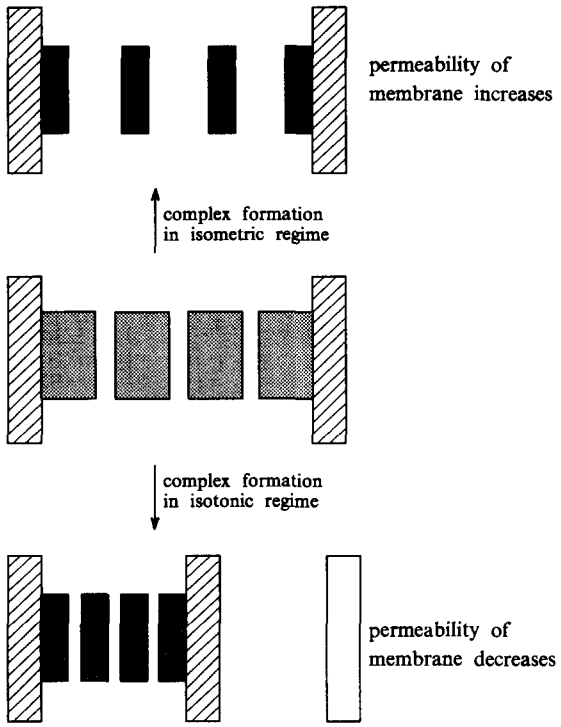


Figure 4. Behaviour of a poly(methyl methacrylate) membrane during the formation of a complex with polyoxyethylene in isometric and isotonic regimes.[39]

If the membrane consists wholly of a polymeric hydrogel, its permeability changes greatly as the degree of swelling of the gel is altered. The permeability of a membrane made from a copolymer comprising 4-acryloylpiperidine (LCT = 5.5 °C), 2-hydroxyethyl methacrylate, and styrene to insulin varies sharply with temperature. Depending on the composition of the copolymer, the permeability either increases or decreases with increase in temperature.[172] A change in the pH or in the electric field alters reversibly the permeability of a poly(methyl methacrylate) membrane by a factor of 50.[173] The complex formation reaction between polyoxyethylene and a poly(methyl methacrylate) membrane can be used both to increase the permeability of the membrane, which has fixed geometrical dimensions (isometric regime), and to decrease the permeability of a freely mounted membrane (isotonic regime) (Fig. 4). In both cases washing of the membrane with a weakly alkaline solution leads to the dissociation of the complex and the restoration of the initial permeability.[39,156]

The acrylamide–acrylic acid copolymer hydrogel, immobilised on porous glass, exists under isometric conditions. Such a membrane allows the passage of aqueous solutions of polyoxyethylene only with $M < 4000$. The collapse of the hydrogel in 50% acetone leads to a sharp increase in the permeability of the membrane: it is now capable of allowing the passage of polyoxyethylene with $M = 80\,000$.[111,174,175]

Thus membranes based on 'smart' polymers can be used to create various systems with feedback.

3. Isolation and purification of biomolecules

The ability of 'smart' polymers in aqueous solutions to form a separate phase after a slight change in conditions has been used to isolate and purify proteins. A general scheme for this process, which has been called affinity precipitation, is illustrated in Fig. 5 (see over).

The conjugate of a 'smart' polymer with a ligand which has an affinity for the given target protein and forms a complex with the latter is added to the initial mixture containing the protein. When the conditions are altered (change in the pH, temperature, and ionic strength, addition of specific complex-forming agents), the polymeric conjugate together with the target protein is segregated as a separate polymeric phase, while the impurities remain in the solution. The polymeric phase is separated from the supernatant. Next the target protein is either eluted from the polymeric phase or the latter is redissolved, altering the conditions in such a way that the complex dissociates, while the polymeric conjugate is reprecipitated but this time without the target protein, which remains in the solution.

This type of approach was first used by Schneider et al.[31] to isolate trypsin. The extract from the pancreas was treated with an acrylamide–*N*-acryloyl-*p*-aminobenzoic acid copolymer containing *m*-aminobenzamidine ligands with a high affinity for trypsin. The trypsin–copolymer complex was precipitated by acidifying the solution to pH 4. The precipitate was separated, washed, and redissolved at pH 8. The polymer was then precipitated but this time at pH 2 (the trypsin–polymer complex is known not to form in an acid medium), whereupon trypsin remained in the solution. After lyophilic drying, the solution contained 90% of trypsin. The copolymer was regenerated (to the extent of 93%) and reused.[31]

Apart from precipitation, reversible flocculation may be used for the purification of biomolecules. The particles of the latex of a copolymer comprising styrene, NIPAA, glycidyl methacrylate, and methacrylic acid are used for this purpose. Thus the antibodies to bovine serum albumin have been isolated from the serum with the aid of the latex containing immobilised bovine serum albumin on its surface.[142]

Examples of the successful employment of the affinity precipitation methods for the isolation and purification of various biomolecules are compiled in Table 3. Mattiasson and coworkers have made a contribution to the development of these methods.[176,179,185–190]

The traditional methods for the purification of proteins by precipitation with ammonium sulfate, polyoxyethylene, or organic solvents are distinguished by simplicity and a high productivity. Their disadvantage is a low specificity. Affinity precipitation makes it possible to combine the simplicity and high productivity of the protein precipitation processes with the high specificity of the affinity chromatographic method. In principle, the same ligands can be used for affinity precipitation as for affinity chromatography. The difference is that affinity precipitation is carried out in a batch regime, which rules out the possibility of the repeated interaction of the protein with the ligand, as in chromatography. Therefore ligands with a high affinity for the protein isolated are preferable for affinity precipitation, which restricts somewhat the choice of the systems employed.[189] Both synthetic and natural polymers are used for affinity precipitation.

The affinity of the target protein for the polymer (for example, the affinity of endo-polygalacturonase for alginate,[187] of agglutinin for chitosan,[176] and of D-lactate dehydrogenase from *Lactobacillus bulgaricus*[186] or xylanase[185] for the methacrylic acid–methyl methacrylate copolymer), is an interesting case, which makes it possible to avoid the complex procedure involving the preparation of the polymer containing the specific ligand.

It is noteworthy that the choice of the polymer is very important for the successful employment of affinity precipitation. The polymeric phase formed should not be too hydrophobic in order not to create an undesirable environment for the protein molecules being isolated.[190] On the other hand, an unduly hydrophilic polymeric phase is difficult to separate from the supernatant, which leads to an appreciable nonspecific trapping of extraneous proteins, i.e. to a decrease in the degree of purification and in the yield of the target protein.[179] The most successful results have been achieved by employing the methacrylic acid–methyl methacrylate copolymer

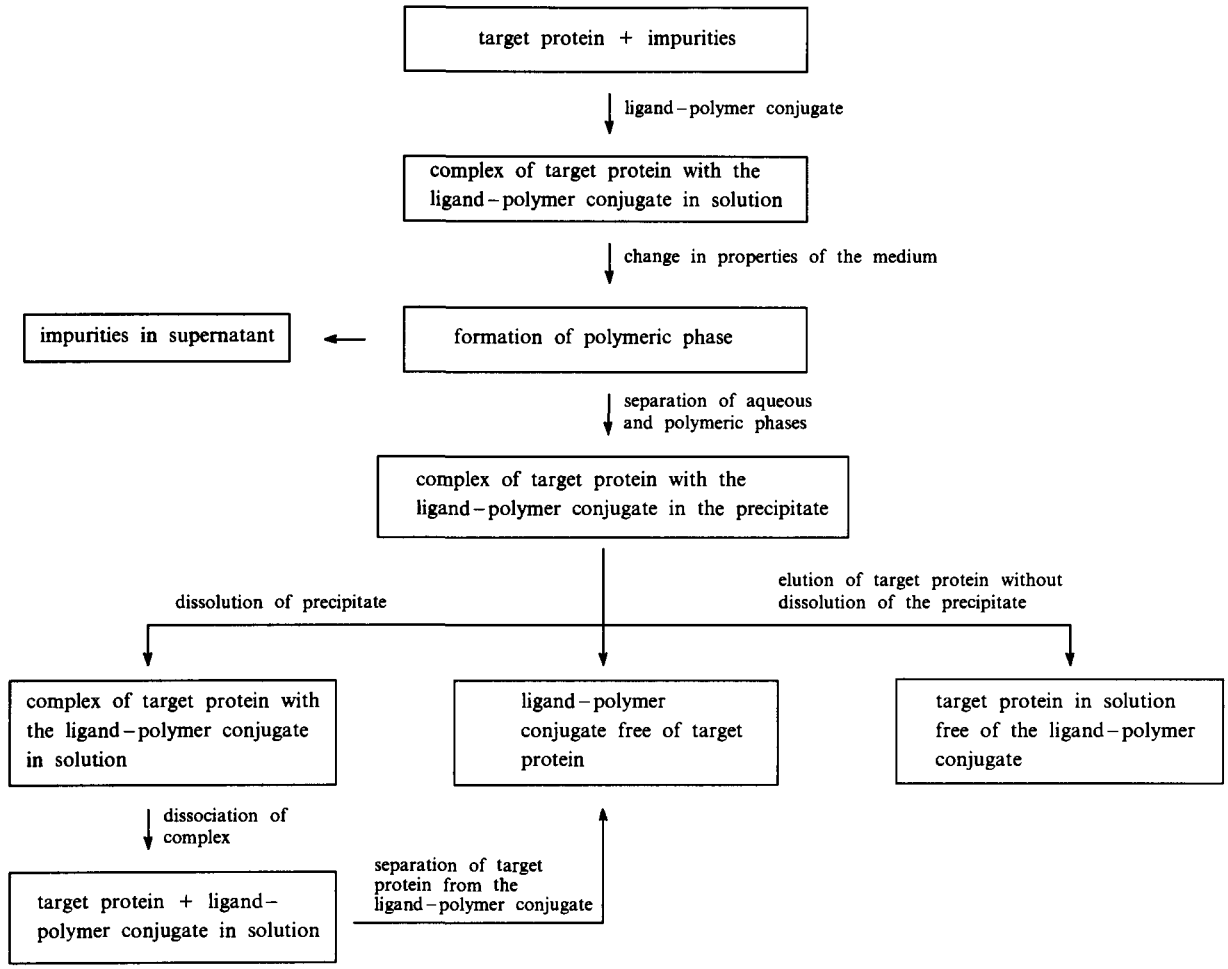


Figure 5. General scheme employed in affinity precipitation methods.

(Eudragit S 100, Table 3). The optimum selection of the conditions makes it possible to attain a tenfold degree of purification of the protein combined with 70%–80% yields.[133,134]

Aqueous solutions of polyoxyethylene and dextran form two immiscible polymeric phases — hydrophilic and hydrophobic — containing more than 80%–95% of water. The hydrophilic and hydrophobic phases consist of dextran and polyoxyethylene respectively. The different distributions of the substances between these two phases are widely used to isolate and purify many biomolecules.[191] One of the problems in this approach is the need to separate the target product from the phase-forming polymer after the mechanical separation of the phases. A convenient way of solving this problem has been proposed by Tjerneld and coworkers.[131,132,192,193]

The principle of the proposed method is illustrated in Fig. 6. A solution of dextran or hydroxyethyl-substituted starch was used as the hydrophilic phase, while the hydrophobic phase consisted of ethylene oxide–propylene oxide copolymers, the aqueous solutions of which separate into aqueous and polymeric phases on heating. When clarified baker's yeast homogenate is added to the two-phase polymer system, enzymes with affinity for the hydrophobic phase (glucose 6-phosphate dehydrogenase, 3-phosphoglycerate kinase, and hexokinase) are extracted into this phase. The extraction of the target product into the hydrophobic phase is facilitated by the addition to the system of the conjugate of the hydrophobic monomer with a ligand having affinity for the target protein (for glucose 6-phosphate dehydrogenase, such a ligand is the dye Procion Yellow).[193] After the mechanical phase separation in the centrifuge, the hydrophobic phase is heated to 24 °C, whereupon the copolymer is segregated in a separate concentrated polymeric phase, whilst the purified enzymes remain in the aqueous phase. The degree of purification and the yield were 5.3% and 50% for glucose 6-phosphate dehydrogenase, 15.3% and 67% for hexokinase, and 15.4% and 72% for 3-phosphoglycerate kinase respectively.[132] The results are entirely comparable with the results of the chromatographic purification of the proteins by traditional methods.

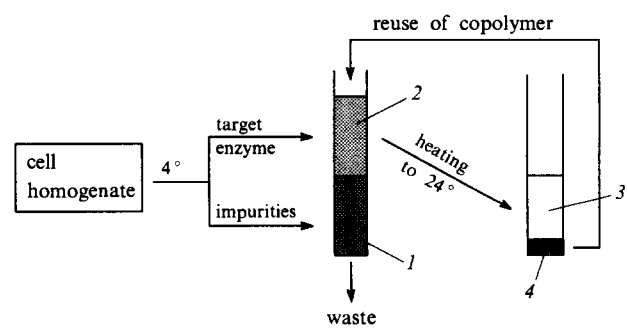


Figure 6. Purification of enzymes in a two-phase system with separation from the phase-forming polymer at a temperature above the LCT.[132] (*1*) Hydrophilic phase — dextran or hydroxypropylstarch; (*2*) hydrophobic phase — copolymer at a temperature below the LCT; (*3*) aqueous phase containing the purified enzyme; (*4*) concentrated polymeric phase — copolymer at a temperature above the LCT.

Table 3. Conditions necessary for the formation of the polymeric phase.

Target product	Ligand	Polymer	Method of formation of polymeric phase	Ref.
Wheatgerm agglutinin	[a]	chitosan	change in pH	176
Trypsin	trypsin inhibitor from soya beans	"	"	177
	p-aminobenzamidine	NIPAA – *N*-acryloyloxy-succinimide copolymer	change in temperature	178
	trypsin inhibitor from soya beans	alginate	addition of Ca^{2+}	179
	"	PVCL	change in temperature	180
Protein A	IgG	hydroxypropylmethylcellulose acetate-succinate	change in pH	181
Human IgG	protein A	galactomannan	addition of tetraborate	182
Alkaline protease	*p*-aminobenzamidine	NIPAA	change in temperature	183
β-Glucosidase	[a]	chitosan	change in pH	184
Hind III restriction endonuclease	λ-phage DNA	NIPAA	change in temperature	183
Xylanase from *Trichoderma viridie*	[a]	Eudragit S 100	change in pH	185
D-Lactate dehydrogenase from *Lactobacillus bulgaricus*	[a]	"	"	186
Endopolygalacturonase from *Aspergillus niger*	[a]	"	"	187
D-lactate dehydrogenase from *Leuconostock mesenteroides ssp. cremoris*	Cibacron Blue	"	"	188
Lactate dehydrogenase, pyruvate kinase from pig muscle	"	"	change in temperature	133
Alcohol dehydrogenase from baker's yeast	"	"	"	134

[a] The target protein exhibits an affinity for the polymer itself.

Another way of separating the target protein from the phase-forming polymer involves the combination of extraction in a two-phase polymer system with affinity precipitation.[194,195] A conjugate of the Eudragit S 100 copolymer with an affine ligand [human immunoglobulin (IgG) (in the purification of recombinant protein A)[194] or Cibacron Blue (in the purification of lactate dehydrogenase)[195]] is added to the polyoxyethylene–hydroxypropylstarch two-phase polymer system. By virtue of the hydrophobic properties of the polymer, the complex of the target protein with the conjugate is extracted into the hydrophobic phase, which is then separated by centrifugation and the target protein–conjugate complex precipitated by acidification. As a result, the recombinant protein A is purified by a factor of 26 (yield 80%),[194] whilst lactate dehydrogenase is purified by a factor of 12 (yield 50%).[195]

An interesting example of the use of the PVCL-based 'smart' polymer has been demonstrated by Galaev et al.[196] Polyvinylcaprolactam forms stable complexes with dyes, including Cibacron Blue, and is sorbed effectively in a chromatographic carrier containing similar ligands (for example Sepharose Blue). At temperatures above the LCT, the polymer exists in the compact conformation, where each polymer molecule can

interact only with a few ligand molecules, leaving the rest accessible for interaction with enzyme molecules. When the temperature is reduced, the PVCL passes to the uncoiled more flexible conformation. Segments of the polymer molecules acquire the ability to interact with a larger number of dye molecules and begin to compete with the sorbed enzyme for the ligand, ultimately displacing it.

Such a system is the first example of the successful purification of an enzyme by elution solely as a result of changing the temperature without any alteration of the composition of the buffer. The column with Sepharose Blue was treated with a solution of PVCL at room temperature and was washed until traces of the polymer were absent from the eluate. At 45 °C, the unpurified pig muscle extract was deposited on this column and was washed in a buffer until the complete absence of the protein from the eluate, after which the column was cooled to room temperature and the homogeneous lactate dehydrogenase was eluted with the same buffer. A 17-fold purification with a yield of 90% was achieved.[196]

The examples described demonstrate the extensive possibilities of the use of 'smart' polymers for increasing the efficiency of traditional methods for the purification of proteins and for the creation of new ones.

4. Immobilisation of biocatalysts

The ability of polymers to form a separate phase in aqueous solutions following a slight change in external conditions can be used to create reversibly soluble biocatalysts, provided that the enzyme molecule is bound covalently to the polymer. The reversibly soluble biocatalyst acquires the advantages of immobilised enzymes (ease of separation from reaction mixture and the possibility of multiple employment) but at the same time it makes it possible to overcome the disadvantages of immobilised and solid matrix enzymes such as diffusional difficulties in the transport of substrates and products (particularly high-molecular mass ones) and the impossibility of using the enzymes in reactions with insoluble substrates or products.

Catalysts which are reversibly soluble as a function of pH have been obtained by the covalent binding of lysozyme to alginate,[197] of trypsin to the acrolein–acrylic acid copolymer,[29] and of cellulase,[198] amylase,[26] α-chymotrypsin, and papain[119] to methacrylic acid–methyl methacrylate copolymers, carboxymethylcellulose, hydroxypropylmethylcellulose phthalate, and cellulose acetate-phthalate. A reversibly soluble cofactor has been obtained by the covalent binding of NAD to alginate with the aid of diepoxyoctane.[199]

Margolin and coworkers[149,151] studied in detail the behaviour of α-chymotrypsin, penicillinamidase, alcohol dehydrogenase, and urease bound covalently to the polyanion or polycation in the nonstoichiometric polymeric complex of polymethacrylic acid and modified poly(*N*-ethyl-4-vinylpyridinium) bromide. The enzymes in the polymeric complexes are readily precipitated from solution on acidification from pH 6.1 to pH 5.7 and are separated by centrifugation. The polymeric precipitate is redissolved in a buffer solution at pH 6.1 and the immobilised enzyme can be used repeatedly. In the precipitate, the α-chymotrypsin bound covalently to the polyanion is entirely accessible to a high-molecular-mass inhibitor, in contrast to the chymotrypsin bound to the polycation, which is accessible to the extent of only 20%. The enzyme bound to the polycation is present within the hydrophobic core of the complex; it is effectively protected by this environment, which increases its thermal stability.[149]

Enzymes which are reversibly soluble as a function of temperature have been obtained by the covalent binding of α-chymotrypsin and penicillinamidase to PVCL,[200] of trypsin,[74] alkaline phosphatase,[178] and thermolysin[201] to poly-NIPAA, and of lipase and wheat germ to the graft-copolymer comprising NIPAA and the acrylamide–acrylic acid copolymer.[202] The reversible flocculation of latexes has been used to obtain reversibly soluble (more precisely reversibly dispersable) biocatalysts also in affinity precipitation. Trypsin[203] and papain[141] preparations were obtained in this way.

Enzymes which are reversibly soluble as a function of Ca^{2+} concentration are formed on covalent binding of phosphoglyceromutase, enolase, peroxidase, and pyruvate kinase to α_{s1}-casein. The enzyme–casein conjugate is soluble at a Ca^{2+} concentration below 20 mM, but is fully precipitated at a Ca^{2+} concentration in excess of 50 mM. When the Ca^{2+}-binding EDTA is added, the precipitate redissolves.[204]

The use of reversibly soluble biocatalysts in reactions which are difficult or impossible to carry out with the aid of enzymes immobilised on insoluble matrices, for example in the hydrolysis of high-molecular-mass substrates (casein,[141,201] dextrin, and starch[26]), in the hydrolysis of insoluble substrates [cellulose[198] and unpurified starch (corn flour)[26,205–208]], and in the preparation of the insoluble benzyl ester of benzyloxycarbonyl-L-tyrosyl-N^{ω}-nitro-L-arginine[119] and of insoluble phenylglycine[209] is of practical interest.

In the hydrolytic cleavage of corn flour to glucose on treatment with amylase, the reaction product (glucose) inhibits the hydrolysis. The use of a reversibly soluble amylase conjugate increases the efficiency of the hydrolysis. The hydrolysis was carried out at pH 5, at which the amylase conjugate is soluble. After each 24 h, the pH was reduced to 3.5, the unhydrolysed solid residue and the precipitated conjugate were separated by centrifugation, the conjugate was redissolved in a fresh portion of the substrate at pH 5, and the hydrolysis was continued. After five repetitions of the cycle, 101 g of glucose was obtained from 150 g (30 × 5) of the unpurified starch. The activity of the amylase after the fifth cycle ws 96% of the initial value.[205]

The cyclic conversion of the unpurified starch to sugar has been used for the preparation of ethanol by fermentation.[205,207,208] The fermentation by yeast in the presence of a biocatalyst was carried out at pH 5 in a reactor with a conical bottom. The fermentation liquid was periodically acidified to pH 4, whereupon the yeast cells flocculated and the biocatalyst precipitated. The precipitate with the unhydrolysed substrate was separated by allowing it to stand for 10 min, after which it was treated with a fresh portion of the substrate. Ethanol was obtained from the supernatant (80% of the initial volume). After five cycles, 61 g of ethanol was obtained from 150 g of the unpurified starch; the productivity was 0.85 g litre^{-1} h^{-1}.[205,207]

Reversibly soluble amylase has been used also to convert (under continuous fermentation conditions) unpurified starch in ethanol[208] or into lactic acid.[206] In the preparation of ethanol, the fermentation, the separation of the cells and the biocatalyst, and their resuspension were carried out in three separate reactors. The continuous fermentation regime made it possible to increase the productivity to 2 g litre^{-1} h^{-1}.[208] A bioreactor with cells of *Lactobacillus casei* suspended in a κ-carrageenan gel was used in the preparation of lactic acid. The amylase conjugate was separated and resuspended in two other reactors. A productivity of 3.1 g litre^{-1} h^{-1} was attained, which is three times higher than for cyclic batch fermentations.[206]

The formation of a water-insoluble polymeric phase by polymers constitutes a convenient method for the immobilisation of enzymes and cells. This process is achieved in the following way: at a temperature below the LCT, the enzyme is dissolved or the cells suspended in a concentrated aqueous solution of the polymer, after which the initial solution is added dropwise to the aqueous solution at a temperature above the LCT. The insoluble polymeric phase formed in the drop 'traps' the enzyme or the cells. After the addition of stabilisers (ovalbumin, egg powder, α-carboxymethylcellulose, tannin) to the initial solution, the polymer particles acquire sufficient stability and do not coagulate on stirring. Trypsin and carboxypeptidase B (stabilised beforehand by covalent binding to the vinylpyrrolidinone–acrolein copolymer),[210] fungal and bacterial cells,[211] and hybridoma cells[212] have been immobilised in a PVCL gel in this way.

The 13:1 NIPAA–vinylferrocene copolymer has been used simultaneously both as a mediator of charge transfer in the enzyme electrode and for the immobilisation of glucose oxidase on the electrode surface.[213–215] At a temperature below 22 °C, the polymer gel film on the surface of the electrode is in a swollen state. The pores in the gel are sufficiently large to allow the permeation of glucose oxidase molecules into their interior and the gel may be 'charged' with the enzyme. At a temperature above 35 °C, the gel collapses, the pores become markedly narrower, and the enzyme is no longer capable of diffusing from the gel, but the gel remains permeable to the low-molecular-mass substrate (glucose). Under these conditions, the glucose concentration is measured with the aid of the electrode. An advantage of such an electrode is the possibility of replacing rapidly and conveniently the inactivated enzyme by fresh enzyme. For this purpose, it is sufficient to wash the electrode below 22 °C in order to remove the inactivated enzyme, charge it with the fresh enzyme, and induce the collapse of the gel by heating it to a temperature above 35 °C.[213]

Thermoresponsive hydrogels were first used for the immobilisation of biocatalysts by Hoffman and coworkers.[216–218] Thus, β-D-galactosidase was immobilised in poly-NIPAA-TH grains (grain size 200–400 μm in the swollen state; critical temperature 37–40 °C). The overall productivity of the bioreactor with the immobilised enzyme at 35 °C differs slightly from its productivity at 30 °C (both temperatures are below the critical temperature). However, cyclic heating and cooling of the reactor between these two temperatures at a rate of 1 °C per minute increases the productivity of the reactor by a large factor. The swelling on cooling and contraction on heating of the TH grains intensify the mass transfer of the substrate and the products into the interior of the grains, the TH operating under these conditions as a pump actuated by a change in temperature and ensuring a more effective supply of the substrate and removal of the products.[217] A similar increase in productivity has been observed also for *Arthrobacter simplex* cells immobilised in poly-NIPAA-TH. The cells catalyse the conversion of hydrocortisone into prednisolone.[218]

Whereas the cyclic heating–cooling between two temperatures below the critical temperature increases the productivity of the bioreactor, heating to a temperature above the critical temperature leads to the complete arrest of the enzymic reaction. The activity of β-D-galactosidase immobilised in poly-NIPAA-TH falls virtually to zero at 50 °C despite the fact that this is the optimum temperature for the soluble enzyme.[219]

exo-1,4-α-Glucosidase has been immobilised in PMVE-TH with a critical temperature of 38 °C. It is noteworthy that the permeability of the TH to the substrate diminishes by five orders of magnitude on heating from 32 to 42 °C, whereupon the reaction stops almost completely. On cooling the TH to 32 °C, the reaction is renewed.[220] A similar effect has been observed also for α-chymotrypsin incorporated in PMVE-TH.[221]

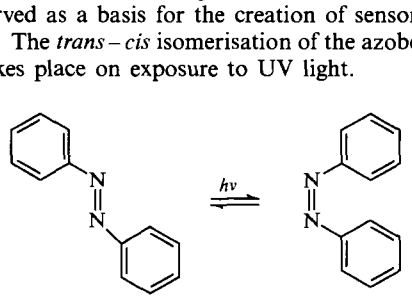
On collapse of the TH, the polymer chains approach one another and the medium within the TH becomes more hydrophobic. Both these factors limit the mobility of the macromolecules incorporated in the gel and hence increase the thermal stability of the immobilised enzyme at temperatures above the critical value.[222] A formal kinetic description of the behaviour of α-chymotrypsin incorporated in a cross-linked poly-NIPAA-TH has been published.[223–225] The temperature dependence of the activity of the immobilised α-chymotrypsin ceases to obey the Arrhenius law at temperatures close to the temperature of the collapse of the NIPAA-TH. This is expressed by the appearance on the Arrhenius plot of a section with an apparent negative activation energy. An increase in the concentration of the cross-linking agent leads to a shift of the break point on the Arrhenius plot towards higher temperatures and to a less marked decrease in the activity of the enzyme.[224]

Thus the biocatalysts obtained by immobilising enzymes and cells with the aid of 'smart' polymers acquire new and unusual properties. They can combine the advantages of homogeneous and heterogeneous catalysts, can serve as convenient 'chemical switches' sensitive to slight changes in external conditions, and are distinguished by a higher productivity as a result of the operation of the 'thermal pump'.

5. Sensor systems

Solutions and hydrogels of 'smart' polymers are sensitive to slight changes in the properties of the external medium, i.e. they function as complete sensors for these properties. For example, a set of solutions of polymers with different LCT can serve as a thermometer. The response of the polymers to changes in the properties of the medium is due to a change in the balance between the hydrophobic and hydrophilic interactions. Covalent binding to the polymer of acceptor molecules capable of undergoing a change in their hydrophobic properties in the presence of the agent to be detected (a definite substance or light) leads to the appearance of two states of the polymer — in the absence of the substance to be detected (characterised by a critical temperature T_1) and in its presence (characterised by a critical temperature T_2). Usually $T_2 > T_1$. If a temperature in the range $T_1 < T < T_2$ is fixed, then the transition from one state of the polymer to the other can be achieved under isothermal conditions with the aid of the agent to be detected. The latter induces a visible change in the solution or hydrogel, which has served as a basis for the creation of sensor systems.[226]

The *trans–cis* isomerisation of the azobenzene chromophore takes place on exposure to UV light.



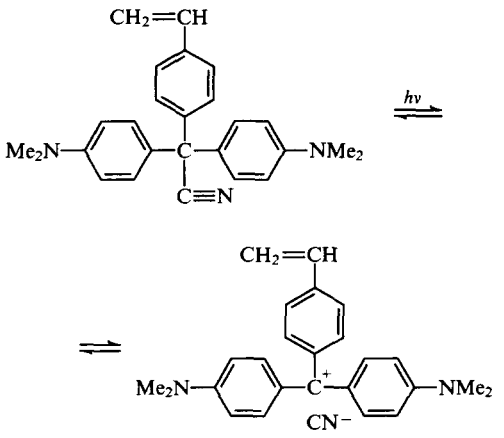
This transition is accompanied by an increase in the dipole moment from 0.5 D (for the *trans*-form) to 3.1 D (for the *cis*-isomer), which indicates an increase in the hydrophilicity of the polymer. The incorporation of a hydrophobic comonomer [*N*-(4-phenylazophenyl)acrylamide] (2.7 mol%) in a copolymer with NIPAA lowers the LCT to 19.4 °C, whilst UV irradiation increases it to 26.0 °C (as a result of the transition of the azobenzene chromophore to the more hydrophilic *cis*-form).[226]

We shall now consider the dimethylacrylamide–4-phenylazophenyl acrylate (7.5 mol%) system.[227] At a temperature slightly above the LCT in the absence of UV irradiation (visible light), the solution is turbid owing to the formation of an insoluble polymeric phase. UV irradiation increases the LCT (from 14 to 21 °C) and the copolymer, which is at a temperature below the LCT, gradually dissolves (the system becomes transparent). When UV irradiation ceases, the LCT is reduced, the copolymer again forms an insoluble polymeric phase, and the system once more becomes turbid. From the foregoing, it is clear that aqueous solutions of most copolymers constitute a sensor responding to UV irradiation.[226]

It is noteworthy that the phase transition in the copolymers becomes sensitive to UV irradiation for a strictly defined content of the acceptor comonomer. This emphasises yet again that the maintenance of a very fine balance between the hydrophobic and hydrophilic interactions is needed for the manifestation of critical phenomena in polymer solutions.

Another molecular acceptor of light quanta is triarylmethyl cyanide (the leuco-derivative of triphenylmethane), which dissociates reversibly on UV irradiation. The NIPAA copolymer containing only 1 mol% of the leuco-nitrile ligands has a LCT of 29.2 °C. After UV irradiation, the copolymer becomes more hydrophilic to such an extent that it loses the capacity for the clearly expressed formation of a polymeric phase following an

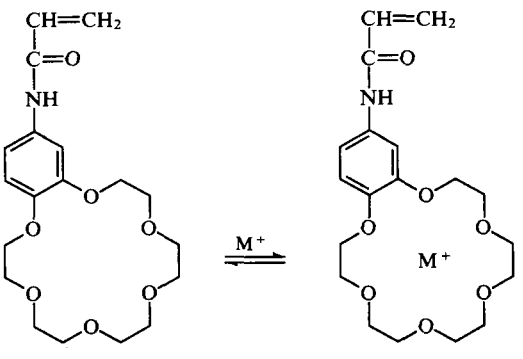
increase in temperature.[227] However, when the leuco-nitrile ligands are incorporated in poly-NIPAA-TH, the critical temperature for the collapse increases from 30 °C in the absence of UV irradiation to 32.6 °C (under UV irradiation). At 32 °C, UV irradiation induces the reversible transition of the gel from the collapsed to the swollen state, whereupon the degree of swelling of the gel changes almost by a factor of 10.[228]



On the other hand, the change in the hydrophilicity of the azobenzene chromophore on UV irradiation is insufficient to induce the collapse. The poly-NIPAA gel containing 10.8 mol% of the chromophore does not collapse, but is gradually dehydrated when the temperature is raised. UV irradiation induces an increase in the degree of swelling by only ~25%,[226] but the change in polarity within the hydrogel and the associated change in its permeability to substrates make it possible to regulate the activity of the enzymes immobilised in polyacrylamide gels containing photosensitive ligands.[229-231]

Another approach involves the use of heat derived from the absorbed light to raise the temperature of the TH, which leads to the collapse of the gel. Thus illumination of poly-NIPAA-TH containing Cu-chlorophyllin as the chromophore, with the power of the illumination exceeding 85 mW, at 31.5 °C results in the collapse of the gel.[232]

The change in the hydrophobicity of the acceptor molecule needed for the isothermal transition of the polymer from one state to another may be induced not only by UV irradiation but also by the introduction of various additives.[226,233] Thus the copolymer of NIPAA with the crown-ether **9** (11.6 mol%) has a LCT of 31.5 °C. In the presence of Na^+, the LCT increases to 33.0 °C, whilst in the presence of K^+ it increases to 38.9 °C. Thus the introduction of Na^+ and K^+ cations leads to the dissolution of the copolymer at 32 °C, the copolymer being insoluble in their absence. At 37 °C, this effect is induced only by the addition of K^+ cations. A similar effect has been observed also for poly-NIPAA-TH containing 12 mol% of the crown-ether. The thermoresponsive hydrogel which has collapsed at 33.8 °C swells by a factor of 10 in the presence of 30 mM potassium sulfate.



9

The thermoresponsive hydrogel can be caused to pass from one state to another also under the influence of the products of the reaction catalysed by the enzyme immobilised in the TH. For example, the TH of the NIPAA–acrylic acid copolymer with immobilised urease collapses at 32.4 °C. When urea is added to the collapsed gel (at 33.4 °C), the enzymic reaction results in the formation of ammonia, which increases the pH of the medium. Under these conditions, the LCT of the copolymer increases and the gel swells, its volume increasing by a factor of 7 in 15 min.[234] In a buffer without urea, the TH collapses again.

Rabbit liver esterase hydrolyses the nonpolar ethyl butyrate to more polar products — ethanol and butyric acid. The change in polarity occurring under these conditions is sufficient to induce the swelling of the collapsed poly-NIPAA-TH.[235]

Concanavalin A (a lectin) immobilised in poly-NIPAA-TH can bind various carbohydrates, including the negatively charged dextran sulfate and the neutral methyl α-D-mannopyranoside. Dextran sulfate bound to concanavalin A increases the swelling of the collapsed gel by a factor of 5 as a result of the mutual repulsion of the negative charges on dextran sulfate. The displacement of dextran sulfate by the neutral methyl α-D-mannopyranoside again induces the collapse of the gel. The swelling–contraction cycle can be repeated many times with excellent reproducibility.[235]

The examples quoted above demonstrate the extensive possibilities of the employment of 'smart' polymers for the creation of exceptionally simple, reliable, and fairly sensitive sensor systems. However, this does not exhaust all the possibilities. The phase transition in solutions of such polymers has been used by Hoffman and coworkers[237-239] to devise a new method of precipitation immunoassay (PRECIPIA). The essential features of this method are explained in Fig. 7. *N*-Isopropylacrylamide was copolymerised with monoclonal antibodies to the κ-chain of human immunoglobulin G (IgG) modified by *N*-hydroxysuccinimidylacrylamide. The polymeric conjugate was incubated for 1 h at room temperature with the IgG solution being analysed, poly-NIPAA (to facilitate the thermoprecipitation of the conjugate), and monoclonal antibodies to the γ-chain of human IgG labelled with fluorescein or phycoerythrin. The temperature was raised to 45 °C, the resulting polymeric phase was separated by centrifugation and dissolved in a cold buffer solution, and the fluorescence was measured.

This system is not inferior as regards sensitivity to the traditional heterogeneous immunoassay methods, but makes it possible to overcome their significant disadvantage — the need for incubation in the course of many hours due to the diffusional hindrance to the interaction of the antigen with the antibody immobilised on an insoluble matrix. Since the antigen–antibody interaction during precipitation immunosassay takes place in solution, the incubation time can be shortened to only 1 h.[237-239]

6. Controlled delivery of medicinal drugs

An effective medicinal preparation is not simply a chemical substance but one which is supplied at an appropriate time and at an appropriate place in the organism. The creation of systems for the directed transport and controllable delivery of medicinal substances is one of the hot spots in modern pharmacochemistry. A significant role is assigned to polymers in this process.[68,240,241] Above we have already spoken of the industrial employment of reversibly soluble polymers for the formation of a protecting shell around peroral medicines.

The use of hydrogels for the controllable delivery of medicines is based on their ability to undergo a sharp change in the degree of their swelling and hence in their permeability in response to changes in the medium. The pathological processes occurring in the organism are as a rule associated with changes in the pH, temperature, and concentrations of specific substances. Thus it becomes possible to create systems with feedback, where the pathological process initiates the release of the medicinal drug.

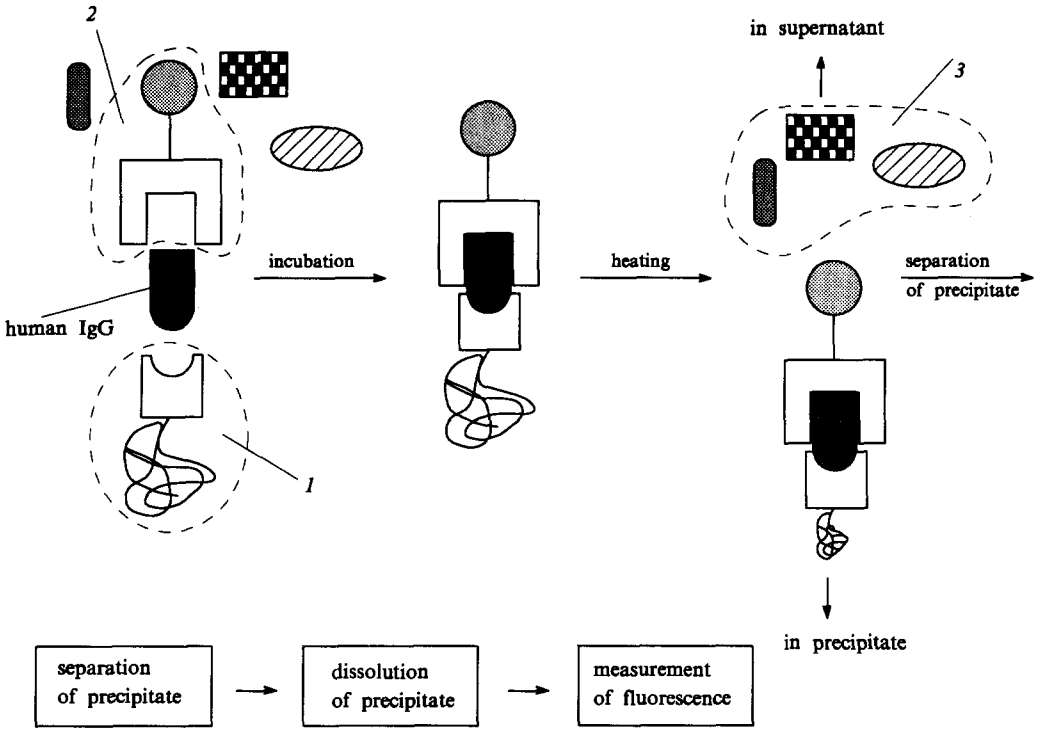


Figure 7. The precipitation immunoassay method.[237] (*1*) Conjugate of poly-NIPAA with monoclonal antibodies to the κ-chain of human IgG; (*2*) monoclonal antibodies to the γ-chain of human IgG with a fluorescent label; (*3*) extraneous proteins.

The gel in the swollen state is 'charged' with the medicinal drug. In the collapsed state, the gel does not give up the drug, diffusion becoming possible only after the swelling of the gel. The transition of the gel from the collapsed to the swollen state may be induced by various factors. Thus the change in the pH of the medium from 5 to 7 leads to the virtually complete arrest of the liberation of caffeine from the gel based on the copolymer of ketyl methacrylate and 2-(*N*,*N*-dimethylamino)ethyl methacrylate.[33] On the other hand, UV irradiation accelerates the diffusion of *p*-aminobenzoate from the poly(2-hydroxyethyl methacrylate) gel containing the azobenzene chromophore.[242] The formation of a charge-transfer complex between triethylamine and the copolymer of 2-hydroxyethyl methacrylate and methacryloyl-β-hydroxyethyl 3,5-dinitrobenzoate increases the swelling of the polymer membrane in water and hence the liberation of Methyl Orange from it.[243] An electric potential of 3–6 V initiates the liberation of edrophonium chloride from the gel based on the butyl methacrylate–2-acrylamido-2-methylpropanesulfonic acid copolymer. In the absence of an electric field, the positively charged medicinal drug is not liberated owing to its interaction with the negatively charged polymer.[244]

The liberation of glucose, insulin, or indomethacin from TH based on the copolymers of NIPAA and alkyl methacrylates ceases completely when the temperature is raised from 20 to 30 °C and is renewed on subsequent cooling to 20 °C. The thin film of the collapsed polymer, formed on the surface of the TH grains when the temperature is raised above the critical value, plays a critical role in the regulation of the diffusion process.[92,244–250] A similar sharp retardation of diffusion as a result of the formation of a collapsed gel film on the surface has been observed also for TH based on interpenetrating polymer networks comprising polyacrylic acid and the acrylamide–butyl methacrylate copolymer.[251] The kinetics of the release of the medicinal drug can be regulated (changing the reaction order from zeroth to first) by altering the nature of the TH, for example by employing interpenetrating polymer networks of poly-NIPAA and poly(methylene glycol ether) of different compositions.[252,253] When the TH collapses rapidly, there is a possibility of the formation of solution-filled cavities, the contents of which are not involved in the exchange with the surrounding medium.[92]

The reversible sorption on the surface of latex particles may be used for the temperature-controlled release of substances. Up to 65% of fluorescence-labelled dextran (M = 70 000), sorbed by the poly-NIPAA latex, is released into the solution on heating. When the temperature is reduced, the entire desorbed dextran is again bound to the latex.[138]

The most interesting approach has been developed by Hoffman and coworkers.[254,255] The authors used hydrogels sensitive to changes both in the pH and temperature. At 37 °C and pH 1.4 (the conditions within the stomach), the TH based on copolymers of NIPAA with acrylic acid and polydimethylsiloxane are in the collapsed state. Indomethacin or amylase, incorporated in the TH grains, hardly diffuse to the outside. At 37 °C and pH 7.4 (the conditions within the intestine), the TH swells markedly and the substances incorporated in it are rapidly released to the surrounding medium: more than 90% of indomethacin is released after 5 h. Thus a system has been created with directional transport and a prolonged release of the medicinal drug.

The creation of an artificial pancreas, i.e. a device releasing insulin in response to changes in the concentration of glucose, makes it possible to solve serious problems in the treatment of the numerous patients suffering from sugar diabetes. The development of such systems is therefore arousing unflagging interest.[256] Definite advances on these lines have been achieved by employing 'smart' polymers. The enzyme glucose oxidase, which oxidises glucose to gluconic acid, is usually employed as the glucose sensor. This reaction is accompanied by a decrease in pH, which in fact initiates the release of insulin. Technically this is achieved in different ways, for example by employing a membrane consisting of the 60:20:20 2-hydroxyethyl acrylate–*N*,*N*-diethylaminomethacrylate–4-trimethylsilylstyrene copolymer. In the swollen state, such a membrane contains 30% of water at pH 6.3 and 53% at pH 6.15, its permeability to insulin increasing in this case by a

factor of 42. Capsules made of this copolymer and containing glucose oxidase and insulin released insulin approximately five times faster in the course of 2–3 h in the presence of 0.2 M glucose. After the removal of glucose, the rate of release of insulin fell to the initial value.[257]

The swelling of the gel in the presence of glucose has been used in a mechanical device consisting of two compartments. The first compartment contained a glucose-sensitive gel and the second a solution of insulin. The solution of insulin was simply forced out by the swollen gel from the device through a valve.[33]

The complex of poly(vinyl alcohol) with the vinylpyrrolidinone–*m*-acrylamidophenylboronic acid may be used as the glucose sensor instead of glucose oxidase.[157] In this case, the hydroxy-groups of glucose displace the hydroxy-groups of poly(vinyl alcohol), as a result of which the polymeric complex decomposes. When glucose has been removed, the complex is reformed. A communication concerning the creation of an artificial pancreas operating in accordance with a similar principle has appeared recently.[258]

An interesting approach to the employment of 'smart' polymers for the controllable delivery of medicinal drugs has been proposed by Tirrell.[259] Among the numerous polyelectrolytes, polyethylacrylic acid possesses the fairly unique ability to undergo a change in conformation in the physiological pH range 7.4–6.5. The transition from the uncoiled to the compact conformation is accompanied by intensification of the interaction of the polymer with lipid membranes.[260] Poly-ethylacrylic acid, immobilised covalently on the surfaces of the vesicles formed by phosphatidylcholine, induces a reorganisation of the large vesicles on transition to the compact conformation, converting them into more compact micelles. The contents of the vesicles are then released into the external medium.

IV. Conclusion

The author hopes that he has succeeded in demonstrating the extensive possibilities for the employment of 'smart' polymers in various branches of biotechnology and medicine. There is no doubt that the examples presented do not exhaust all the possibilities. This field is developing dynamically judging from the constantly growing number of publications. For example, a communication has appeared quite recently[261] stating that the graft-copolymerisation of NIPAA makes it possible to convert a hydrophilic surface (at a temperature below the LCT) into a hydrophobic one (at a temperature above the LCT). This may be used for the directed transport of microparticles with a medicinal drug in the organism or for the segregation and purification of biomolecules (hydrophobic chromatography). The cells of microorganisms also interact in different ways with hydrophilic and hydrophobic surfaces.

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Specific features of the reactivity of organotellurium compounds

I D Sadekov, V I Minkin

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Abstract. The characteristic features of the reactivity of the principal classes of organic compounds of tellurium(II) and tellurium(IV) are examined and compared with the analogous compounds of sulfur and selenium. The factors determining the specific features of the chemical behaviour of organotellurium compounds are characterised. It is shown that the possibility of the convenient introduction of tellurium-containing functional groups, their structural modification, elimination, the low-temperature elimination of the tellurium atom as a result of the low energy of the C – Te bond, and the high nucleophilicity of the tellurolate anions and diorganyl tellurides together with other properties create preconditions for the development of a new methodology in organic synthesis. The bibliography includes 446 references.

I. Introduction

The first representative of organotellurium compounds — diethyl telluride — was obtained by Woehler[1] more than 150 years ago, but the principal data concerning the method of synthesis, reactivity, and structure of organic derivatives of tellurium have been obtained during the last 20 – 25 years. These compounds have been considered in monographs,[2–5] while individual classes of acyclic and cyclic tellurium-containing compounds have been the subject of review articles.[6–22] Together with profound analogies between the structure and reactivity of organic compounds of tellurium and [other] higher chalcogens, the studies which have been carried out have revealed significant characteristic features of the chemical behaviour of organotellurium compounds compared with their sulfur and selenium analogues. The present authors' previous review was devoted to the structure of the latter.[23] The present, more complete review takes into account new data which have accumulated during recent years. All the research results analysed are classified in terms of the specific features of organotellurium compounds which distinguish them from those of the other chalcogens and not in terms of the individual classes of such compounds, as was done in previous reviews.[23]

The specific structure and chemical behaviour of organic derivatives of tellurium are determined mainly by the following factors.

1. The increased nucleophilicity and halophilicity of the RTe^- and Te^{2-} anions compared with those of the other organochalcogen derivatives.

2. The reduced thermodynamic and kinetic stability of the tellanyl derivatives RTeX.

3. The ability of the tellurium atom in various coordination states to form extremely stable (compared with sulfur and selenium atoms) intramolecular coordinate bonds with electron-excess centres (oxygen, nitrogen), which play an important role in the stabilisation of the corresponding organotellurium compounds and which influence the stereochemistry of their reactions.

4. The unusual tendency of derivatives of dicoordinate tellurium — diorganyl tellurides R_2Te and diorganyl ditellurides R_2Te_2 — to enter into oxidative addition reactions with formation of structures containing tellurium in the Te(IV) and Te(VI) oxidation states.

5. The fact that the nucleophilicity of diorganyl tellurides is the highest in the series of diorganyl chalcogenides R_2M (M = O, S, Se, Te).

6. The high polarisation of the $Te=X \rightleftarrows Te^+ - X^-$ bonds (X = CR_2, NR, O) which is responsible for the specific reactions of π-telluranes.

7. The sharply increased stability of derivatives of tetracoordinate tellurium — σ-tellanes R_2TeX_2 and $RTeX_3$ as well as tetraorganyltellanes R_4Te — compared with the analogous selenium and sulfur derivatives.

8. The low energy of the C – Te bond (compared with those of the C – S and C – Se bonds).

These specific properties are responsible for the increasing application of organotellurium compounds in preparative organic chemistry (see the relevant reviews[24–31]).

I D Sadekov, V I Minkin Institute of Physical and Organic Chemistry of the Rostov State University, prosp. Stachki 194/3, 344104 Rostov-on-Don, Russian Federation. Fax (7-863) 228 56 67

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II. Nucleophilic and halophilic properties of tellurolate and telluride anions

The usual methods of synthesis of organic anions RM^- containing Group VIA elements (M = O, S, Se) from the corresponding hydride derivatives RMH are virtually impossible to apply in the case of their tellurium analogues. Until recently, only a few alkanetellurols had been described. These are thermally unstable and are extremely readily oxidised to ditellurides not only by atmospheric oxygen[2,3] but even by dilute H_2SO_4;[32] tellophenols have not been isolated in a pure form. (Trimethylsilyl)silanetellurol[33] $(Me_3Si)_3SiTeH$ and 2,4,6-trialkyltellurophenols[34] 2,4,6-$R_3C_6H_2TeH$ (R = Me, Pr^i, Bu^t), obtained by protonating the lithium salts of tellurols, are relatively stable by virtue of the presence of bulky organic groups. The organyltellurolate anions **1** are therefore usually obtained by reducing diorganyl ditellurides with alkali metal tetrahydroborates in alcohol or a benzene–alcohol mixture[2,3] and with alkali metals in liquid ammonia,[2,3,32,35–38] ether,[39] tetrahydrofuran (THF),[40,41] THF–dimethylformamide (DMF),[42] and hexamethylphosphoramide (HMPA)[43] or by the reactions of organolithium derivatives with elemental tellurium in ether or THF.[2,3] The tellurolate anions are oxidised extremely readily even by atmospheric oxygen and are therefore employed only in situ. These anions exhibit the highest nucleophilicity in the series of analogous derivatives of Group VIA elements. Although there are hitherto virtually no quantitative literature data on the nucleophilicity parameters of the tellurolate anions (such as the Swain–Scott parameter n[44] or the Ritchie parameter N_+[45]), the high basicity and polarisability of RTe^- guarantee that their nucleophilicity is even higher than the current record holders on these scales — the RS^- and RSe^- anions.

Quantitative kinetic data on the relative reactivities of the benzenechalcogenolate anions PhM^- (M = S, Se, Te) have been obtained only for $S_{RN}1$ reactions. In the interaction of 2-quinolinyl radicals, the relative rate constants increase in the sequence PhS^- (1.0) < $PhSe^-$ (5.8) < $PhTe^-$ (28.0),[46] while in the case of the 9-anthranyl radicals the increase is in the sequence PhS^- (1.0) < $PhSe^-$ (1.4) < $PhTe^-$ (3.2).[47]

By virtue of their high nucleophilicity, the tellurolate anions **1** readily add both to activated (α-ethynylcarbonyl compounds[43,48–55]) and nonactivated triple bonds,[43,50,52,53,55–58] which leads to the vinyl tellurides **2** and **3** in high yields.

$$R^1C{\equiv}CCOR^2 + ArTe^- \longrightarrow \underset{\mathbf{1}}{} \underset{TeAr}{R^1C{=}CHCOR^2} \quad \mathbf{2}$$

R^1 = Alk, Ar; R^2 = H, Alk, Ar, OR.

$$R^1C{\equiv}CH + R^2Te^- \longrightarrow \underset{\mathbf{3}}{R^1CH{=}CHTeR^2}, \quad \underset{TeR^2}{R^1C{=}CH_2} \quad \mathbf{3a}$$

R^1 = Alk, Ar, CH_2OH; R^2 = Ar, Me.

The addition of the tellurolate anions to activated triple bonds is regiospecific and is always accompanied by the formation of only type **2** compounds. In the case of the esters of ethyne-1-carboxylic acids, only the (*Z*)-isomers or mixtures of (*Z*)- and (*E*)-isomers with the former greatly predominating (more than 90%) are formed.[51] The preferential formation of (*Z*)-isomers was observed also in the reactions of activated ethynes, but these reactions are less regiospecific and, together with compounds **3**, the formation of the isomeric alkenes **3a** is observed.[53,55,58]

The addition of potassium telluride, generated from tellurium in a superbasic medium [KOH/HMPA(DMSO)/H_2O], first investigated by Trofimov et al.,[59] leads to vinyl telluride as the main product. (For further details about this and similar reactions, see the review of Gusarova et al.[12]) (*Z*)-Divinyl tellurides **4** have been synthesised in high yields by the reaction of Na_2Te (obtained by the reduction of tellurium with sodium tetrahydroborate in an aqueous alcoholic solution of NaOH) with monosubstituted ethynes.[58] In certain cases, the 1,1-disubstituted isomers **4a** are formed in yields up to 10% together with the tellurides **4**.[58]

$$RC{\equiv}CH + Na_2Te \longrightarrow \underset{\mathbf{4}}{(RCH{=}CH)_2Te}, \quad \underset{\mathbf{4a}}{(H_2C{=}CR)_2Te}$$

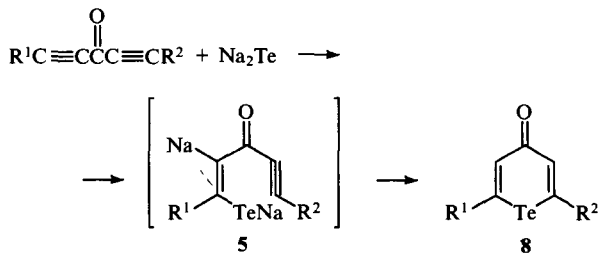
R = Ph, 4-ClC_6H_4, 4-BrC_6H_4, 4-MeC_6H_4, 4-$MeOC_6H_4$,

$HOCH_2CH{=}CMe$, $\overline{CH_2CH_2OCH_2CH_2NCH_2}$,

$\overline{CH_2(CH_2)_4CH{=}C}$, $\overline{CH_2(CH_2)_3OCHOCH_2}$.

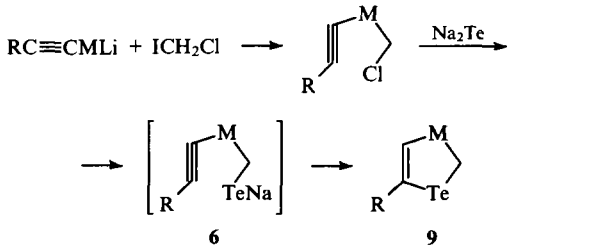
The intramolecular nucleophilic addition reactions of the tellurolate anions **5**–**7**, formed as intermediates in the interaction of Na_2Te with the corresponding ethynes, have been used for the synthesis of certain tellurium-containing heterocycles which are difficult to obtain by other methods. 2,6-Diorganyltellurapyran-4-ones **8**,[60–64] 2-*H*-1,3-thiatellurols **9** (M = S),[65] 2*H*-1,3-ditellurols **9** (M = Te),[66] and 1-thia-4-telluracyclohexa-2,5-dienes **10**[67] have been obtained by this procedure (Scheme 1).

Scheme 1

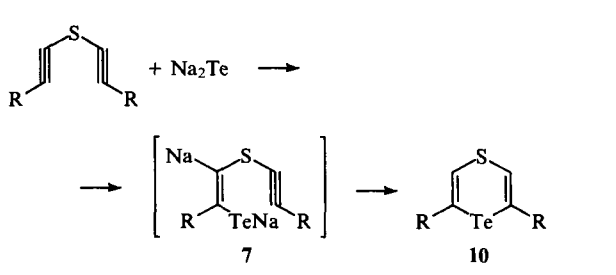


$R^1 = R^2$ = $SiMe_3$, Me, Bu^t, Ph; R^1 = Ph,

R^2 = $SiMe_3$, H, $(CH_2)_3OH$, 2-C_4H_3S, $(CH_2)_3OSiMe_2Bu^t$, 4-FC_6H_4, 2,5-$F_2C_6H_3$, 4-$MeOC_6H_4$.



M = S, R = Me, Et, Bu^t, Ph; M = Te, R = H, Me, Et, Ph.



R = H, Me, Bu^t.

In the last case, sodium telluride reacted much faster than sodium selenide and especially sodium sulfide.

The reactions involving nucleophilic addition of arenetellurolate anions to an activated double bond have been much less investigated.[57,68] A series of β-aryltellurapropionic

acids,[68] their esters,[57] and β-phenyltellurapropionitriles[57] have been synthesised with their aid in 31%–62% yield.

$$R^1CH{=}CHCOOR^2 + ArTe^- \longrightarrow ArTeCHCH_2COOR^2 \quad (R^1)$$

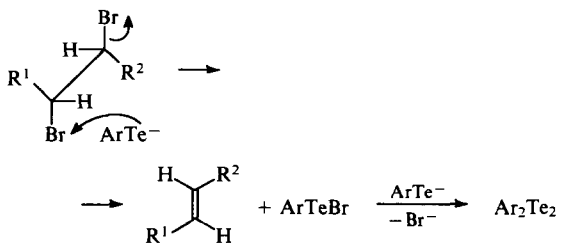
R^1 = H; R^2 = Na; Ar = Ph, 4-MeC_6H_4, 4-$EtOC_6H_4$;

R^1 = H, Me; R^2 = Et; Ar = Ph.

$$RCH{=}CHCN + PhTe^- \longrightarrow PhTeCHCH_2CN \quad (R)$$

R = H, Me.

Organyltellurolate anions are not only more nucleophilic than other chalcogenolate anions but also exhibit more clearly expressed X-philic properties[69] (especially halophilic properties). As a result of this, sodium thiophenetellurolate debrominates vicinal dibromides, affording alkenes in 75%–100% yields.[70] This reaction, which proceeds with high *anti*-stereospecificity, is of definite preparative value, since it can be carried out catalytically in the presence of small amounts of ditelluride (1 mmol per 10 mmol of the halogen-containing substrate) and $NaBH_4$, which reduces the ditelluride obtained back to the tellurolate anion.

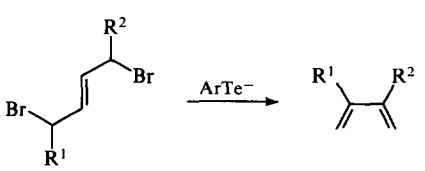


Ar = 2-C_4H_3S; R^1 = R^2 = Me, Ph, CO_2Et; R^1 = H; R^2 = C_8H_{17};

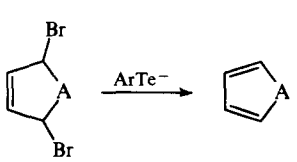
R^1 = CO_2H; R_2 = Me, Ph; R^1+R^2 = —$(CH_2)_4$—.

It is noteworthy that substituted 1,2-dibromocyclohexanes undergo similar debrominations also on treatment with sodium thiophenoxides.[71,72] However, in the case of 1,2-dihaloethanes only the products of the nucleophilic substitution of the halogen atoms by phenylthio-groups are formed.[73]

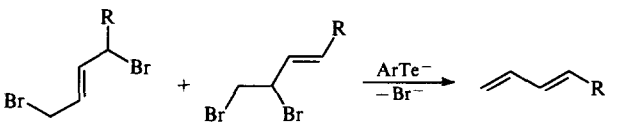
On the other hand, just as the debromination of the vicinal dibromo-derivatives described above is an example of β-halophilic elimination, the synthesis of 1,3-dienes from 1,4-dibromoalk-2-enes or their mixtures with 1,2-dibromoalk-3-enes on treatment with di(2-thienyl)ditelluride, used in catalytic amounts, and $NaBH_4$ is a δ-halophilic elimination reaction.[74] The reactions take place with high yields (60%–100%) and lead to mixtures of the (*E*)- and (*Z*)-isomers in proportions of ~9 : 1.



R^1 = R^2 = Me, Ph.



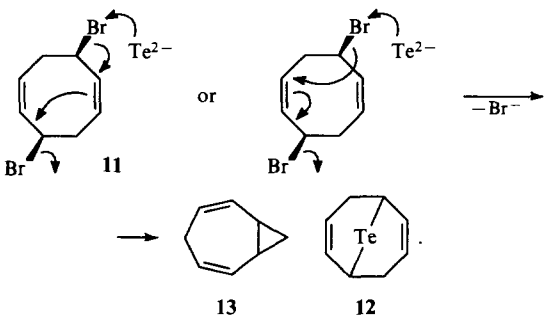
A = —$(CH_2)_2$— , —$(CH_2)_3$— , —$CH(CO_2Me)$—.



R = Et, Bu, C_6H_{13}, $(CH_2)_7OAc$, $(CH_2)_8OAc$, $C_{12}H_{25}$.

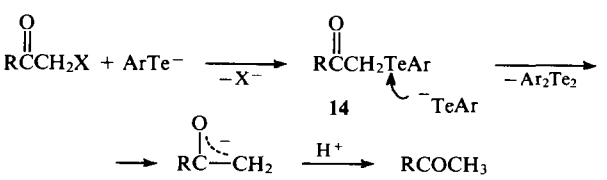
Examples of elimination of a similar kind are not known for the sulfur and selenium nucleophiles.[69]

An instance of ε-halophilic elimination is also known for the telluride anion.[75] Thus, when 3,7-dibromocycloocta-1,5-diene **11** reacts with Na_2Te, bicyclo[5.1.0]octa-2,5-diene **13** is formed together with the expected 9-tellurabicyclo[3.3.1]nona-2,6-diene **12** (yield 18%) in accordance with the following scheme:



An analogous reaction is not observed when Na_2S is employed.

Another possible type of X-philic reaction — the reduction of C–Hal bonds — occurs when sodium (lithium) 2-thiophenetellurolate interacts with α-halocarbonyl compounds. For stoichiometric amounts of the reactants, the final reaction products are the corresponding ketones (or carboxylic acids) and ditellurides and not the products of the nucleophilic substitution, i.e. (2-thienyltelluro)carbonyl derivatives.[76] This is the result of the attack by the tellurolate anion on the tellurium atom of the intermediate tellurides **14**, which leads to the ditellurides and the corresponding enolates. This mechanism has been confirmed both by the isolation in certain cases of type **14** tellurides (R = $CH_2CONHPh$) and by the formation of the benzaldehyde chalcone (yield 48%) when the enolate (R = Ph) is used as the trapping agent.



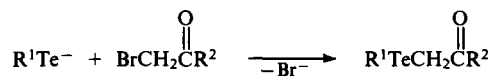
X = Cl, Br, I; R = Ph, 4-BrC_6H_4.



X = Cl, Br; R^1 = H, R^2 = Ph, 1-$C_{10}H_7$; R^1 = R^2 = Ph.

Similar results had been obtained earlier for the thiolate[77,78] and selenolate[78] anions. However, for these species the preferred mode of reaction (reduction or nucleophilic substitution) is determined primarily by the nature of the halogen. For stoichiometric amounts of the reactants and at reduced temperatures, α-chloro- and α-bromoketones afford mainly the products of nucleophilic substitution, while α-iodoketones give rise to the products of the reduction reactions. Tellurolate anions reduce all α-haloketones to ketones at room temperature.[76] However, at a very low temperature (−78 °C)

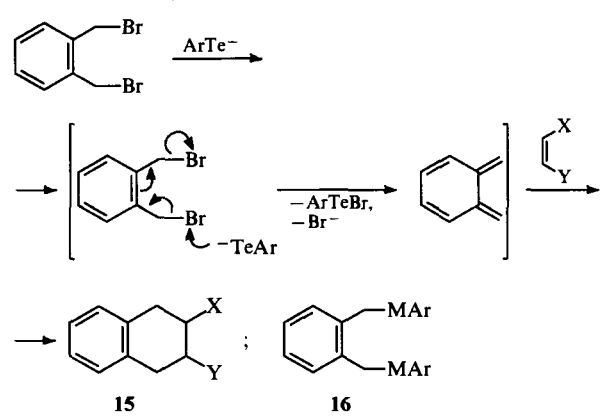
α-bromocarbonyl compounds afford the α-organyltellura-carbonyl compounds **14a** in fairly high yields (55%–92%) on interaction with tellurolate anions.[79] On the other hand, α-chloroketones are reduced even at −78 °C.



R^1 = Bu, Ph, CH_2=CH, BuC≡C, Me_3SiC≡C;

R^2 = OR^3 (R^3 = Li, Et, 4-$NO_2C_6H_4$).

The available data do not permit the quantitative characterisation of the halophilicities of S, Se, and Te organyl-chalcogenolate anions. However, bearing in mind the higher halophilicity of the methaneselenolate anion compared with the sulfur analogue (in the reaction with benzyl halides[80]) and the easy reduction of phenacyl phenyl sulfide by the thiophene-2-tellurolate anion,[76] one could postulate that the halophilicity increases from S to Te. The higher halophilicity of the tellurolate anions compared with the structurally related selenolate anions is indicated also by the result of the reactions of α,α′-dihalo-*o*-xylenes with these anions.[81] In the presence of an excess of the dienophile, the reactions of α,α′-dibromo(iodo)-*o*-xylenes with arenetellurolate anions (generated by the reduction of the corresponding diaryl ditellurides with $NaBH_4$) in boiling xylene, which proceed via the intermediate formation of *o*-quinodimethane, lead to the Diels–Alder adducts **15** in 20%–53% yields. The most probable mechanism of these reactions[81] is presented below.



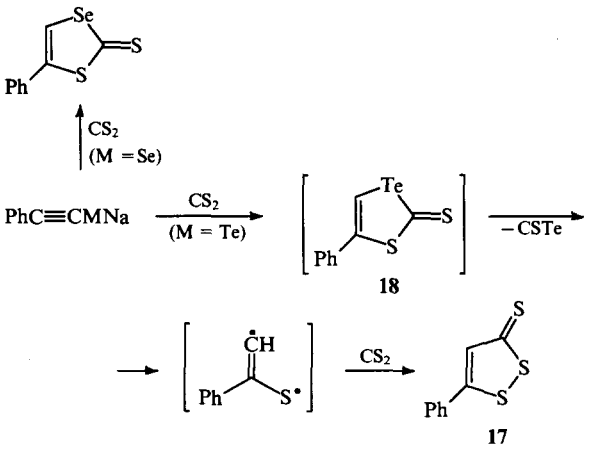
15 **16**

Ar = Ph, 3-MeC_6H_4, 3-ClC_6H_4, 4-$MeOC_6H_4$;

X = Y = CO_2Et; X = H, Y = CO_2Et, CN, Me.

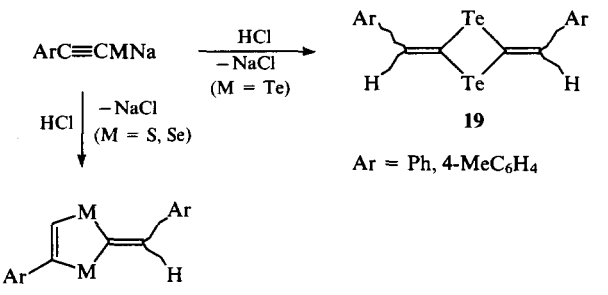
Under the same conditions, sodium benzeneselenolate gives rise to only the product of nucleophilic substitution at the C(sp^3) atoms — α,α′-bis(phenylseleno)-*o*-xylene **16** (M = Se) in 75% yield together with the product of nucleophilic addition to the double bond — ethyl phenylselenopropionate — when ethyl acrylate is employed as the dienophile.[81] Incidentally, the α,α′-bis(aryltello)-*o*-xylenes **16** (M = Te) are also formed in the reaction of arene-tellurolate anions, since the product of the oxidation of compounds **16** — *o*-phthalic aldehyde — has been isolated in ~30% yield in all cases. The preferential formation of the telluride **16** (M = Te, Ar = 4-$EtOC_6H_4$) (yield 50%) has also been observed when the reaction was carried out at room temperature.[82]

The reactions examined below, the mechanisms of which are frequently obscure, are evidently not associated with the nucleophilic or halophilic properties of the organyltellurolate anions. However, the diversity of these reactions compared with the other RM^- (M = S, Se) anions makes it possible to consider them in the present section. In particular, a specific behaviour compared with ethynethiolate(selenolate) anions and geminal dithiolate (diselenolate) dianions, has been observed in certain reactions of their tellurium analogues. Thus, in contrast to sodium phenylethyneselenolate, which affords 5-phenyl-1,3-thia-selenole-2-thione on interaction with CS_2,[83] the product obtained in the similar reaction of sodium phenylethynetellurolate was 5-phenyl-1,2-dithiole-3-thione **17**.[84] The possible process mechanism, involving the dissociation of the C–Te bond in the intermediate 1,3-thiatellurole **18**, is presented below.[84]



18 **17**

Another example of the specific behaviour of the phenyl-ethynetellurolate anion is its protonation (in solution in DMSO) by an ethereal solution of HCl. The only products of this reaction are the *cis*- and *trans*-1,3-ditelluretanes **19**[84–86] and not their isomers — benzylidene-4-aryl-2*H*-1,3-ditelluroles, which was suggested[87] when the reaction was first described. A mixture of the same compounds **19** is also formed in the reaction of phenyl-ethyne with powdered tellurium under highly basic conditions.[88] On the other hand, the protonation of structurally similar thiolate and selenolate anions leads to the benzylidene-4-aryl-2*H*-1,3-dichalcogenoles **20**.[89]



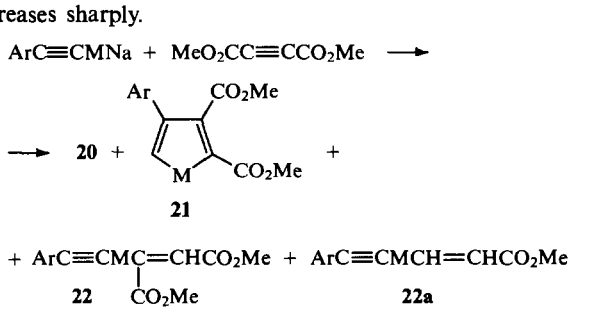
19

Ar = Ph, 4-MeC_6H_4

20

Ar = Ph

The interaction of phenylethynechalcogenolate anions with dimethyl ethynedicarboxylate results in the formation of a mixture of the corresponding chalcogenophenes **21**, the 1,3-dichalcogenoles **20**, and the products **22** and **22a** of the nucleophilic addition of the anions to the triple bond.[84,90] On passing from sulfur to tellurium, the yield of such adducts increases sharply.

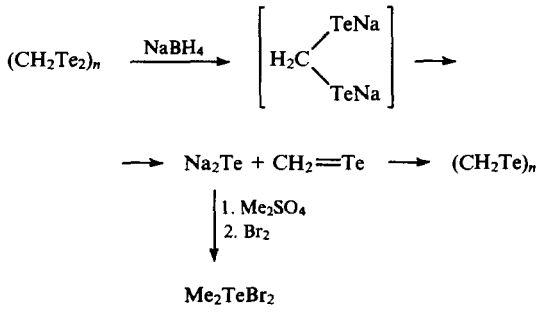


21

22 **22a**

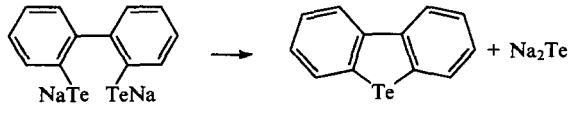
M = S, Se, Te

Significant differences have been observed also in the behaviour of geminal dichalcogenolate anions. Whereas the disodium salt of methanediselenol[91] is fairly resistant to heating and undergoes in solution the usual chemical reactions, its tellurium analogue, obtained by reducing poly(methylene ditelluride)[92] with $NaBH_4$ in ethanol, readily disproportionates to sodium telluride and telluromethanol, which polymerises subsequently to poly(methylene telluride).[93]

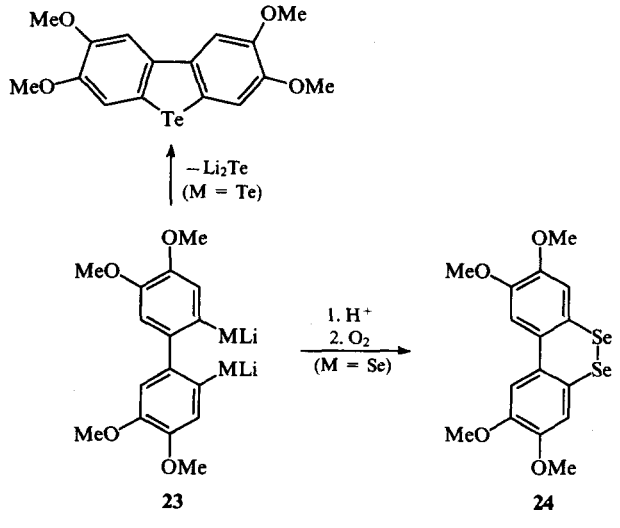


The mechanism of the formation of poly(methylene telluride) involving the reduction of poly(methylene ditelluride) with $NaBH_4$ in methanol and the subsequent alkylation of the ditellurolate dianion by methylene bromide (iodide) therefore appears erroneous.[94] Evidently, poly(methylene telluride) is formed via the disproportionation of the dianion, as described above, and not as a result of the alkylation reaction.

The sodium salt of bipyridyl-2,2'-ditellurol also undergoes a similar disproportionation with elimination of sodium telluride.[95] The second reaction product, isolated in a yield exceeding 90%, is dibenzotellurophene.



With the aid of this reaction, it is possible to account for the formation of various final products in the reactions of 2,2'-dilithio-4,4',5,5'-tetramethoxybiphenyl with tellurium and selenium.[96] In the former case, the product is the corresponding dibenzotellurophene, while the dilithio-derivative of the diselenole **23** (M = Se), which is incapable of undergoing the disproportionation reaction described above, is converted into the heterocyclic diselenide **24**, albeit in a very low yield.



23 **24**

III. Kinetic lability of organotellanyl halides

In contrast to the selenium and especially sulfur analogues, the tellanyl derivatives RTeX (X = Hal, OCOMe, SCN, N_3) are relatively unstable compounds, which readily decompose at room temperature both in the crystalline state and in solution.

Tellanyl halides, which are mainly aromatic derivatives, have been most thoroughly investigated among the tellanyl derivatives. The stability of arenetellanyl halides ArTeX increases in the sequence Cl < Br < I as the electronegativities of the atoms in the Te–X bonds approach equality. Thus the bromo-derivatives decompose fully at room temperature in 24 h, while arenetellanyl iodides in the crystalline state can be stored without decomposition for several weeks.[97] In the case of alkanetellanyl halides, the chloro-derivatives are more stable, while alkanetellanyl iodides decompose in several minutes.[98] The overall mechanism of the decomposition of aryltellanyl halides involves the formation of diorganyltellurium dihalides and elemental tellurium.[26,99]

$$2\,RTeX \longrightarrow R_2TeX_2 + Te$$

Such instability is predominantly kinetic in nature and is induced both by the relative ease (compared with other chalcogenyl halides) of dissociation of the chalcogen–halogen bond in solvating solvents and by the increased capacity of compounds of dicoordinate tellurium for associative oxidative addition reactions. Individual decomposition reactions of organyltellanyl halides are also facilitated by the comparative ease of elimination of the tellurium atom.

The principal methods for the stabilisation of organyltellanyl halides are associated either with the generation in their molecules of significant steric hindrance to the access of the reactants to the TeX groups or with the coordination of the Te(II) centre, which results in its transition to a more stable higher oxidation state. Thus the increased stability of biphenyl-2-tellanyl[100] and naphthalene-2-tellanyl[101] iodides, compared with other aryltellanyl halides, can be accounted for by the steric shielding of the TeI groups. The naphthalene derivative is thus the first arenetellurenyl iodide isolated in an analytically pure form. On the other hand, the first stable alkanetellanyl halides were tris(trimethylsilyl)methanetellanyl halides $(Me_3Si)_3CTeX$ (X = Cl, Br, I), obtained by oxidising the corresponding ditellurides with the halogen or SO_2Cl_2.[102] The stability of these compounds is undoubtedly associated with the bulky tris(trimethylsilyl)methyl group. However, the high stability of tris(trimethylsilyl)methanetellanyl pseudohalides $(Me_3Si)_3CTeX$ (X = CN, NCO, NCS, NCSe, N_3), obtained by the exchange reaction between tris(trimethylsilyl)methanetellanyl iodide and the corresponding AgX, is also noteworthy.[103]

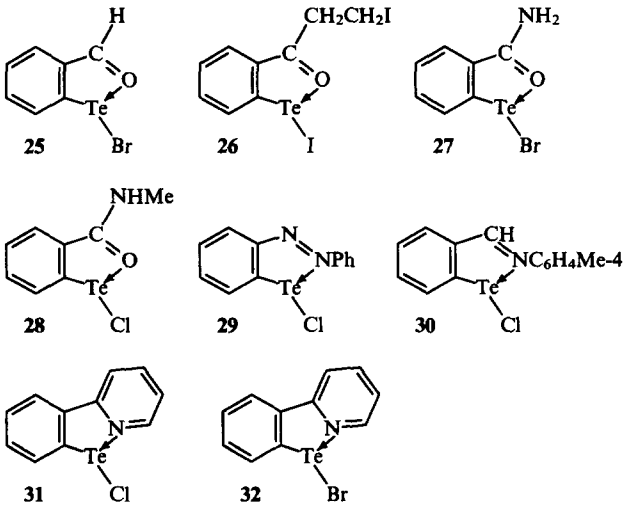
A second way of stabilising tellanyl halides involves the formation of complexes with neutral ligands,[2,3] the tellurium atom playing the role of the coordination centre.

IV. Intramolecular Te←O(N) coordination as a factor stabilising derivatives of dicoordinate tellurium

The most effective procedure for increasing the stability of tellanyl halides and other tellanyl derivatives involves the introduction in the *o*-position relative to the Te–Hal functional group of substituents capable of forming stable intramolecular Te←O(N) coordinate bonds involving their O or N atoms.[104–106] Compounds of this kind are also useful synthons in preparative organic chemistry and in the first place in the chemistry of tellurium-containing heterocycles.

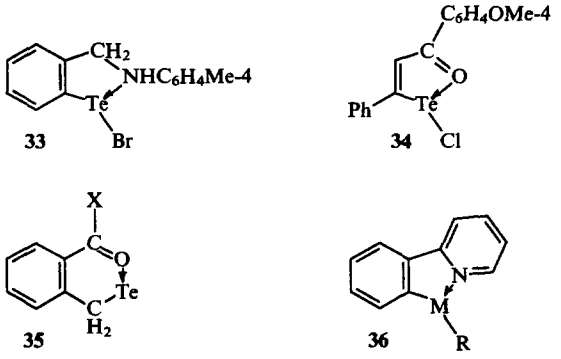
1. Tellanyl halides

Tellanyl halides are stabilised by substituents such as CHO,[107,108] COR,[51,109–118] $CONR_2$,[119,120] NO_2,[121] N=N,[122] CH=N [104,123–127] (this bond can also be part of the pyridine ring [128–130]), and CH_2NR_2.[127,131,132] The lengths *d* of the intramolecular Te←O and Te←N coordinate bonds, which belong to the class of three-centre four-electron (hypervalent) bonds, are in the range 2.21–2.37 Å (compounds **25**–**32**) and are much smaller than the sums of the van der Waals radii of the elements (3.60 Å for Te and O and 3.70 Å for Te and N),[133] approaching the lengths of the usual covalent bonds. The replacement of the sp^2-hybridised by the sp^3-hybridised nitrogen atom weakens somewhat the intramolecular coordination, which lengthens the Te–N bond (of the bond lengths in compounds **30** and **33**).



Compound	*d*(Te–O)/Å	Ref.	Compound	*d*(Te–N)/Å	Ref.
25	2.31	108	**29**	2.21	122
26	2.368	118	**30**	2.239	104, 124
27	2.237	119	**31**	2.236	130
28	2.25	119	**32**	2.236	130
34	2.19	51	**33**	2.375	129

The intramolecular Te←O coordinate bonds stabilise not only arenetellanyl halides but also vinyltellanyl (compound **34**)[51] and alkanetellanyl (compounds **35**)[134] halides.

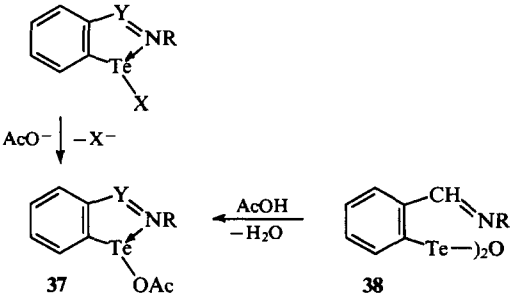


Comparison of the properties of compounds with the same structure of the organic ligand and of the chalcogen-containing groups is desirable for the quantitative characterisation of the relative strengths of the intramolecular O(N)→M coordinate bonds in the series M = S, Se, Te, the measure of which may be either the difference (Σ) between the van der Waals radii of M and O(N) [M···O(N)] or the Pauling bond order (*n*). Although there are comparatively few data, they make it possible to infer that the strength of bonds of this kind increases on passing from sulfur to tellurium. Thus comparison of the Se←N (2.813 Å) [135] and Te←N (2.695 Å) [129] bond lengths in *p*-ethoxyphenyl 2-(2-pyridyl)phenyl chalcogenides **36** with the sums of the van der Waals radii of selenium and nitrogen (3.55 Å) [133] and of tellurium and nitrogen (3.70 Å) [133] indicates the greater strength of the coordinate bonds involving a tellurium atom.

X-Ray diffraction data for benzoisotellurazole [136] and 1,2,5-telluradiazole [137] and their selenium analogues may serve as indirect evidence for the greater strength of the coordinate bonds with participation of tellurium atoms. Strong intermolecular Te···N bonds have been noted for tellurium-containing heterocycles in crystals. Their lengths are 2.40 Å for benzoisotellurazole and 2.764 Å for 1,2,5-telluradiazole (the sum of the van der Waals radii of Te and N is 3.70 Å).[133] The Se···N bonds have not been found in benzoisoselenazole, while in 3,4-diphenyl-1,2,5-selenazole they are much weaker than in telluradiazole. The anomalous physical properties of benzoisotellurazole and 1,2,5-telluradiazole compared with other chalcogen-containing heterocycles, namely the high melting points and sparing solubility in the usual organic solvents, are also explained by the presence of these intermolecular bonds.

2. Aryltellanyl acetates

Aryltellanyl acetates without intramolecular Te←O(N) coordinate bonds have not been obtained. However, stable tellanyl acetates **37** containing an azo-group or an azomethine group in the *o*-position relative to TeOAc group have been synthesised by the exchange reactions of the corresponding telluranyl halides with AcONa [138] or AgOAc [104,126] and also by the interaction of aryltellanic acids **38** with acetic acid.[126]



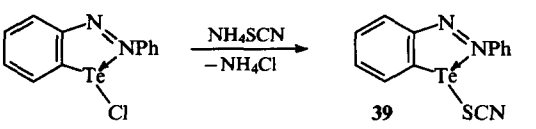
Y = N, R = Ph;

Y = CH; R = 4-MeC_6H_4, 4-$MeOC_6H_4$, 2,4,6-$Me_3C_6H_2$.

The lengths of the coordinate bonds in compounds **37** (Y = N, R = Ph) and **37** (Y = CH, R = 4-MeC_6H_4) are 2.26 Å [138] and 2.297 Å [104] respectively.

3. Aryltellanyl thiocyanates

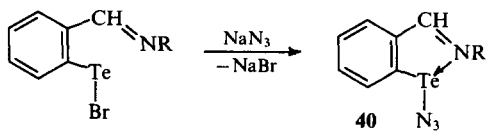
The interaction of equimolar amounts of diaryl ditellurides and thiocyanogen leads to unstable alkyltellanyl thiocyanates, which have been isolated in the form of complexes with thiourea, 2-picoline, and other nitrogen heterocycles.[139] However, the tellanyl thiocyanate **39**, containing the intramolecular Te←N coordinate bond (2.243 Å),[138] is extremely stable in the crystalline state.



It is noteworthy that the lengths of the intramolecular Te←O(N) coordinate bonds in the tellanyl derivatives ArTeX are in the range 2.130–2.375 Å (depending on the nature of X).[104–106] An increase in bond length for different X in the following sequence is then observed: Cl < Br < I < S_2CNMe_2, which agrees with the sequence based on decreasing electronegativity of the substituents X.

4. Arenetellanyl azides

The intramolecular Te←N coordination also ensures a high stability of the arenetellanyl azide **40**, obtained by the reactions of the corresponding arenetellanyl bromides with NaN_3.[126] The attempts to obtain the selenium analogues of these compounds from benzeneselanyl chloride and Me_3SiN_3 led actually only to diphenyl diselenide as a result of the rapid decomposition of the benzeneselanyl azide formed initially.[140] (By virtue of the steric hindrance due to the methyl groups, mesityleneselanyl azide is more stable and can be isolated on a preparative scale).[140] Bearing in mind that the selenyl derivatives ArSeX are in general always more stable than the analogous tellurium compounds, one must rule out the possibility of obtaining arenetellanyl azides from compounds in which the tellurium atom is not involved in intramolecular coordination.



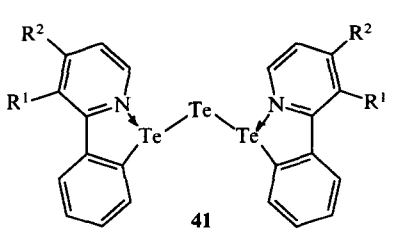
40

R = Ph, 4-MeC_6H_4.

5. Other derivatives of dicoordinate tellurium

Intramolecular Te←O(N) coordinate bonds increase the stability not only of the tellanyl derivatives RTeX but also certain other derivatives of dicoordinate tellurium: tritellurides, aryl cyclopentadienyl tellurides, and bis(organylthio)tellurides.

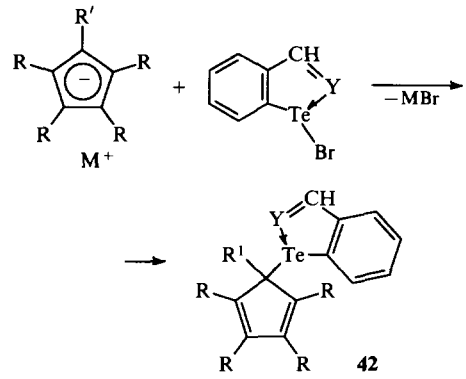
The first representative of tritellurides isolated in a pure form was bis[tris(trimethylsilyl)methyl] tritelluride $[(Me_3Si)_3C]_2Te_3$.[141] The stability of this compound is due to the presence of the bulky tris(trimethylsilyl)methyl group, which gives rise to steric hindrance to attack on the tritelluride bridge. On the other hand, the kinetic and thermal stabilities of type **41** tritellurides are associated with the intramolecular Te←N coordination in these compounds.[128,129] The Te←N bond length in bis[2-(2-pyridyl)phenyl]tritelluride **41** ($R^1 = R^2 = H$) is 2.554 Å.[128]



41

$R^1 = R^2 = H$; $R^1 + R^2$ = —(CH=CH)$_2$—.

Although aryl cyclopentadienyl sulfides and selenides are thermally stable, the attempts to obtain aryl cyclopentadienyl tellurides by the reaction of metal cyclopentadienides with benzenetellanyl bromide were unsuccessful.[142] However, the stable tellurides **42** have been obtained by the reactions of arenetellanyl bromides containing the *o*-formyl or *o*-aldimine groups, capable of forming strong intramolecular Te←O(N) coordinate bonds.

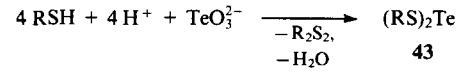


42

R = CO_2Me; R′ = CO_2Me; Y = O, NPh, 2-MeC_6H_4N;

R = CO_2Me; R′ = Me; Y = NPh, 4-$MeOC_6H_4N$.

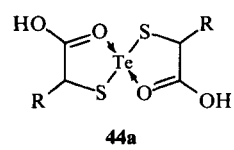
Yet another class of derivatives of dicoordinate tellurium, the stability of which is a consequence of the presence of the Te←O coordinate bonds comprises the bis(organylthiyl) tellurides **43**. Bis(benzenethiyl) telluride **43** (R = Ph) and bis(naphthalene-2-thiyl) telluride **43** (R = 2-$C_{10}H_7$), obtained by the interaction of the corresponding thiols with Na_2TeO_3, decompose very rapidly into diaryl disulfides and tellurium when they are kept in the crystalline state and especially in solutions.[143]



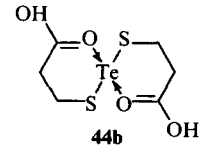
43

R = Ph, 2-$C_{10}H_7$.

Compounds **44a–c**, the carboxy-groups of which are capable of forming Te←O coordinate bonds, are much more stable.[143] According to the authors, two coordinate O←Te bonds are formed in their molecules.

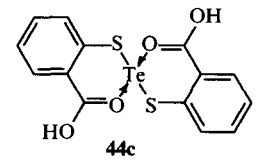


44a



44b

R = H, Me.



44c

According to IR spectroscopic data, a stronger Te←O bond and hence a more powerful stabilisation effect are manifested for five-membered chelates compared with six-membered ones.

V. Oxidative addition reactions of dicoordinate tellurium derivatives

One of the characteristic features of dicoordinate tellurium derivatives — diorganyl tellurides R_2Te and diorganyl ditellurides R_2Te_2 — is their ability to enter into oxidative addition reactions. Derivatives of dicoordinate sulfur and selenium undergo similar reactions. However, whereas in the case of tellurides (ditellurides) the reaction products are the stable σ-tellanes R_2TeX_2 or $RTeX_3$ with covalent Te–X bonds, the oxidation of the sulfides and selenides R_2M (M = S, Se) by the halogens X_2 results in the formation (depending on the nature of the chalcogens M and the halogens X) of either the charge-transfer complexes $R_2M\cdots X_2$

(M = S, Se, X = I; M = S, X = Br) or of σ-chalcogenanes R_2MX_2 (M = S, Se, X = F, Cl; M = Se, X = Br) (for a more detailed description see Section VIII).

Data on the most typical oxidation-reduction addition reactions of various types of organic derivatives of tellurium(II) are presented below.

1. Diorganyl tellurides

Diorganyl tellurides having different structures — dialkyl, aryl alkyl, and diaryl tellurides — readily combine with chlorine,[2,3] bromine,[2,3] iodine,[2,3] and fluorine (diluted with an inert gas)[144,145] under mild conditions (room or reduced temperatures), forming the corresponding σ-tellanes $R^1TeX_2R^2$. The latter are stable crystalline compounds which can be effectively purified by the usual recrystallisation. They are readily reduced to diorganyl tellurides in yields which are in many cases close to quantitative. Various reductants are employed: Na_2S, $K_2S_2O_5$ ($Na_2S_2O_5$), Na_2SO_3, $NaHSO_3$, $Na_2S_2O_3$, $Na_2S_2O_4$, $LiAlH_4$, $NaBH_4$, $N_2H_4 \cdot H_2O$,[2,3] thiourea dioxides,[146,147] zinc powder in benzene or acetic acid, $SnCl_2$, methyl (ethyl)magnesium iodide,[2,3] and lithium diethylamide.[148] The conversion of diorganyl tellurides into σ-tellanes with subsequent reduction of the latter is therefore employed for the isolation of diorganyl tellurides from reaction mixtures and for their purification.

One of the few compounds incapable of undergoing some of the reactions indicated above is $(CF_3)_2Te$.[149] Whereas the reactions of chlorine and bromine lead to the corresponding σ-tellanes, on interaction with iodine, a weaker oxidant, tellurium diiodide is not formed.

Thionyl chloride and sulfuryl chloride are used as oxidants instead of gaseous chlorine in the synthesis of tellurium dichloride.[2,3] Diorganyl tellurides may be oxidised also by certain metal salts: $FeCl_3$,[150] $HgCl_2$,[150] $CuCl_2$,[150–152] and $CuBr_2$.[152] It is noteworthy that, whereas diaryl tellurides are converted only into diaryltellurium dichlorides on treatment with $CuCl_2$,[150–152] the reaction of diethyl telluride with the same oxidant proceeds in a different manner:[153]

$$Et_2Te + CuCl_2 \longrightarrow Et_2TeCl_2 + Et_2Te \cdot CuCl.$$

Diorganyl tellurides are converted into the corresponding tellurium difluorides not only on treatment with fluorine[144,145] but also on reaction with SF_4,[154] XeF_2,[145,155,156] ClF,[156] Ph_2SF_2,[144] and $(4\text{-}MeC_6H_4)_3BiF_2$.[157–159]

$$Ar_2Te + XY \longrightarrow Ar_2Te\begin{matrix}X\\Y\end{matrix}$$

X = Y = NCS; X = Br, Y = I, CN; X = I, Y = Cl.

Diorganyl tellurides also enter into reactions involving the oxidative addition of thiocyanogen,[160–165] the interhalogens (ICl, IBr),[164] and halogen cyanides (BrCN, ICN),[164] forming the corresponding σ-tellanes in high yields.

The oxidation of diorganyl tellurides by lead tetraacetate, which occurs in benzene or toluene solutions at room temperature, leads to diorganyltellurium diacetates in high yields.[166–168]

$$R_2Te + Pb(OAc)_4 \xrightarrow[-Pb(OAc)_2]{} R_2Te(OAc)_2$$

R = Ar, Alk.

The reactions of diorganyl tellurides with certain oxidants, leading to σ-tellanes, proceed via the intermediate formation of telluroxides. Thus the interaction of diorganyl tellurides with benzoyl peroxide affords low yields of diorganyltellurium dibenzoates.[169,170] This mechanism is confirmed by the formation of diaryltellurium dicarboxylates in the reactions of diaryl telluroxides with percarboxylic acids[171,172] and their anhydrides.[171,173]

$$R_2Te + (PhCOO)_2 \xrightarrow[-(PhCO)_2O]{} [R_2TeO] \xrightarrow{(PhCO)_2O} R_2Te(OCOPh)_2$$

The results of the reactions of tellurides with dilute HNO_3, leading to diorganyltellurium dinitrates, have also been explained in terms of the 'telluroxide' mechanism.[2,3]

$$R_2Te + HONO_2 \longrightarrow [R_2TeO] \xrightarrow[-H_2O]{HONO_2} R_2Te(ONO_2)_2$$

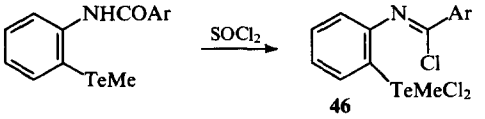
Finally, the interaction with one equivalent of *m*-chloroperbenzoic acid leads to the mixed σ-tellane **45**.[174] Taking into account the foregoing, the most probable mechanism of the formation of this σ-tellane can be represented as follows:

$$R^1R^2Te + ArCO_3H \xrightarrow[-ArCO_2H]{} [R^1R^2TeO] \xrightarrow{ArCO_2H} R^1R^2Te\begin{matrix}OCOAr\\OH\end{matrix}$$

45

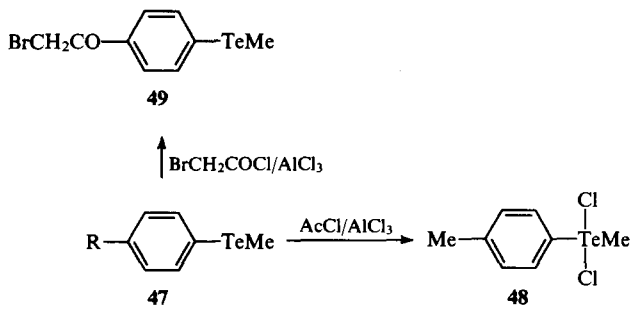
Ar = 3-ClC_6H_4.

The thermodynamic stability of σ-tellanes is the driving force of many of the reactions of diorganyl tellurides leading ultimately to σ-tellanes, while in the similar reactions of diorganyl sulfides, the formation of σ-sulfanes is not observed. Thus the arylation of diaryl ditellurides by arenediazonium salts in the presence of copper(II) halides[151,152] (see Section V) leads to diaryltellurium dihalides in high yields, while the arylation of diaryl disulfides under similar conditions results in the formation of only diaryl sulfides.[175,176] The synthesis of σ-tellanes is achieved by oxidising the diaryl tellurides formed initially with copper(II) salts.[152] Similarly the Sandmeyer reaction of 2-aminophenoxatellurane with CuCl terminates with the formation of 1,1,2-aminophenoxatellurane and not 2-chlorophenoxatellurane.[177] Another example is provided by the interaction of *N*-aroyl derivatives of *o*-methyltelluroaniline with $SOCl_2$.[178] This entails not only the conversion of the amide groups into the –N=C(Ar)Cl groups but also the oxidation of Te(II) to Te(IV), a consequence of which is the formation of the σ-tellanes **46**. These compounds are convenient synthons in the synthesis of 2-arylbenzotellurazoles.[178]



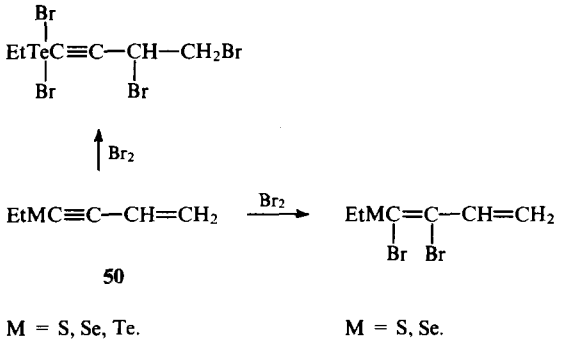
46

It is also of interest to note that the interaction of 4-methylphenyl methyl telluride **47** (R = Me) with acetyl chloride in the presence of $AlCl_3$ involves the oxidation of the initial telluride to the σ-tellane **48**[109] and not acetophenone, as in the case of the analogous selenium derivative.[179] Incidentally, the acylation of the telluroanisole **47** (R = H) by α-bromoacetyl chloride in the presence of $AlCl_3$ proceeds in the usual way, leading to the expected 4-methyltelluro-α-bromoacetophenone **49** in 52% yield.[180]



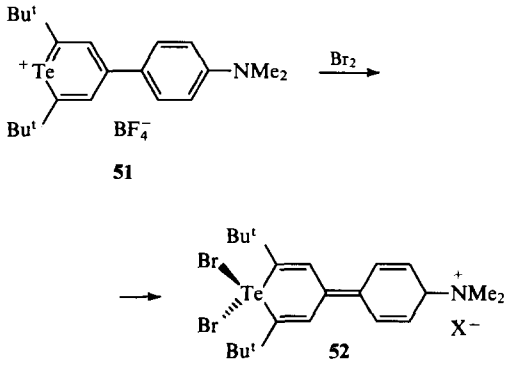
R = H, Me.

The vinylethynyl tellurides **50** behave differently in their reactions with bromine from their selenium and sulfur analogues. Whereas the latter readily combine with bromine only at the triple bond, the tellurides combine with two molecules of bromine: at the double bond and at the tellurium atom.[181]



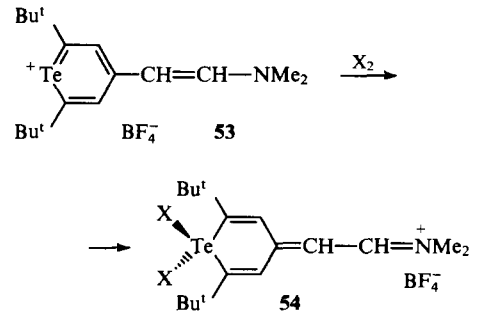
M = S, Se, Te. M = S, Se.

The reactions involving the oxidative addition of the halogens to the tellurium atom of tellurapyrylium salts containing a powerful electron donor (the dimethylamino-group) in the *p*-position relative to the heteroatom are of special interest. Bromine reacts under comparatively mild conditions with 4-(4′-dimethylaminophenyl)tellurapyrylium tetrafluoroborate **51**, which leads to the telluranes **52** in 90%–97% yields.[182] In the presence of an excess of bromine, the BF_4^- anions are exchanged for Br_3^-.

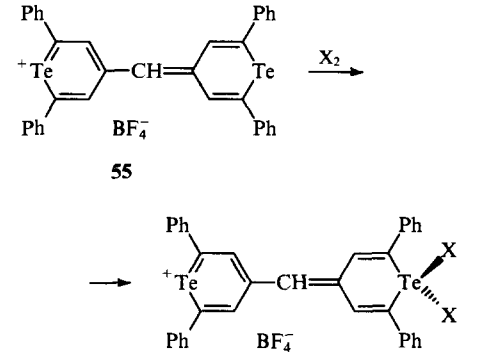


$X^- = BF_4^-, Br_3^-$.

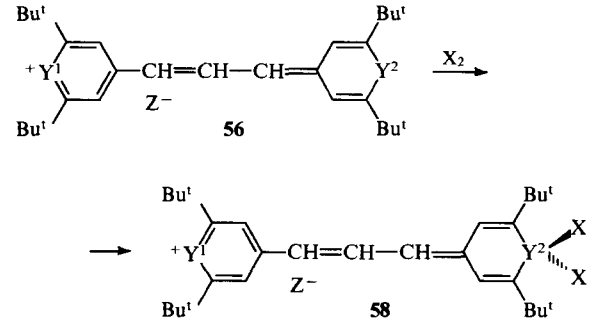
The analogous reactions with the tellurapyrylium dye **53** lead to the dibromo-derivative **54** (X = Br) and the diiodo-derivative **54** (X = I) in 67% and 91% yields respectively.[182]



The symmetrical tellurapyrylium monomethine dyes **55** and trimethine dyes **56** also enter into reactions in which the halogens undergo oxidative addition. The tellurapyrylium fragment is then retained in the σ-tellanes **57** and **58** formed.[182,183]



57, X = Cl, Br, I.



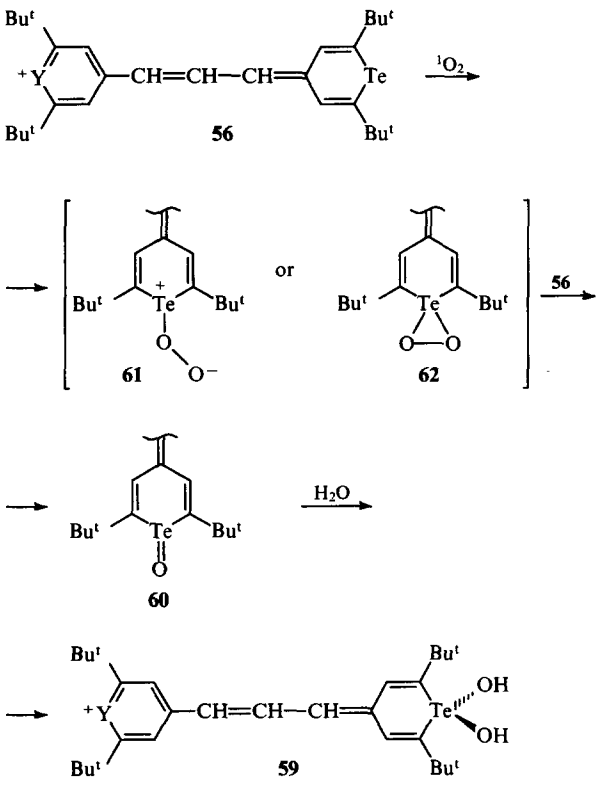
$Y^1 = Y^2 = Te$; X = Cl, Br, I;

$Z = BF_4^-, CF_3SO_3^-, PF_6^-$.

It is noteworthy that the trimethine pyrylium dyes of type **56** ($Y^1 = Y^2 = O$, S, Se) also enter into reactions with chlorine and bromine.[183,184] However, these are much slower than those involving the tellurapyrylium analogues and, which is most important, the trimethine bridges and not the heteroatoms are attacked.

Other examples of oxidative addition reactions, which take place only for the tellurapyrylium trimethine dyes **56** ($Y^1 = O$, S, Se, Te, $Y^2 = Te$) and are not characteristic of other structurally similar compounds without a tellurium atom, involve the oxidative addition of H_2O_2 or singlet oxygen in the presence of water, which results in the formation of the dihydroxytellanes **59**.[185–188] The latter reaction is carried out by the UV irradiation of solutions of the tellurium-containing dyes **56**, whereupon singlet oxygen is formed (the dyes **56** with Y = O, S, Se, or Te and $Y^2 = Te$ serve as effective photosensitisers for the singlet O_2 generation process) and oxidises compounds **56** to the tellur-oxides **60**. It has been suggested[185] that the latter are formed via the pertelluroxides **61** or telluradioxiranes **62**. The subsequent

hydration of the telluroxides **60** leads to the dihydroxytellanes **59**. Such hydration reactions are characteristic of dialkyl and alkyl aryl telluroxides.[2,3,189]

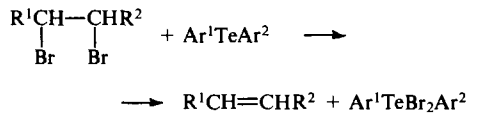


The interaction of other type **56** pyrylium cations, not containing tellurium atoms, with singlet oxygen is slower and the molecular π-skeletons are then involved in the reactions and not the heteroatoms.[186]

One of the characteristic properties of the dihydroxytellanes **59** is the relatively slow thermal reductive elimination of H_2O_2 in aqueous methanol solutions, which leads to the reformation of the initial compounds **56**. This can be used for the photochemical conversion of water and oxygen into H_2O_2.[187,188] Another possible application of the above reaction is photodynamic therapy: tellurapyrylium dyes function under these conditions as photosensitisers of the formation of singlet oxygen or the superoxide radical-anion, which are cytotoxic agents. A useful property of tellurapyrylium dyes is their ability to absorb in the near IR region, where biological tissues are transparent.

The ability of diorganyl tellurides to be converted by various oxidants into derivatives of tetracoordinate tellurium prevents in a number of instances the employment of reagents which are normally used for the conversion of the functional groups. Thus, in contrast to the sulfur and selenium derivatives, carboxylic acids containing telluride functional groups are converted into the corresponding acid chlorides on treatment with alkyl dichloromethyl ethers in the presence of anhydrous $ZnCl_2$,[51,54,56,111,113,117,190–192] whilst the use of PCl_5 or $SOCl_2$ for these purposes leads merely to the oxidation of tellurium(II) to tellurium(IV).

The appreciable 'affinity' of diorganyl tellurides for the halogens permitted the employment of these compounds as dehalogenating agents in the synthesis of alkanes from organic dihalides. Vicinal[193–195] and geminal[196] dibromo-derivatives are converted, with fairly high yields, into the corresponding alkenes on treatment with diaryl tellurides[193,195] or their cyclic analogue — phenoxatellurane.[194,196]

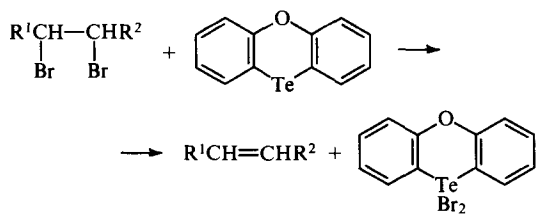


$R^1 = Ph$; $R^2 = CO_2H, CO_2Et, COPh$, 2-pyridyl;

$R^1 = R^2 = Ph$; $R^1 + R^2$ = cholesteryl,

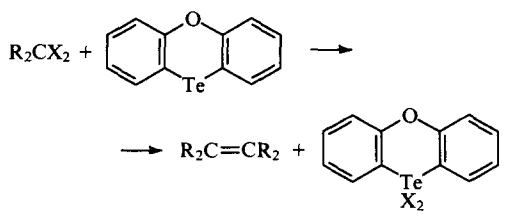
$Ar^1 = Ar^2 = Ph, 4\text{-}MeOC_6H_4$; $Ar^1 = 4\text{-}MeOC_6H_4$;

$Ar^2 = 1\text{-}C_{10}H_7, 2\text{-}C_{10}H_7$.



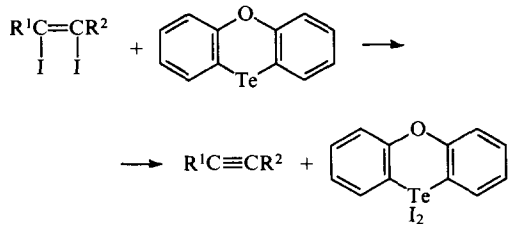
$R^1 + R^2 = -(CH_2)_3-$, $-(CH_2)_4-$, 1,8-naphthylidene;

$R^1 = Ph$; $R^2 = H, CO_2H, CO_2Et$; $R^1 = Me$; $R^2 = CO_2H$.



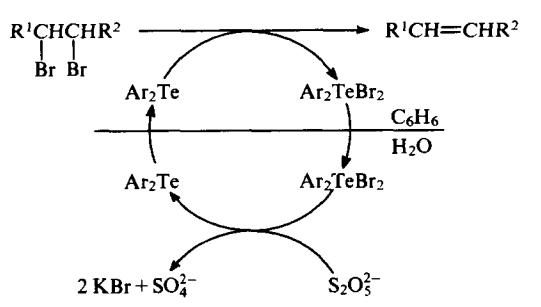
$R = Ph, CO_2Et$; $R + R = C_{12}H_8$, X = Cl, Br.

In terms of its dehalogenating capacity, phenoxatellurane is superior to diaryl tellurides, since it reduces not only 1,2-dibromoalkanes but also 1,2-diiodoalkenes, which leads to ethynes in yields exceeding 80%.[194]



$R^1 = Ph$, $R^2 = H, CO_2H$.

An important advantage of diaryl tellurides over other dehalogenating agents is the possibility of using them in catalytic amounts (the optimum amount is 5% of the mass of the halogen-containing substrates).[195] The reactions lead in this case to a two-phase system (benzene–water) and the tellurium dibromides formed are reconverted into the tellurides on treatment with potassium metabisulfite, which by itself does not reduce the vicinal dibromo-derivatives. The foregoing considerations can be illustrated by the following scheme:



2. Diorganyl ditellurides

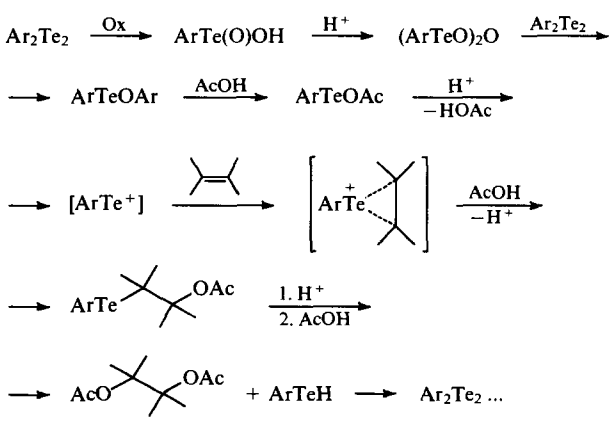
Like diorganyl tellurides, diorganyl ditellurides R_2Te_2 undergo oxidative addition reactions under mild conditions (at room or reduced temperature in the absence of catalysts). When solutions of these compounds are treated with the halogens [$Cl_2(SOCl_2$, SO_2Cl_2), Br_2, I_2,[2-4] F_2, XeF_2,[197] or ClF [198]], the Te–Te bonds are ruptured and organyltellurium trihalides $RTeHal_3$ are formed in high yields. On treatment with various reductants, the latter can be reconverted into the corresponding ditellurides. The ease of the interconversions $R_2Te_2 \rightleftarrows RTeX_3$ is used (depending on the relative availability of these compounds) for their synthesis and purification. It has been shown in relation to aryltellurium triiodides that the halogen oxidative addition reactions proceed in stages.[199] The first stage of this process is the rapid formation of arenetelluranyl iodides, which are then converted into complexes **63** and finally into the triiodides **64**.

$$R_2Te_2 + I_2 \longrightarrow RTeI \rightleftharpoons \underset{\mathbf{63}}{RTeI \cdot I_2} \longrightarrow \underset{\mathbf{64}}{RTeI_3}$$

The reactions with other oxidants have been less thoroughly investigated. Thus, according to Pant's data,[166,167] the oxidation of diaryl ditellurides with lead tetraacetate affords, judging from the ^1H NMR spectra of the reaction mixture, aryltellurium triacetates. However, as a consequence of the ready hydrolysis of the latter, the attempts to isolate them from solutions were unsuccessful.

Diaryl ditellurides are catalysts of the oxidation of aromatic alkenes by various oxidants (O_2, Bu^tO_2H, H_2O_2, *m*-$ClC_6H_4CO_3H$) in methanol or acetic acid in the presence of H_2SO_4 to the vicinal dimethoxy- and diacetoxy-derivatives.[200] It has been suggested[200] that these reactions proceed via the intermediate formation of arenetellurinic acids ArTe(O)OH or their derivatives. This has been confirmed by the fact that, when the anhydrides of arenetellurinic acids $[ArTe(O)]_2O$[201] are refluxed with alkenes in acetic acid, they convert the latter into vicinal diacetates; the second reaction product is the corresponding ditelluride. The possible mechanism of these reactions[200,201] is presented in Scheme 2.

Scheme 2



Thus the intermediate formation of arenetellurinic acids or their anhydrides in the oxidation of diaryl ditellurides with Bu^tO_2H, H_2O_2, etc. under the conditions described above is evident; however, these reactions have not been investigated separately.

The ionisation potentials of the chalcogens (in eV) decrease in the sequence S(10.36) > Se(9.75) > Te(9.01).[202] As a result of this, diorganyl ditellurides are much stronger reductants than their sulfur and selenium anaogues and are capable of undergoing certain reactions which are not characteristic of the latter two classes of organochalcogen compounds.

The reducing properties of diaryl ditellurides have been used in preparative organic chemistry for the synthesis of alkenes from vicinal dibromo-derivatives.[203] Organic dibromo-derivatives convert diaryl ditellurides into arenetelluranyl bromides: under the reaction conditions (refluxing in toluene or acetic acid), the latter disproportionate to diaryltellurium dibromides and tellurium. Alkenes are obtained predominantly in the (*E*)-form in 68%–100% yields.

$$R^1\underset{Br}{CH}\!-\!\underset{Br}{CHR^2} + Ar_2Te_2 \longrightarrow$$

$$\longrightarrow R^1CH{=}CHR^2 + ArTeBr \longrightarrow Ar_2TeBr_2 + Te$$

Ar = 4-$MeOC_6H_4$, 4-$EtOC_6H_4$; $R^1 = R^2 = H$, Ph, CO_2H; R^1 = Ph, $R^2 = CO_2H$.

Being strong one-electron reductants, diaryl ditellurides enter into reactions which cannot be carried out with the analogous sulfur derivatives. Thus the interaction of diaryl ditellurides with arenediazonium halides leads to a mixture of equimolar amounts of diaryltellurium dihalides and diaryl tellurides in accordance with the mechanism presented below:[152]

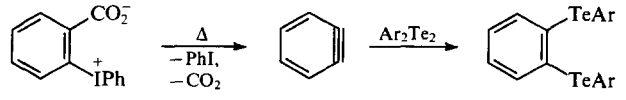
$$Ar^1_2Te_2 + Ar^2N_2X \xrightarrow[-N_2]{} Ar^1Te^{\cdot} + (Ar^2)^{\cdot} + Ar^1TeX,$$

$$Ar^1Te^{\cdot} + (Ar^2)^{\cdot} \longrightarrow Ar^1TeAr^2,$$

$$Ar^1TeX + Ar^2N_2X \xrightarrow[-N_2]{} Ar^1TeX_2Ar^2.$$

On the other hand, diaryl disulfides are arylated by arenediazonium halides only in the presence of copper(II) halides, which promote the formation of free aryl radicals.[175,176]

The M–M bond energy (kJ mol^{-1}) in the diorganyl dichalcogenides R_2M_2 decreases in the sequence S(264.0) > Se(202.0) > Te(149.8).[203] This is the reason for the strikingly manifested ability of diorganyl ditellurides to undergo other reactions (other than the reactions with the halogens) involving the dissociation of these bonds. Thus diaryl ditellurides containing electron-donating substituents in the *p*-positions in the arene rings add readily to dehydrobenzene, obtained by the thermal decomposition of 2-phenyliodonium benzoate, forming *o*-bis-(aryltelluro)benzenes in 50%–64% yields.[205-206] Diphenyl disulfide does not enter into this kind of reaction.



Ar = 4-MeC_6H_4, 4-$MeOC_6H_4$, 4-$TeOC_6H_4$.

Mercury tellurophenoxides, which are stable under the usual conditions, are formed under extremely mild conditions—shaking of solutions of diaryl ditellurides with mercury at room temperature.[207-209] On heating, these compounds decompose into diaryl tellurides and HgTe.[209]

$$Ar_2Te_2 + Hg \longrightarrow (ArTe)_2Hg \xrightarrow{\Delta} Ar_2Te + HgTe$$

Ar = Ph, 4-$MeOC_6H_4$, 4-$EtOC_6H_4$.

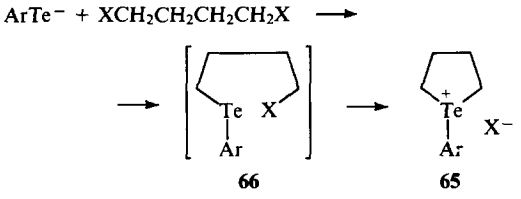
It is probable that the interaction of diaryl ditellurides with powdered copper in boiling dioxane, leading to high yields of diaryl tellurides, also proceeds via the intermediate formation of copper(II) tellurophenoxides.[210-215] This reaction is frequently used as a preparative method of synthesis of diaryl tellurides and for the elimination of traces of diaryl ditellurides from the latter. In contrast to diaryl ditellurides, diaryl disulfides give rise to stable copper(I) thiophenoxides on heating with copper powder in *N,N*-dimethylacetamide.[216]

$$ArSCu \xleftarrow[M = S]{Cu/\Delta} Ar_2M_2 \xrightarrow[M = Te]{Cu/\Delta} Ar_2Te + CuTe$$

VI. Nucleophilic properties of dicoordinate tellurium derivatives

1. Diorganyl tellurides

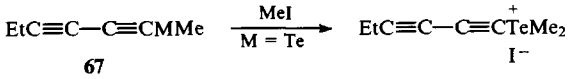
Diorganyl tellurides of various types readily give rise to telluronium salts on interaction both with compounds containing activated neighbouring electron-accepting groups [esters of carboxylic α-bromoacids, α-bromoacetophenones, α-bromoacetone, chloro(bromo)acetonitriles] and with nonactivated alkyl halides.[2,3] The increased nucleophilicity of the tellurium atom, compared with the other chalcogens, in diorganyl tellurides results in the formation of telluronium salts on interaction of not only dialkyl and alkyl aryl tellurides but also diaryl tellurides with haloalkanes.[2,3] Furthermore, iodobenzene can be used as the halogen-containing substrate in relation to dimethyl telluride.[217] The interaction between these compounds leads to dimethylphenyltelluronium iodide in ~50% yield. In contrast to diaryl tellurides, diphenyl sulfide[218] and diphenyl selenide[219] form salts on treatment with haloalkanes only in the presence of Ag^+ cations. A similar difference between the reactivities has been observed also in the alkylation of chalcogen-containing heterocycles. Thus whereas benzo[*b*]tellurophene is alkylated by methyl bromide,[220] benzo[*b*]thiophenium and dibenzo[*b*]thiophenium salts have been obtained by the alkylation of the corresponding heterocycles only in the presence of $AgClO_4$ or $AgBF_4$.[221] The high nucleophilicity of the tellurium atom in diorganyl tellurides is also indicated by data[222] on the interaction of arenetellurolate anions with 1,4-dihalobutanes. 1-Aryl-1-telluroniacyclopentane halides **65** were obtained instead of the expected 1,4-bis(aryltelluro)butanes. These compounds are probably formed as a result of the intramolecular alkylation of the intermediate 1-aryltelluro-4-halobutanes **66**.



Ar = Ph, 4-TeOC$_6$H$_4$; X = Cl, Br.

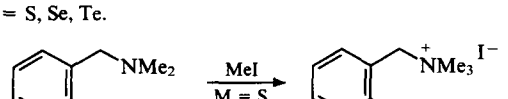
However, one should note that, according to the data of Hope et al.,[223] the main products of the reactions of lithium benzene- and methane-tellurolates with 1,4-dihalobutane are the corresponding tellurides and 1-telluracyclopentane.

Significant differences between the reactivities, determined by the nature of the chalcogen atoms, are observed also in the alkylation of alkylchalcogeno-1,3-diynes **67**[224] and 2-dimethylaminobenzyl methyl chalcogenides **68**.[116]

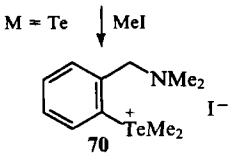


67

M = S, Se, Te.



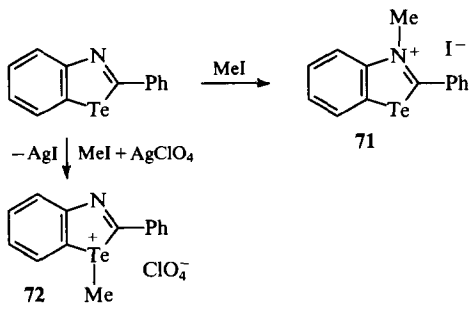
68 **69**



70

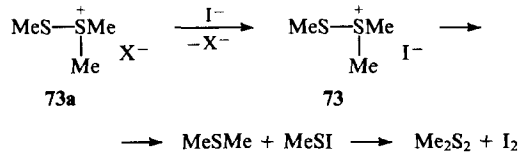
Among the methyl chalcogenides **67**, only the telluride is alkylated by methyl iodide, the telluronium salt being formed in this reaction in an almost quantitative yield.[224] More interesting data have been obtained on the alkylation of compound **68**. In the case of 2-dimethylaminobenzyl methyl selenide **68** (M = Se), the object of attack is the nitrogen atom; the iodide of methyl 2-*N*,*N*,*N*-trimethylammoniabenzyl selenide **69** is formed in an almost quantitative yield. On the other hand, the tellurium analogue is alkylated exclusively at the tellurium atom, which leads to the telluronium salt **70** in a high yield.[116]

In relation to 2-phenylbenzotellurazole, it has been shown for the first time that the alkylation of N,Te-containing organic compounds can be achieved at different nucleophilic centres depending on the nature of the alkylating agents.[225,226] Refluxing of 2-phenylbenzotellurazole in an excess of MeI leads to the immonium salt **71** (yield 90%), while treatment of the same heterocycle with methyl iodide in the presence of an equivalent amount of $AgClO_4$ results in the formation of the telluronium salt **72** in an almost quantitative yield. Compound **72** is the first example of benzochalcogenazoles for which alkylation at the chalcogen atom has been achieved.



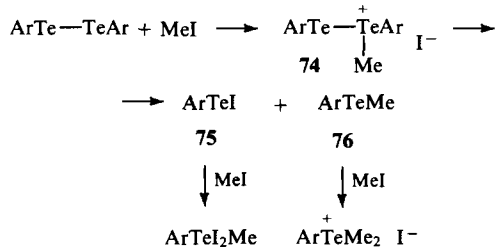
2. Diorganyl ditellurides

The alkylation of dialkyl disulfides by alkyl halides proceeds fairly effectively in the presence of HgI_2 or on treatment with trimethyloxonium 2,4,6-trinitrobenzenesulfonate.[227] We may note that methylthio(dimethyl)sulfonium iodide **73**, obtained by treating the sulfonate **73a** with the I^- ion, decomposes in accordance with the mechanism presented below:



X = 2,4,6-(NO$_2$)$_3$C$_6$H$_2$SO$_3$.

On the other hand, the alkylation of diaryl ditellurides evidently takes place under milder conditions in the presence of compounds similar to HgI_2 or the oxonium cation. Thus refluxing of di(*p*-anisyl) ditelluride in an excess of MeI leads to a mixture of *p*-anisylmethyltellurium diiodide and *p*-anisyl-(dimethyl)telluronium iodide.[228,229] Evidently the intermediate *p*-anisyltelluro(methyl)*p*-anisyltelluronium iodide **74** decomposes, like the iodide **73**, to *p*-anisyltellanyl iodide **75** and *p*-anisyl methyl telluride **76**. The latter products react with the excess MeI, affording the observed products.



The formation of type **74** telluronium salts is not ruled out also in the reactions of dialkyl ditellurides with phenylethyne and MeI under the conditions of phase transfer catalysis (PTC).[230,231]

VII. Reactions determined by the polarisation of the Te=X bonds (X = CR_2, NR, O)

π-Telluranes include telluronium ylides, tellurimides, and telluroxides:

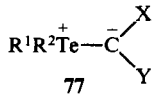
$$R_2Te{=}CR'_2 \longleftrightarrow R_2\overset{+}{T}e{-}\overset{-}{C}R'_2, \quad R_2Te{=}NR' \longleftrightarrow R_2\overset{+}{T}e{-}\overset{-}{N}R',$$

$$R_2T{=}O \longleftrightarrow R_2\overset{+}{T}e{-}\overset{-}{O}.$$

The reactivities and methods of synthesis of these compounds differ significantly from those of their sulfur (and to a lesser extent selenium) analogues. The principal factors responsible for the specific behaviour of π-telluranes compared with other π-chalcogenanes are the more intense polarisation of Te=X bonds (a greater contribution of the polar resonance structures Te^+-X^-) and hence the increased basicity of derivatives of tricoordinate tellurium. A characteristic feature of all π-telluranes without exception is their ability to be converted under the influence of different electrophiles into derivatives of tetracoordinate tellurium — the σ-telluranes R_2TeX_2.

The complete analogy of the electronic structures of organic derivatives of I(III) and Te(IV) should also be reflected in the similarity of the chemical properties of these compounds. The hypothesis[232] that organic derivatives of Te(IV), in particular π-telluranes, can be used in organic synthesis for the same purpose as organic derivatives of I(III) is therefore valid.[233]

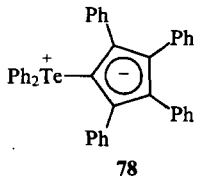
The number of telluronium ylides and imides described hitherto[7,10] is relatively small compared with their sulfur analogues. The doubly stabilised telluronium ylides **77**,[234–238] the diphenyltelluroniacyclopentadiene **78**,[239–241] and the diaryltelluronia-4,5-dicyanoimidazolylylidenes **79**[242] have been isolated on a preparative scale and characterised. The monostabilised and unstabilised telluronium ylides, compounds **80**[243–246] and **81**[247–249] respectively, have been used only in situ. Among tellurimides, only those which contain strongly electron-accepting groups at the nitrogen atom have been described.[250–256]



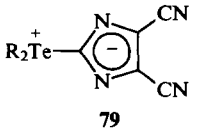
77

X+Y = $COCH_2CMe_2CH_2CO$, *o*-COC_6H_4CO;

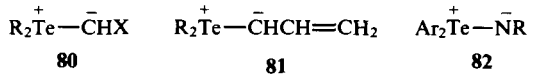
X = CO_2R; Y = CO_2R, CN, NO_2; X = Y = CN



78



79



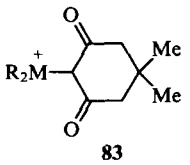
80 **81** **82**

X = CO_2R, CN, COR, $CONHBu^t$

X = SO_2R, COR (R = CCl_3, *m*-$O_2NC_6H_4$, *p*-$O_2NC_6H_4$).

We shall consider initially the properties and reactions common to all π-telluranes.

1. In contrast to dialkyl and alkyl aryl sulfoxides, the corresponding telluroxides are always isolated, by virtue of their high basicity, in the form of hydrates having the structure of σ-telluranes — diorganyltellurium dihydroxides $R_2Te(OH)_2$.[2,3,10,189] The basicity constants of the chalcogenoxides R_2MO[171,257–259] increase, like those of the telluronium ylides **83** (M = Te),[235] in the sequence M = S, Se, or Te. Thus the basicity constants of di(4-methoxyphenyl)chalcogenoxides $(4\text{-}MeOC_6H_4)_2MO$ have the following values in acetonitrile (the constants for the compounds with M = S or Se have been recalculated in relation to this solvent): S (4.2),[257] (5.4),[258] Se (9.1),[259] Te (14.9).[171] The telluroniadimedone ylides **77** (X+Y = $-COCH_2CMe_2CH_2CO-$) are somewhat weaker bases, comparable in strength to aromatic amines.[260] Indeed, $pK_a = 10.59$[235] for diphenyltelluroniadimedone ylide **83** (M = Te, $R^1 = R^2 = Ph$) is virtually identical with pK_a for aniline determined under identical conditions.[260] It follows from the pK_a for the diorganylchalcogenoniadimedone ylides **83**[235] that the basicity of the ylides increases sharply in the sequence S, Se, Te.

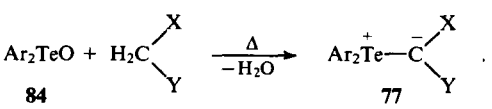


83

R = Me, M = S ($pK_a = 9.67$), Te ($pK_a = 12.07$);

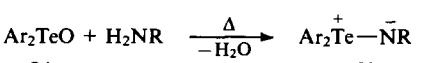
R = Ph, M = Se ($pK_a = 9.59$), Te ($pK_a = 10.59$).

By virtue of the high basicity of the oxygen atom in the diaryl telluroxides **84**, their reactions with reactive methylene compounds, leading to the telluronium ylides **77**,[236,237] do not require, in contrast to the synthesis of the corresponding sulfonium ylides, the use of any kind of dehydrating agents of the type of Ac_2O, PCl_5, $SOCl_2$, dicyclohexylcarbodiimide, etc.[7,10] The reactions are carried out by refluxing a mixture of equimolar amounts of the components in C_6H_6 or $CHCl_3$, the water formed in the reaction being simultaneously distilled away.



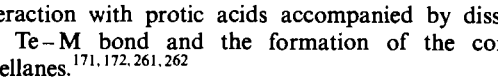
84 **77**

The syntheses of the tellurimides **82** from the diaryl telluroxides **84** and amides also take place under similar conditions.[251–253]



84 **82**

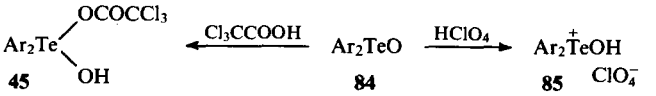
2. A characteristic feature of all π-telluranes is their interaction with protic acids accompanied by dissociation of the Te–M bond and the formation of the corresponding σ-tellanes.[171,172,261,262]



77, 82, 84

R^1 = Alk, Z = C(X)Y (**77**), NR^2 (**82**), O (**84**); X = F, Cl, Br, I, $OCOR^3$.

The reactions of diaryl telluroxides with acids proceed stepwise. For the equimolar reactant ratio, either type **45** hydroxytelluranes[171] (see above) or type **85** telluronium salts[171] are formed depending on the nature of the acids.



45 **84** **85**

In contrast to diaryl telluroxides, their sulfur analogues do not react with acids. On the other hand, the interaction of the doubly stabilised sulfonium ylides (dinitromethylides) with solutions of halides in organic solvents afford sulfides and not σ-sulfuranes.[263] Selenonium dinitromethylides occupy an intermediate position: depending on the nature of the hydrogen halides and the reaction conditions, either σ-selenanes or selenides are

formed.[264] The characteristic features of the reactions of the doubly stabilised chalcogenonium ylides with HHal noted above can be evidently attributed to the sharp increase in stability of the tetracoordinate derivatives of the chalcogens in the series S, Se, Te (for further details see Section VIII).

3. The diaryl telluroxides **84** [171-173] and tellurimides **82** [262] readily react with carboxylic acid anhydrides, affording the corresponding σ-tellanes, i.e. diaryltellurium dicarboxylates **86** and diacylamides (in the case of tellurimides).

$$\underset{\textbf{82, 84}}{Ar_2\overset{+}{T}e-\overset{-}{Z}} + (R^1CO)_2O \longrightarrow \underset{\textbf{86}}{Ar_2Te(OCOR^1)_2} + \underset{Z = NR^2}{Z(COR^1)_2}$$

Z = O (**84**), NR^2 (**82**); R^1 = Alk.

Diaryl sulfoxides do not react with anhydrides, while diaryl selenoxides behave similarly to diaryl telluroxides, giving rise to diarylselenium dicarboxylates.[171]

The reactions of π-telluranes and, in particular, of diaryl telluroxides with carboxylic acids and their anhydrides are important for the following two reasons.

a. They are convenient preparative methods of synthesis of diaryltellurium dicarboxylates, which make it possible to obtain virtually any compounds **86** in nearly quantitative yields. The methods for the formation of these compounds described earlier, namely the exchange reactions of diaryltellurium dihalides with silver salts of acids,[167,265] or the oxidation of diaryl tellurides by lead tetraacetate [166,167] require either the use of expensive silver salts or make it possible to obtain only diacetates. The interaction of diaryl tellurides and of the corresponding carboxylic acids with hydrogen peroxide (molar ratios 1:2:1) (yields 82%-92%) is a convenient preparative modification, which makes it possible to avoid the preliminary synthesis of diaryl telluroxides.[266]

$$Ar_2Te + H_2O_2 \xrightarrow[-H_2O]{} \underset{\textbf{84}}{[Ar_2TeO]} \xrightarrow[-H_2O]{RCOOH} \underset{\textbf{86}}{Ar_2Te(OCOR)_2}$$

b. In view of the ease of the interaction of acids with diaryl telluroxides, one cannot use for the synthesis of the latter the acid reagents widely employed in the preparation of sulfoxides from sulfides: HNO_3, H_2O_2 in acetic anhydride, peracids, etc.[267]

We may also note the ability of diaryl telluroxides to interact with acyl chlorides[171] (diaryl sulfoxides do not interact with the latter). For equimolar reactant ratios, a 1:1 mixture of diaryltellurium dichlorides and diaryl tellurium dicarboxylates **86** is formed.

$$\underset{\textbf{84}}{Ar_2TeO} + RCOCl \longrightarrow Ar_2TeCl_2 + \underset{\textbf{86}}{Ar_2Te(OCOR)_2}$$

However, in the presence of an excess of acyl chlorides, diaryltellurium dichlorides and carboxylic acid anhydrides are obtained in high yields.[171]

$$\underset{\textbf{86}}{Ar_2Te(OCOR)_2} + 2\,RCOCl \longrightarrow Ar_2TeCl_2 + 2\,(RCO)_2O$$

Later[268] this reaction was used as a preparative method of synthesis of acid anhydrides with different structures.

4. The telluronium ylides **77** [261] and imides **82** [262] react under mild conditions with the halogens, the reaction involving the cleavage of the Te-M bonds in the formation of σ-telluranes.

$$\underset{\textbf{77, 82}}{Ar_2\overset{+}{T}e-\overset{-}{Z}} + X_2 \longrightarrow Ar_2TeX_2 + X_2Z$$

Z = C(X)Y (**77**), NR′(**82**); X = Cl, Br, I.

Sulfonium dinitromethylides give rise to dicoordinate sulfur derivatives, i.e. diorganyl sulfides, under analogous conditions.[263]

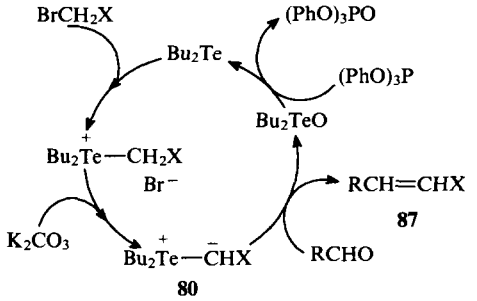
5. The monostabilised telluronium ylides **80**, generated by treating the corresponding telluronium salts with bases (Bu^tOK [243-245]) or NaH [244] and used in situ, are smoothly condensed with aldehydes and ketones, forming α,β-unsaturated esters (nitriles, ketones) **87** in fairly high yields. The (*E*)-isomers are formed preferentially in these reactions.

$$\underset{Y^-}{Bu_2\overset{+}{T}eCH_2X} \xrightarrow[-HY]{HB} \underset{\textbf{80}}{\left[Bu_2\overset{+}{T}e-\overset{-}{C}HX\right]} \xrightarrow[-Bu_2TeO]{R^1R^2C=O} \underset{\textbf{87}}{R^1R^2C=CHX}$$

X = CO_2Et, COPh, CN; Y = Cl, Br; R^1,R^2 = H, Alk, Ar.

On the other hand, the structurally similar sulfonium ylides do not react with aldehydes and ketones,[269,270] although they do react with α,β-unsaturated carbonyl compounds to form cyclopropanes.[269,270]

The ease of the synthesis of telluronium salts from dibutyl telluride and the ability of dibutyl telluroxide (or the corresponding dihydroxide), obtained as a result of the reaction, to be reduced back to the telluride by various reductants [$(PhO)_3P$, Na_2SO_3, $NaHSO_3$, $Na_2S_2O_3$] made it possible to carry out the latter reaction, as well as a series of other reactions involving organotellurium reagents described previously (see the reactions of arenetellurolate anions and diaryl tellurides) under catalytic conditions.[246] The alkenes **87** are formed stereoselectively in high yields when aldehydes and α-bromocarbonyl compounds are treated with catalytic amounts of dibutyl telluride in the presence of K_2CO_3 (as a base) and $(PhO)_3P$ (as a reductant) in accordance with the following mechanism:



X = CO_2Me, COPh, $COPr^i$.

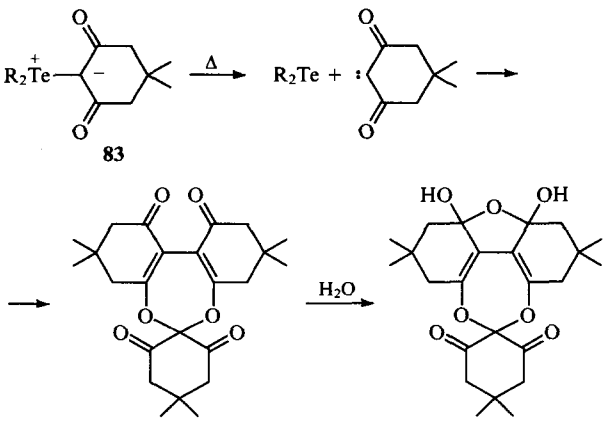
The fact that the alkenes **87** are obtained in high yields in the form of the (*E*)-isomers when aldehydes are condensed with telluronium salts in boiling THF in the absence of bases, i.e. under conditions which rule out the formation of ylides, is of special interest.[245,271]

$$ArCHO + \underset{Y^-}{Bu_2\overset{+}{T}e-CH_2X} \xrightarrow{\Delta} \underset{\textbf{87}}{ArCH=CHX}$$

X = CO_2Me, CN, COPh; Y = Cl, Br.

However, the mechanism of these reactions remains unelucidated.

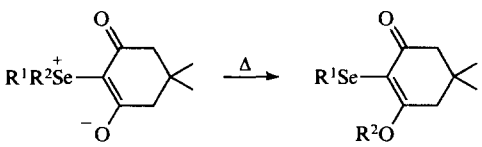
6. The thermolysis of the telluroniadimedone ylides **83** (M = Te) and their selenium analogues **83** (M = Se) proceeds in completely different ways. On heating in inert solvents, the former decompose with formation of tellurides and the product of trimerisation of the carbanionic fragment of compound **88**.[272]



83

88

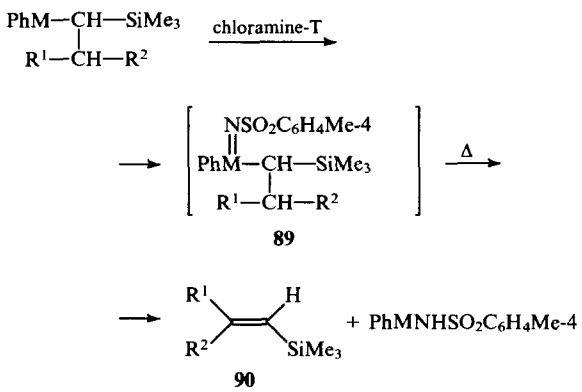
On the other hand, the selenoniadimedone ylides **83** undergo the Stevens thermal rearrangement under the same conditions.[273]



83a

The different results of the thermolytic reactions can be accounted for by the smaller Te^+-C^- bond energy compared with that of Se^+-C^-. This is also confirmed by mass-spectrometric data for the type **83** telluronium[274] and selenonium[275] ylides. In the case of the telluronium ylides, the intensities of the M^+ molecular peaks are extremely low (0.1%–0.3% of the total ionic current), whereas for the selenonium ylides they are fairly intense.

The thermolysis of the chalcogenonium imides **89**, containing S, Se, or Te, takes place in the same way and leads to the vinylsilanes **90** predominantly in the (*E*)-form.[276] The nature of the chalcogen affects only the reaction conditions: sulfur derivatives decompose at 100 °C, those of selenium decompose at room temperature, and those of tellurium decompose in boiling THF.



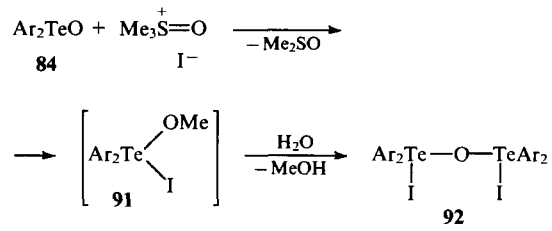
89

90

M = S, Se, Te; $R^1 = C_9H_{19}, C_{11}H_{23}, C_{13}H_{27}, C_{15}H_{31}$; R^2 = H.

7. Extremely significant differences are observed in the reactions of diaryl telluroxides and sulfoxides with alkylating agents. Depending on the nature of the alkylating agents, the sulfoxides undergo both *O*- and *S*-alkylation.[277] On the other hand, the interaction of diaryl telluroxides with various alkylating agents (trimethylsulfoxonium iodide,[278,279] dialkyl sulfates,[279,280] and methyl iodide[279,281]) leads evidently to *O*-alkylation only (it has been suggested that the structure of the intermediates corresponds to the σ-tellanes **91**). However, in most cases the compounds isolated were formed as a result of further reactions of these intermediates, the structure and composition of which are determined by the nature of the groups linked to the tellurium atom and the reaction conditions.

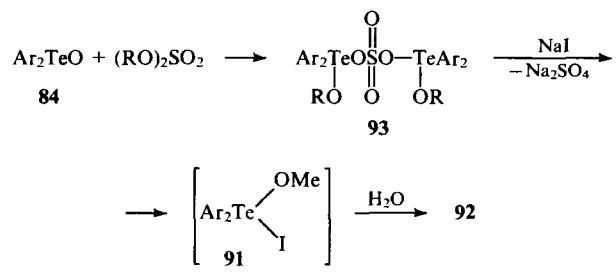
The interaction of the diaryl telluroxides **84** with trimethylsulfoxonium iodide leads ultimately to the bis(diaryliodotellurium) oxides **92**, probably via the intermediate *O*-alkylation product **91**.[278,279]



91

92

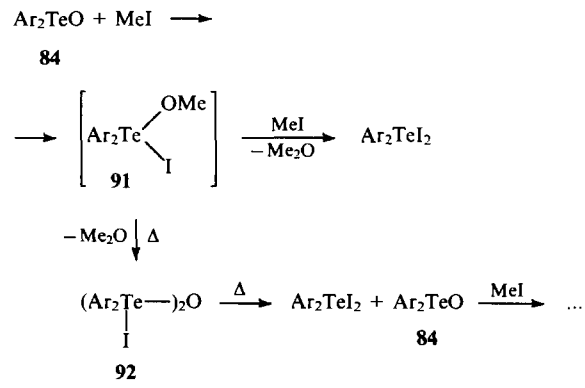
Treatment of diaryl telluroxides with dialkyl sulfates involves the formation of the σ-tellanes **93**,[279,282] which are converted into the oxides **92** on treatment with NaI $2H_2O$.



93

91

Telluroxides and sulfoxides behave quite differently in their reactions with methyl iodide. While dimethyl sulfoxide affords the *S*-alkylation product — trimethylsulfoxonium iodide — on refluxing in an excess of MeI,[277] diaryl telluroxides give rise to diaryltellurium diiodides in high yields under the same conditions.[279,281] The formation of the latter can be explained by the mechanism presented below,[279] which indicates two alternative paths leading to the conversion of diaryl telluroxides into diaryltellurium diiodides.



91

92

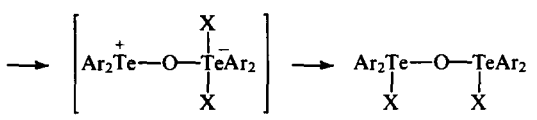
84

The possibility of the formation of tellurium diiodides via the bis(diaryliodotellurium) oxides **92** has been confirmed by the fact that the oxides **92** obtained by independent methods[282] decompose into diaryltellurium diiodides and diaryltelluroxides on heating in solution.

8. The diaryl telluroxides **84** react readily with the σ-tellanes Ar_2TeX_2, forming bis[diarylhalo(acetoxy)tellurium oxides **92** in high yields.[282]

$Ar_2TeO + Ar_2TeX_2 \longrightarrow$

84



92

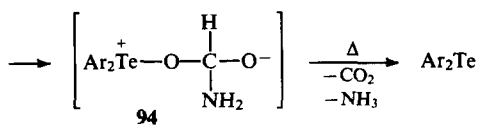
X = F, Cl, Br, I, OCOMe.

Such a reaction is evidently impossible for organosulfur compounds because of the instability of σ-sulfanes — analogues of Ar_2TeX_2.

9. The high nucleophilicity of the diaryl telluroxides **84**, which promotes the formation of the intermediate **94**, results in the ready reduction of compounds **84** to tellurides on heating in an excess of formamide at 120–140 °C. The yields of the tellurides are almost quantitative.[283]

$Ar_2TeO + HCONH_2 \longrightarrow$

84

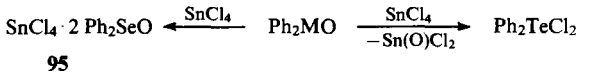


94

The same reagent has been used for the reduction of diaryl selenoxides,[283] whereas diaryl sulfoxides, which are the least basic among the chalcogenoxides, do not react with formamide.

Evidently formamide has significant advantages as a reductant over bis(trimethylsilyl) chalcogenides[284] and phenylselenotrimethylsilane.[285] Indeed, the above reagents, which are in addition synthesised only in moderate yields, have an unpleasant smell and are extremely sensitive to moisture and air. Furthermore, their employment entails the formation of side products [the chalcogens, $(Me_3Si)_2O$, or Ph_2Se_2 and $(Me_3Si)_2O$], which hinders the isolation and purification of diaryl tellurides.

10. The striking tendency of various organotellurium compounds to be converted into tetracoordinate tellurium derivatives is probably responsible for the different results of the reactions of diphenyl telluroxide and diphenyl selenoxide with $SnCl_4$. Whereas Ph_2TeO gives rise to the corresponding σ-tellane, i.e. Ph_2TeCl_2,[286] diphenyl selenoxide affords complex **95** under the same conditions.[287]



95

M = Se, Te.

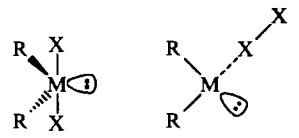
VIII. The increased stability of tetracoordinate tellurium derivatives

The most thoroughly investigated derivatives of tetracoordinate tellurium are σ-tellanes: diorganyltellurium dihalides R_2TeX_2 and organyltellurium trihalides $RTeX_3$. These compounds are at the same time important synthons for the preparation of various derivatives of di-, tri-, penta-, and hexa-coordinate tellurium.[2–5] Tetraorganyltellanes R_4Te have been less thoroughly investigated and the first tellurone reliably described (and so far the only one) is di(4-methoxyphenyl) tellurone.[288]

σ-Tellanes and tetraorganyltellanes exhibit an increased stability compared with the analogous sulfur and selenium derivatives. These compounds have a trigonal-bipyramidal structure; the equatorial and axial bonds, even those with identical substituents, have different lengths. The axial bonds are hypervalent,[289,290] their three-centre orbitals being occupied by four electrons: two from the *p*-orbitals of the chalcogen atoms and one each from the axial substituents. As a result of this, the axial bonds are appreciably lengthened compared with the usual two-centre two-electron covalent bonds. Thus the average lengths of the $Te-C_{eq}$ bonds are 2.127 Å for tetramethyltellane Me_4Te[291] and 2.13 Å for the tetraphenyltellane solvate $Ph_4Te \cdot 0.125C_6H_6$;[292] on the other hand, the $Te-C_{ax}$ bond lengths are 2.292 and 2.29 Å respectively. In the case of nonequivalent substituents, the axial positions are always occupied by the more electronegative ligands in which there is a possibility of delocalisation of the electrons from the nonbonding L^1-M-L^2 orbital (L is the substituent and M the chalcogen). The increased stability of σ-tellanes compared with other σ-chalcogenanes can be explained by the higher energy level of the *p* orbital of tellurium, which favours bonding.[289,290]

1. The σ-tellanes R_2TeX_2 and $RTeX_3$

Depending on the nature of the chalcogen and halogen atoms, the compounds R_2MHal_2 (M = S, Se, Te; Hal = F, Cl, Br, I) have either a covalent structure with a trigonal-bipyramidal configuration of the bond (TBP) at the central atom (compounds **96**) or are charge-transfer complexes (CTC) of type **97**.[293–297] In the latter, the chalcogen atom is coordinated to only one halogen atom and the M···X–X angle is close to 180°.



96 **97**

The formation of compounds of one type or another is determined primarily by the effective electronegativities (EO) of the chalcogen and halogen atoms. In general, if the electronegativity of the halogens is much higher than that of the chalcogens, covalent type **96** TBP structures are formed. Otherwise, the formation of type **97** CTC is to be expected. This rule agrees well with results of X-ray diffraction in other studies on R_2MX_2, the results of which for the structures of the compounds R_2MHal_2 are presented below:

M	F	Cl	Br	I
S	TBP	TBP	CTC	CTC
Se	TBP	TBP	TBP	CTC
Te	TBP	TBP	TBP	TBP

However, one should note that variation of the electronic nature of the groups R linked to the chalcogen atoms can alter the effective electronegativity of the latter, which may affect in its turn the structure of the R_2MHal_2. Thus diorganylselenium dibromides are usually σ-selenanes,[293–296] whereas, judging from the ^{13}C NMR spectra, dibromoselenoxanone[295,296] as well as the diarylselenium dibromides Ar_2SeBr_2 (Ar = 4-NCC_6H_4, 4-$O_2NC_6H_4$, 3,5-$Cl_2C_6H_3$, 2-ClC_6H_4) and $Ar^1Ar^2SeBr_2$ (Ar^1 = 2,6-$Cl_2C_6H_3$, Ar^2 = Ph)[298] are molecular complexes. This is due to the increase in the effective electronegativity of the selenium atom as a consequence of its conjugation with strongly electron-accepting groups.

It follows from the data presented that, regardless of the nature of the chalcogens, the true σ-chalcogenanes are the difluorides and dichlorides. The former are thermally stable for any M, while the stability of the dichlorides increases sharply in the sequence S, Se, Te. Some data on the thermal stabilities of the σ-chalcogenanes R_2MCl_2 as well as $RMCl_3$ and MCl_4 are presented below.

The σ-tellanes R_2TeX_2 are readily reduced to diorganyl tellurides R_2Te by various reductants (see above) and can be converted into telluronium salts, telluroxides, telluronium ylides,

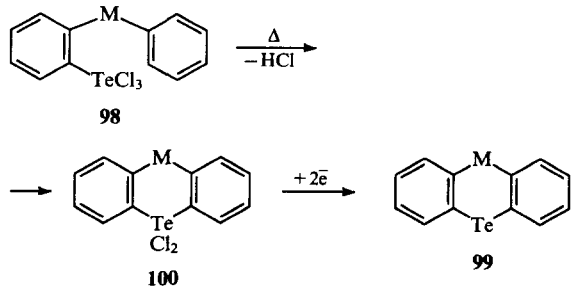
SCl_4 decomposes at −31 °C [299]	$SeCl_4$ melts without decomposition at 305 °C [299]	$TeCl_4$ melts without decomposition at 224 °C [299]
The compounds $RSCl_3$ decompose even at temperatures in the range 5–25 °C [300,301]	The compounds $RSeCl_3$ are stable at room temperature; on heating, they decompose readily into RSeCl and Cl_2 [302–305]	The compounds $RTeCl_3$ are stable up to their melting points [2–5]
The compounds R_2SCl_2 decompose at temperatures below 0 °C; at room temperature, they exist only under a dry chlorine atmosphere [306–310]	The compounds R_2SeCl_2 are stable up to their melting points [299,305]	The compounds R_2TeCl_2 are stable up to their melting points [2–5]

and tetraorganyltellanes.[2–5] On interaction with $TeCl_4$, diaryltellurium dichlorides are converted into aryltellurium trichlorides.[311]

Like other organyltellurium trihalides $RTeX_3$, aryltellurium trichlorides (the most thoroughly investigated representatives of σ-tellanes of this type) are readily reduced to diorganyl ditellurides, hydrolysed to aryltellurium oxide halides, and are converted into diaryltellurium dichlorides (symmetrisation reaction).[311] They also readily form the pertelluranes $[RTeX_4]^-$ and $[RTeX_3Y]^-$ containing a pentacoordinate tellurium atom.[2–5]

Aryl(organyl)tellurium trihalides $RTeHal_3$ are electrophiles, but their reactivity is inferior to that of the corresponding tellurium tetrahalides. The electrophilicity of the aryltellurium trihalides $ArTeHal_3$ (Hal = Cl, Br, I) decreases in the sequence Cl, Br, I.[312] Aryltellurium trichlorides therefore add comparatively readily to double and triple bonds and undergo electrophilic substitution reactions with activated strong electron donors, aromatic substrates, and aliphatic compounds containing activated methyl or methylene groups (ketones, acetic anhydride, etc.).[2–5] The method of synthesis specific to tellurium-containing heterocycles, involving the intramolecular electrophilic cyclisation of the aryltellurium trichlorides **98** having the appropriate structure, is in fact based on the electrophilic nature of the trichlorotelluro-groups.

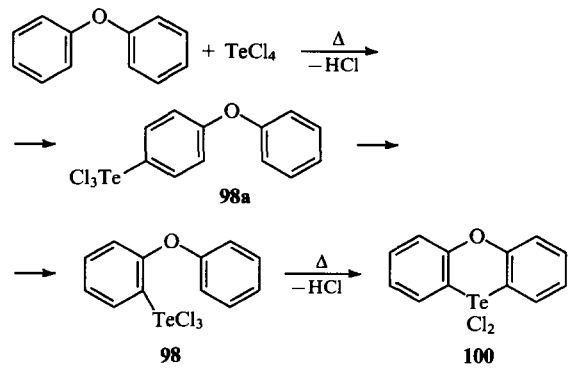
This reaction has been most often employed to synthesise tricyclic tellurium-containing systems **99** with two heteroatoms. The reaction leads to the formation of the corresponding tellurium dichlorides **100**, which are smoothly converted into the heterocycles **99** on treatment with various reductants.



M = CH_2, NH, O, S.

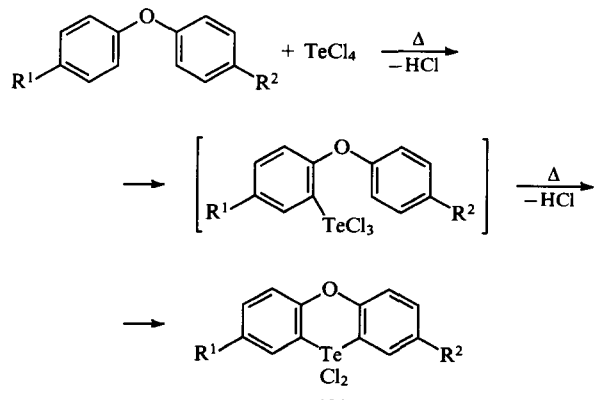
The synthesis is usually carried out by heating the trichloride **98** in suitable solvents or without them. The cyclisation temperatures are determined primarily by the electronic nature of the heteroatoms. As the electron-donating properties of these atoms become more pronounced, the temperature at which the process takes place is reduced. Thus the cyclisation of 2-(phenylamino)phenyltellurium trichloride **98** (M = NH) takes place on refluxing in acetic acid,[313] whereas the cyclisation of the diphenyl ether **98** (M = O) and diphenyl sulfide **98** (M = S) requires heating to 200 °C [314] and 240–250 °C [315] respectively. The weak electron-donating properties of the methylene bridge are evidently the reason why 10,10-dichlorotelluraxanthene **100** (M = CH_2) could not be obtained by heating 2-benzylphenyltellurium trichlorides **98** (M = CH_2).[316] The synthesis of this heterocycle was found to be possible only by carrying out the reaction in the presence of $AlCl_3$, which increases the electrophilicity of the trichlorotelluro group as a result of the formation of the complex $[ArTeCl_2]^+[AlCl_4]^-$.[316,317]

It is of interest to note that 10,10-dichlorophenoxatellurane **100** (M = O) can be obtained in approximately 50% yield by the prolonged heating of equimolar amounts of $TeCl_4$ and diphenyl ether.[314] The primary product of this reaction, isolated in an analytically pure form, is *p*-phenoxyphenyltellurium trichloride **98a**, because, like other electron releasing groups,[2,3,318,319] the OPh group directs the electrophile to the *para*-position. However, on further heating of this compound, the $TeCl_3$ group migrates to the *ortho*-position and the *o*-phenoxyphenyltellurium trichloride thus obtained is converted further into the heterocycle **100** (M = O).



A similar migration of the $TeCl_3$ groups with subsequent cyclisation occurs on heating *p*-(phenylamino)phenyltellurium trichloride (obtained from *p*-chloromercuriodiphenylamine and $TeCl_4$ [313]) in acetic acid and by heating $TeCl_4$ in an excess of Ph_2S at 190–200 °C.[196] The yields of the heterocycles **99** (M = NH, S) are, however, extremely low and amount to 7% and 6% respectively.

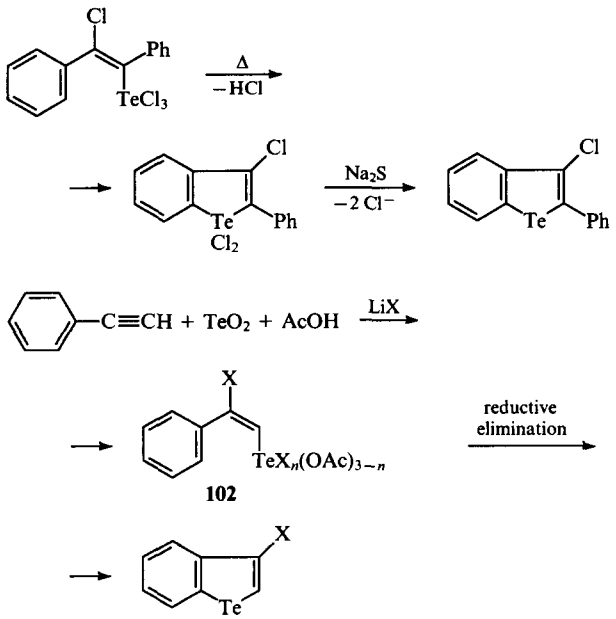
Similar reactions have been used also to synthesise 2,8-disubstituted 10,10-dichlorophenoxatelluranes **101**. The latter are obtained in 14%–50% yields on heating melts of mixtures of 4,4′-disubstituted diphenyl ethers and $TeCl_4$.[177,320–324]



$R^1 = R^2$ = Me,[321] Cl,[322] F;[323]

R^1 = Me, R^2 = H,[320] Cl,[320] F,[324] CO_2H;[320] R^1 = F, R^2 = Cl.[177]

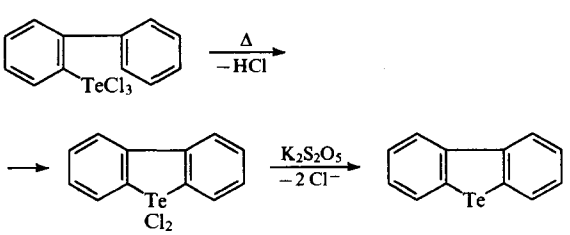
The synthesis of five-membered tellurium-containing heterocycles — substituted benzo[*b*]tellurophenes and dibenzotellurophenes — has also been achieved with the aid of cyclisation reactions of the corresponding aryltellurium trichlorides. Thus the first representative of benzo[*b*]telluro-phenes — 1,1,3-trichloro-2-phenylbenzo[*b*]tellurophene — has been obtained in a yield exceeding 50% by heating 2-chloro-1,2-diphenylvinyltellurium trichloride[325] (the product of the electrophilic addition of $TeCl_4$ to diphenylethyne[326]). A series of 3-halobenzo[*b*]tellurophenes have been synthesised in 21%–92% yields by treating phenylethyne with tellurium dioxide in acetic acid in the presence of LiX.[327,328] The latter reaction evidently proceeds via the intermediate formation of the σ-tellanes **102**, the cyclisation of which leads to the required heterocycles.



102

X = Cl, Br, I.

Brief heating at 210 °C of 2-trichlorotelluriobiphenyl (obtained from 2-chloromercuriobiphenyl and $TeCl_4$) leads to 1,1-dichlorodibenzotellurophene in almost quantitative yield.[329]



Evidently, these reactions, like those examined above, could not be used to obtain the sulfur and selenium heterocycles because the corresponding arylsulfur trichlorides and arylselenium trichlorides are thermally unstable. However, benzo[*b*]thiophene[330] and benzo[*b*]selenophenes[331] as well as dibenzothiophene[332] and dibenzoselenophene[333] have been obtained by the thermal cyclisation of arylchalcogen monohalides ArMX (M = S, Se; X = Cl, Br, I).

2. Tetraorganyltellanes R_4Te and tetraalkoxytellanes $(RO)_4Te$

As in the case of the σ-tellanes R_2TeX_2 and $RTeX_3$ as well as their sulfur and selenium analogues, significant differences between the thermal stabilities of tetraaryltellanes Ar_4Te **103** and other tetraarylchalcogenanes Ar_4M (M = S, Se) are observed. The latter exist only in solutions at very low temperatures [thus the formation of tetrakis(pentafluorophenyl)sulfane in solution on reaction between SF_4 and C_6F_5Li has been detected by the ^{19}F NMR method at −80 °C[334]], decomposing to biaryls and diaryl chalcogenides on raising the temperature. In contrast to them, the tetraaryltellanes **103** are stable crystalline compounds under the usual conditions, melting above 100 °C.[335–338] It is noteworthy that the tetraalkyltellanes **103**, which have been obtained comparatively recently, are thermally stable but are extremely sensitive to air and light.[339–341] The most general method of synthesis of compounds **103** involves the interaction of organolithium or organomagnesium derivatives with $TeCl_4$[335–338,340,341] [Ph_4Te has also been obtained from PhLi, Ph_2TeCl_2, and Ph_3TeCl,[335] whilst $(CF_3)_4Te$ has been synthesised by the reaction of $(CF_3)_2TeCl_2$ with $(CF_3)_2Cd$.[339]]

$$RM + TeCl_4 \xrightarrow[-MCl]{} R_4Te$$

103

M = Li, MgX; R = Ph,[335,337,338] C_6D_5,[338] 4-MeC_6H_4,[337,338] C_6F_5,[336] Me,[340,341] Bu,[341] Me_3SiCH_2,[341] $CH_2{=}CH$,[340] $CH_2{=}CHCH_2$.[341]

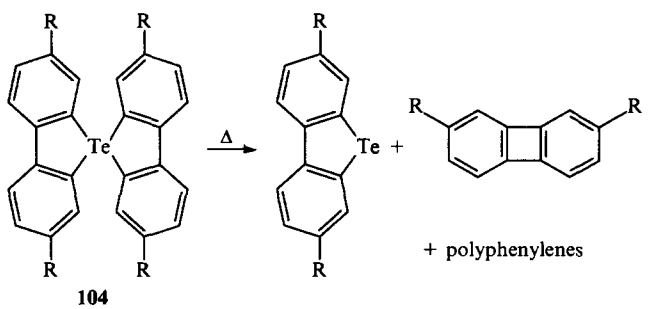
Tetraaryltellanes, which are stable under the usual conditions, decompose smoothly to diaryl tellurides and biaryls on heating.

$$Ar_4Te \xrightarrow{\Delta} Ar_2Te + Ar{-}Ar$$

103

The decomposition of tetraalkyltellanes, especially $(CF_3)_4Te$, proceeds in a more complex manner, considerable amounts of secondary reaction products being formed in addition to dialkyl tellurides and the corresponding hydrocarbons.

The highly stable cyclic tetraaryltellanes **104**[250,255,342,343] (with melting points above 200 °C) decompose on thermolysis similarly to the acyclic tetraaryltellanes **103**: the principal decomposition products are dibenzotellophene and biphenylene.



104

R = H, Me.

The high thermal stability of the recently synthesised hexamethyltellurium Me_6Te is also noteworthy;[344] this compound does not decompose on heating in solution in C_6D_6 in a sealed tube at 140 °C in the course of 4.5 h (for comparison, we may note that tetramethyltellane Me_4Te decomposes fully in 4 h at 120 °C).[344]

The thermal stabilities of tetraalkoxychalcogenanes $(OR)_4M$ (M = S, Se, Te) are also very different. Among the sulfur derivatives, only those which contain perfluorinated alcohol residues are stable.[345] Tetraalkoxyselenanes are stable only below 0 °C,[346,347] decomposing rapidly to dialkyl selenites and dialkyl ethers when the temperature is raised.[346,347]

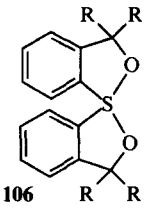
$$(RO)_4Se \xrightarrow{\Delta} (RO)_2Se{=}O + R_2O$$

105

The tetraalkoxytellanes $(RO)_4Te$ (R = Me, Et, Pr^i, Bu)[347–349] are thermally more stable than their sulfur and selenium analogues and can be vacuum distilled without decomposition. Their thermolysis proceeds in a different way from that of

the selenium derivatives. Thus tetraethoxytellane decomposes on heating to ethanol, acetaldehyde, and tellurium.[350]

We may also note that dialkoxydiorganyltellanes $R^1_2Te(OR^2)_2$, obtained by means of exchange reactions of diorganyltellurium dihalides with sodium alkoxides, are thermally stable regardless of the nature of the alkoxy-groups.[351] On the other hand, only those sulfur analogues which contain perfluoroalkoxy-groups, for example $Ph_2S[OC(CF_3)_2Ph]_2$,[306,352] or have the cyclic structure **106**[306] are stable under the usual conditions.



R = H, Me, CF_3.

106

IX. Reactions involving the dissociation of C–Te bonds

The C–Te bonds have the lowest energy among carbon–chalcogen bonds. The bond energies of the latter as well as the M–M bond energies (kJ mol^{-1}) in diorganyl dihalides RM–MR[204] are presented below.

	S	Se	Te
C_{prim}–M	287.0	246.9	213.4
C_{sec}–M	285.8	245.6	302.0
M–M	264.0	202.0	149.8

As a result of the significant decrease in the carbon–chalcogen bond energies in the sequence S, Se, Te, certain reactions, which in the case of organosulfur and organoselenium compounds take place with retention of the C–M bonds, in the case of organotellurium compounds are accompanied by the dissociation of the C–Te bonds. Because of this, certain reactions leading to particular types of acyclic and cyclic sulfur and selenium compounds are inapplicable to the synthesis of the structurally similar tellurium-containing derivatives. On the other hand, the application of organotellurium compounds in preparative organic chemistry is based precisely on the ease of dissociation of the C–Te bond accompanied by elimination of the Te atom. This section deals with the reactions of derivatives of dicoordinate tellurium, principally of diorganyl tellurides of various types, which proceed with dissociation of one or two C–Te bonds (elimination of the Te atom). (Analogous reactions of certain derivatives of tricoordinate tellurium were examined in Section VII, while those of derivatives of tetracoordinate tellurium and the telluroxide elimination reactions have been considered in other reviews.[10,26,27,29,30])

The dissociation of the C–Te bonds in organotellurium compounds in general and in diorganyl tellurides in particular takes place as a result of pyrolysis or photolysis and also on treatment with Raney nickel, transition metals (primarily palladium and its compounds), nontransition metal salts, Group IV element hydrides, as well as a series of oxidants, electrophiles, and nucleophiles.

The gas-phase pyrolysis of dialkyl tellurides[2,3,353,354] is accompanied by the dissociation of both C–Te bonds and makes it possible to obtain ultrapure tellurium. It is believed[2,3,355] that these reactions take place via a radical mechanism. The pyrolysis of dimethyl telluride (330–380 °C) is four times faster than that of Me_2Se.[353] The decomposition in the gas phase of mixtures of volatile dialkyl tellurides and alkyl derivatives of metals (Zn, Cd, Hg, etc.)[356,357] is used for the synthesis of the tellurides of these metals, which have found an application as semiconductors, in the preparation of opto- and acousto-electronic systems, etc.

The synthesis of benzo[*b*]thiophene and of its selenium analogue (in yields of 85% and 40% respectively),[358] as well as selenophene, mixed with benzo[*b*]selenophene,[359] can be achieved by means of the high-temperature reactions of diphenyl disulfide and diselenide with ethyne and propargyl alcohol respectively. On the other hand, diphenyl ditelluride decomposes in similar reactions with liberation of metallic tellurium; for example, benzo[*b*]tellurophene is detected in only trace amounts (1%–2%).[358] The different compositions of the final products of the reactions of 2-iodothiophene with dimethyl selenide and telluride and the formation of considerable amounts of metallic tellurium[360] are also a result of the decrease in the carbon–chalcogen bond energy on passing from selenium to tellurium.

Reactions involving the pyrolytic dissociation of the C–Te bonds have been used in a number of instances for the preparative synthesis of various hydrocarbons. Allyl and benzyl halides interact with lithium telluride, affording 1,5-dienes (yield 60%–93%)[361] and bibenzyl (yield 37%)[24,361] as the main products. These hydrocarbons are the products of the coupling of the allyl(benzyl) radicals arising following the elimination of the tellurium atom from the intermediate diallyl(benzyl) tellurides.

$$R^1CH{=}CHCHX + Li_2Te \xrightarrow[-LiX]{110\ ^\circ C} \left[\left(R^1CH{=}\underset{R^2}{\underset{|}{C}}H\right)_2Te\right] \xrightarrow[-Te]{\Delta} R^1CH{=}\underset{R^2}{\underset{|}{C}}H^{\bullet}$$

$$\longrightarrow R^1CH{=}\underset{R^2}{\underset{|}{C}}H{-}\underset{R^2}{\underset{|}{C}}H{-}CH{=}CHR^1$$

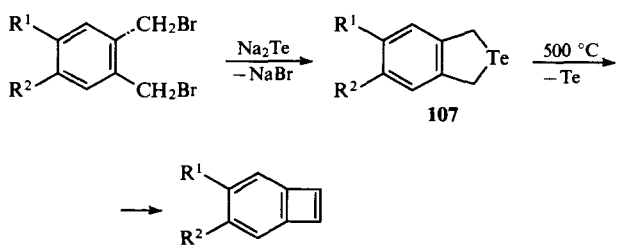
$R^1 + R^2 = -(CH_2)_4-$, $-(CH_2)_5-$, $-(CH_2)_6-$;

$R^1 = R^2 = Me$; R^1 = Ph, $CH_2{=}CH$, Pr, R^2 = H; X = Cl, Br.

$$PhCH_2Br + Li_2Te \xrightarrow[-LiBr]{110\ ^\circ C} [(PhCH_2)_2Te] \xrightarrow[-Te]{\Delta} \longrightarrow PhCH_2^{\bullet} \longrightarrow PhCH_2CH_2Ph.$$

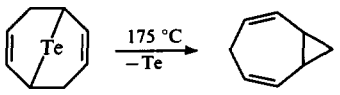
Such reactions, which constitute a new method of synthesis of 1,5-dienes are characteristic of tellurium derivatives only. Indeed, whereas treatment of 3-bromocyclohexene with lithium telluride gives 2,2′-bicyclohexenyl in 81%–86% yield, only the corresponding selenide is formed in the analogous reaction with Li_2Se.[361] However, one should note that the interaction of allyl and benzyl halides with sodium and lithium tellurides at room temperature makes it possible to obtain symmetrical diallyl or dibenzyl tellurides in 50%–100% yields.[341,355,362–366]

The pyrolysis of the cyclic tellurides **107** (the mechanism of their synthesis is presented below) and **12** (see over; the synthesis of this compound was described in Section II) is also accompanied by the elimination of the tellurium atom and the formation of derivatives of cyclobutene[367] and bicyclo[5.1.0]octa-2,5-diene respectively.[75]



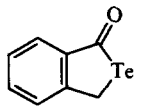
107

$R^1 = R^2 = H$; $R^1 + R^2 = (-CH{=}CH-)$.



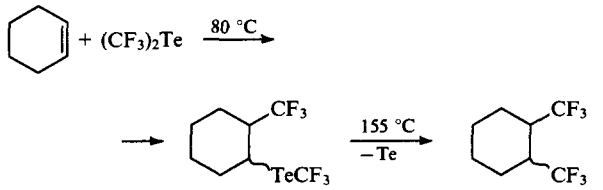
12 13

On the other hand, the attempts to obtain benzocyclobutenone by the vacuum flash photolysis of tellurophthalide **108** were unsuccessful;[134] the elimination of the tellurium atom was not observed under these conditions.



108

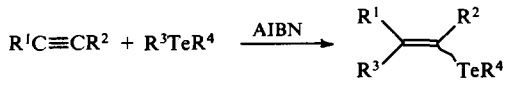
As the electron-accepting properties of the groups linked to the tellurium atom are enhanced, the temperature at which the tellurium atom is eliminated probably decreases. Thus at 80 °C bis(trifluoromethyl) telluride adds to cyclohexene, forming a mixture of *cis*- and *trans*-1-trifluoromethyltelluro-2-trifluoroethylcyclohexanes **109**; the tellurium atoms are eliminated from these compounds at 155 °C.[368]



109

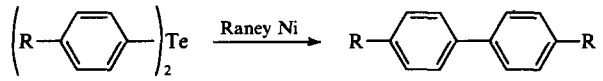
According to the data of Naumann and Wilkes,[368] bis(trifluoromethyl) telluride is superior to CF_3I and $(CF_3)_2Hg$ in terms of its trifluoromethylating capacity in both thermal and photochemical reactions.

Whereas the carbotelluration of cyclohexene (preceding reaction) takes place at 80 °C, the carbotelluration of alkynes is achieved when benzene solutions of equimolar mixtures of alkynes and diorganyl tellurides are refluxed in the presence of catalytic amounts of 2,2′-azobisisobutyronitrile (AIBN).[369,370]



The reaction proceeds via a radical mechanism and leads to a mixture of (*E*)- and (*Z*)-vinyl tellurides in yields ranging from 40% to 100%. The $C(sp^3)$–Te bonds are dissociated exclusively in alkyl phenyl tellurides; the C_{tert}–Te bonds are cleaved more readily than the C_{prim}–Te bonds.[370]

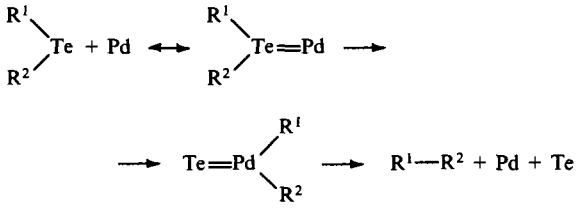
The synthesis of symmetrical biaryls from diaryl tellurides catalysed by Raney nickel is of definite interest for preparative organic chemistry.[371] The reactions are carried out by refluxing diaryl tellurides with a 20-fold molar excess of freshly prepared Raney nickel in 2-methoxyethyl ether for many hours and make it possible to obtain biaryls in 72%–90% yields.



R = OEt, OMe, Me, H, Br.

However, one should note that, according to Horner and Doms,[372] Ph_2Te is reduced under the influence of Rany nickel to benzene. Tellurium is then evidently converted into nickel telluride because on treatment with inorganic acid after the reaction H_2Te is evolved.

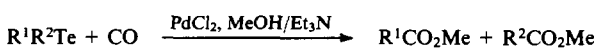
A more general method of synthesis of hydrocarbons of different composition (yield 76%–100%), based on the elimination of tellurium atoms from diorganyl tellurides, involves treatment of the tellurides R^1TeR^2 with palladium generated in situ from $Pd(OAc)_2$ and Et_3N.[373]



R^1 = 4-$MeOC_6H_4$; R^2 = 4-$MeOC_6H_4$, Ad^t, $C_{15}H_{31}$;

$R^1 = R^2 = PhCH_2CH_2$; $R^1 = PhCH_2CH_2$, $R^2 = CH_2Ph$.

Palladium(II) salts promote the insertion of carbon monoxide in the Te–C bonds of diorganyl tellurides, which leads to either carboxylic acids[43,374] or their methyl esters[53] depending on the conditions. The most convenient procedure for carrying out these reactions involves treatment of solutions of diorganyl tellurides in MeOH/Et_3N at room temperature with carbon monoxide in the presence of stoichiometric amounts of palladium(II) salts.[53] The reactions can also be carried out in the presence of catalytic amounts of $PdCl_2$ when the reaction mixtures contain oxidants, the most effective of which is $CuCl_2$.[53] It is believed[43,53] that the reactions proceed via the intermediate formation of the monomeric complexes $(R_2Te)_2PdCl_2$ or dimeric complexes $[R_2TePdCl_2]_2$ with subsequent migration of the organic groups from Te to Pd, the insertion of CO in the Pd–C bond, and the hydrolysis of the acylpalladium intermediates.

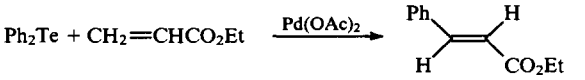


$R^1 = Ph$;

R^2 = PhCH=CH, EtO_2CCH=CH, PhC≡C, $C_6H_{13}C$≡C, Ph, $C_{12}C_{25}$.

It is noteworthy that, when the salts of other transition metals capable of forming complexes with diorganyl tellurides [Rh(III), Ru(III), Ir(III)] are used, the carbonylation reactions have very low yields (for $RhCl_3 \cdot 3H_2O$) or do not occur at all. The ability of triorganyl chalcogenides R_2M to enter into the reactions considered above increases sharply in the following sequence of the elements M: S ≪ Se < Te.[43,53] Thus Ph_2S does not enter into the reaction, Ph_2Se forms methyl benzoate in 14% yield, whereas in the reaction involving Ph_2Te the yield of the ester increases to 86%.

The arylation of alkenes by diorganyl tellurides also proceeds via arylpalladium intermediates formed when phenyl groups migrate from Te to Pd.[375] Thus the interaction of diphenyl telluride with ethyl acrylate in the presence of $Pd(OAc)_2$ leads to the formation of (2*E*)-phenyl acrylate in a yield exceeding 90% (biphenyl is a side product of the reaction).



It is noteworthy that Ph_2Se undergoes a similar reaction, but its rate is much slower than that of the reaction with Ph_2Te.

Under comparatively mild conditions, one or both C–Te bonds in diorganyl tellurides are cleaved by the triorganyl-substituted hydrides of Group IVA elements R_3XH (X = Si, Ge, Sn; R = Et, Bu, Ph).[376–382] The composition of the final reaction product (dissociation of one or two bonds) then depends on the nature of the hydride. Thus Et_3SiH and Et_2Te afforded compounds **110** and **111** in comparable yields at 200 °C,

Et_3GeH gave rise to the analogous compounds at 140 °C, but the reaction of Et_3SnH (even at 20 °C) led to the formation of only bis(triethylstannyl) telluride **111** (X = Sn).[376,377]

$$R_3XH + Et_2Te \xrightarrow[-C_2H_6]{} \underset{\mathbf{110}}{R_3X{-}TeEt} + \underset{\mathbf{111}}{R_3X{-}Te{-}XR_3}$$

The mild conditions in the reactions of diorganyl tellurides with triorganyltin hydrides and the high yields of the hydrocarbons makes it possible to employ diorganyl tellurides in the synthesis of the latter.[378–382] Ph_3SnH or Bu_3SnH are usually employed in these reactions. Diorganyl selenides are reduced to hydrocarbons in high yields (heating with Ph_3SnH at 120 °C).[378] However, organic sulfides are inert to Ph_3SnH.[378] The reduction of tellurides and selenides by tin hydrides probably proceeds via a S_H2 mechanism;[378,383] the rate of reduction of tellurides is then higher than that of selenides.

$$R_3SnH \longrightarrow R_3Sn^{\bullet} + H^{\bullet}$$

$$R_3Sn^{\bullet} + R^1_2Te \longrightarrow R_3Sn{-}TeR^1 + R^{1\bullet}$$

$$R^{1\bullet} + R_3SnH \longrightarrow R^1H + R_3Sn^{\bullet}$$

The dissociation of one (more rarely two) C–Te bond is observed in the protodetelluration and halodetelluration reactions of diorganyl tellurides. These reactions are most characteristic of alkyl aryl tellurides containing in the *ortho*-position functional groups capable of being coordinated to the Te atom; the weaker of the two C–Te bonds, namely $C(sp^3)$–Te, is then cleaved. Thus treatment of alkyl *o*-carbonylaryl tellurides by hydrogen halides (usually HBr) affords high yields of the *o*-halotellurocarbonyl compounds **112** stabilised by strong intramolecular O→Te coordinate bonds.[107,114,116,384]



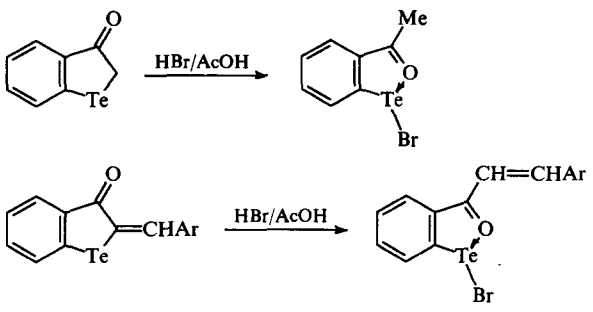
112

X = Cl, Br, I; $R^1 = R^3 = H$; $R^2 = CH_2CO_2Et, CH_2CH(OEt)_2$;[107]

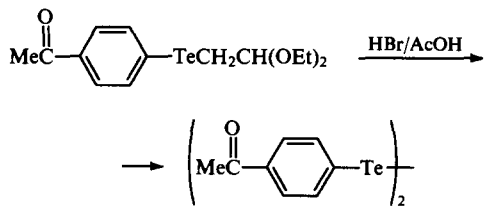
$R^1 = R^2 = Me$; R^3 = H, 4-Cl, 4-Me, 5-Me;[116]

R^1 = Me,[384] Ph;[114] R^2 = Bu; R^3 = H; X = Br.

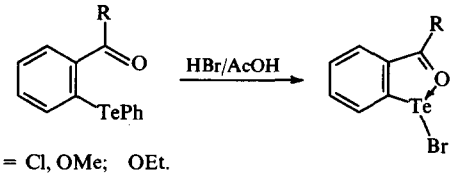
The $C(sp^3)$–Te bonds in telluroindoxyl[112] and telluroaurones[110] dissociate under similar conditions.



The presence of the COR groups in the *ortho*-positions relative to the TeR groups is a necessary condition for the formation of arenetellurenyl halides. Indeed, in the case of the diethyl acetal of *p*-acetylphenyltelluraacetaldehyde the hydrolysis leads only to the corresponding ditelluride.



It is of interest to note that not only the $C(sp^3)$–Te bond but also the C_{Ar}–Te bonds are cleaved by HBr when coordinating groups are present in the *ortho*-position in the molecules. Treatment of derivatives of 2-carboxyphenyl phenyl telluride (but not the acid itself) with HBr in acetic acid leads to tellanyl bromides in high yields.[113] Bearing in mind the ease of the reduction of the tellanyl bromides obtained to ditellurosalicylic acid, this reaction can be regarded as a convenient preparative method of synthesis of the latter.



R = Cl, OMe; OEt.

The $C(sp)$–Te bonds in the ethynes **113**[385,386] and **114**[387] and in alkylchalcogenovinylethynes **50a**[386,388] are very readily cleaved by acids in the presence (or absence) of Hg^{2+} salts.

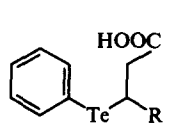
$RC{\equiv}CMMe$	$MeMC{\equiv}CMMe$	$CH_2{=}CHC{\equiv}CMMe$
113	**114**	**50a**

R = Me, Ph.

Whereas phenyl(methyl)thio- and phenyl(methyl)seleno-ethynes are hydrated with formation of the methyl esters of phenyl(methyl)thio(seleno)acetic acids, their tellurium analogues afford only the products of the cleavage of the $C(sp)$–Te bonds ($PhC{\equiv}CH$) and the product of partial dehydration — PhCOMe in the case of compound **113** (R = Ph, M = Te).[385] Whereas bis(methylseleno)ethyne **114** (M = Se) gives rise to a small yield of the addition product of the triple bond in its reaction with acetic acid in the presence of Hg^{2+} salts, its tellurium analogue undergoes only protodetelluration.[387] The product of the addition of acetic acid to the triple bond can be obtained under mild conditions from 1-methyltellurobut-3-en-1-yne **50a** (M = Te) in a low yield.[388] However, under more severe conditions this telluride is protodetellurated,[388] although the sulfur and selenium compounds having analogous structures are entirely stable under these conditions.[388]

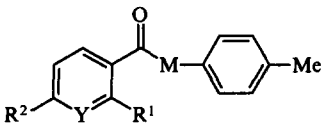
The ease with which protodetelluration takes place prevents in many instances the application in the synthesis of tellurium-containing compounds of reactions such as those employed in the chemistry of their sulfur and selenium analogues. Thus 3-phenyltelluropropionic acid **115** (R = H)[191] and its phenyl analogue **115** (R = Ph)[109] do not cyclise on treatment with perfluoroacetic acid (PFA) under the conditions employed to obtain selenachromanones,[389] but decompose with liberation of metallic tellurium. Similarly the attempts to synthesise telluro-chromanone by the pyrolysis of β-(*o*-carboxyphenyltelluro)-propionic acid or by the Dieckmann condensation of its diester were unsuccessful: the reactions occurred with cleavage of the $C(sp^3)$–Te bonds and led to ditellurosalicylic acid.[191]

Here it is appropriate to mention that one of the methods of synthesis of thia- and selena-xanthones — the photocyclisation of the esters **116** (M = S, Se) is inapplicable to the synthesis of telluraxanthones. UV irradiation of solutions of the telluroesters **116** (M = Te) leads to a complex mixture of products as a consequence of the cleavage of the C–Te bonds.[114,390,391]



115

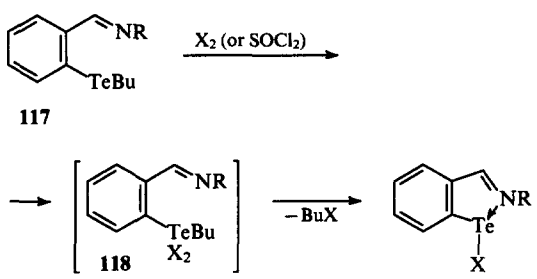
R = H, Ph



116

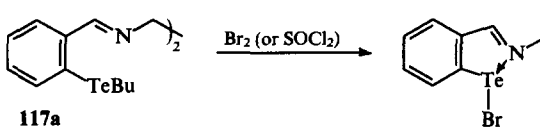
M = S, Se, Te; $R^1 = R^2 = H$; R^1 = H, R^2 = OMe; R^1 = Cl, SMe, OMe, SO_2Me; R^2 = H, Y = N, CH.

Reactions involving the oxidative addition of the halogens to alkyl aryl tellurides (see Section V and also Refs. 2–4) usually lead to stable alkylaryltellurium dihalides. However, when the *o*-tellurated azomethines **117**[104,123,124,126] and **117a**[125] react with the halogens or SO_2Cl_2, the C(sp^3)–Te bonds are cleaved, which leads to the formation of the corresponding tellanyl halides in high yields. The reactions evidently proceed via the σ-tellane intermediates **118**, the existence of which in solutions at a low temperature has been demonstrated with the aid of ^{1}H NMR spectra.[104] When the temperature is raised to room temperature, butyl halide molecules are eliminated.



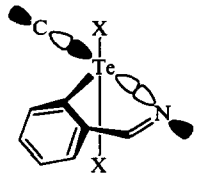
117

118

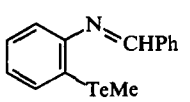


117a

The driving force of these reactions is, as in the protodetelluration reactions examined above, the marked stabilisation of tellanyl halides (which are 10-Te-3-telluranes according to the N–X–L nomenclature[392]) as a result of the coordination of the N(O) atoms to the tellurium atoms. In addition, there are favourable steric conditions for the N–Te and n(N) → σ*(Te–Bu) electron delocalisations in the intermediates **118**. As can be seen from the orbital interaction model **118a**, such delocalisation weakens the Te–C bond, which forms an angle of approximately 180° with the Te←N bond.

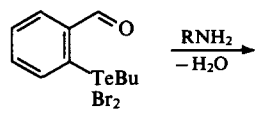


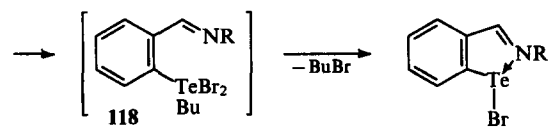
118a



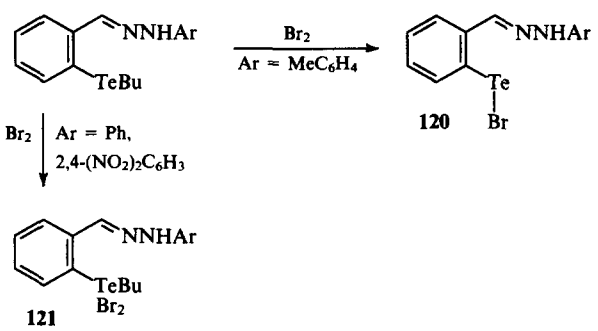
119

There are many examples of reactions facilitating the dissociation of the C–X bonds, which occurs when the interacting fragments are arranged in such a way that appreciable overlap of the n(O)–σ*(X–C) or n(N)–σ*(X–C) orbitals and hence partial population of the antibonding σ*(X–C) orbitals are ensured. In fact, benzylidene-2-methyltelluroaniline **119**, in which there is no N→Te coordination, gives rise to stable tellurium dihalides. The interaction of *o*-dibromo(butyl)tellurobenzaldehyde with primary amines gives rise to *o*-halotellurobenzylideneamines and not the σ-tellanes **118**.[104,124]



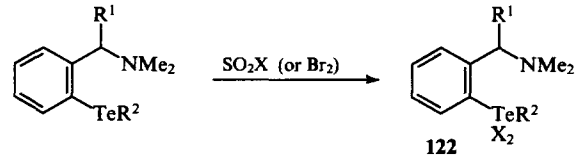


Thus, regardless of the nature of the substituents in the *N*-aryl rings of the azomethines **118**, their halogenation always leads to arenetellanyl halides. On the other hand, similar reactions with the arylhydrazones of 2-butyltellurobenzaldehyde proceed differently.[393] Electron-donating substituents in the arylhydrazone rings (Ar = MeC_6H_4) favour the cleavage of the C(sp^3)–Te bond on bromination, which leads to the formation of the tellanyl bromide **120**; when Ar = Ph or 2,4-$(NO_2)_2C_6H_3$, the arylhydrazones of 2-dibromo(butyl)tellurobenzaldehyde **121** are formed.



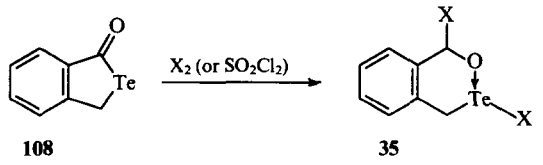
The reactions examined above, involving the halogenolysis of *o*-butyltellurobenzylideneamines and the arylhydrazones of 2-butyltellurobenzaldehyde are excellent illustrations of the influence of intramolecular N→Te coordinate bonds on the reactivity of organotellurium compounds (for other examples, see Section X).

It is noteworthy that, when 2-alkyltellurobenzyldimethylamines are treated with SO_2Cl_2[131] or Br_2,[131,132] the stable σ-tellanes **122** are formed. This is evidence that the coordinate bonds involving an sp^3-hybridised nitrogen atom are weaker than those involving an sp^2-hybridised nitrogen atom.



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

The cleavage of the C(sp^3)–Te bond at low temperatures takes place also in the halogenolysis of tellurophthalide **108**.[134] The tellanyl halides **35** formed in this reaction are the first examples of stable alkanetellanyl halides, their stability being due to the presence of the O→Te coordinate bonds.



108 35

X = Cl, Br, I.

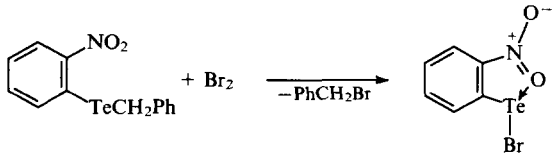
The halogenolysis of aryl benzyl tellurides, accompanied both by the dissociation of the C(sp^3)–Te bonds and by an increase in the coordination number of the tellurium atom, proceeds fairly specifically under the influence of $SOCl_2$ or SO_2Cl_2.[364,394]

$$RTeCH_2Ph \xrightarrow{X} RTeCl_3 + PhCH_2Cl$$

R = 4-MeOC$_6$H$_4$, 2-C$_{10}$H$_7$; X = $SOCl_2$, SO_2Cl_2.

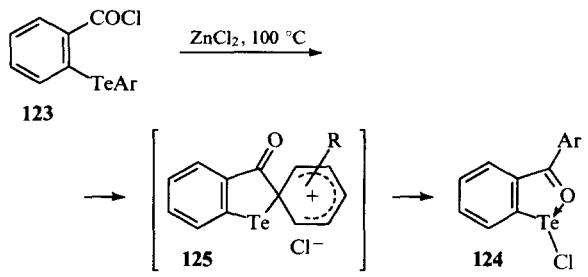
$$(PhCH_2)_2Te \xrightarrow{Br_2} PhCH_2Br + TeBr_4$$

Treatment of benzyl 2-nitrophenyl telluride with bromine entails the formation not of a tribromotelluro-derivative but of a tellanyl bromide stabilised by the O→Te coordinate bond.[121]



The C–Te bond dissociates also on interaction of bis(pentafluorophenyl)telluride with an excess of ClF, which results in the formation of considerable amounts of $C_6F_5TeF_4Cl$ and TeF_5Cl together with $(C_6F_5)_2TeF_4$.[156]

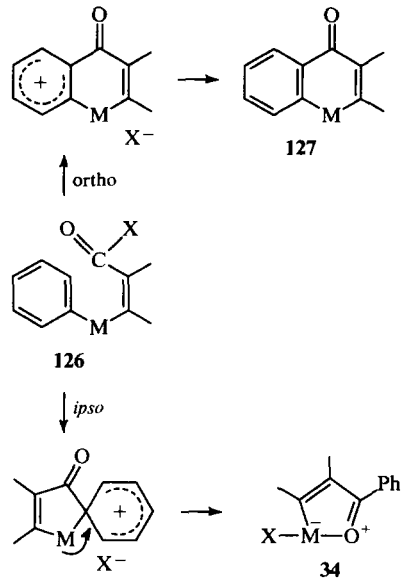
The cleavage of the C–Te bonds with simultaneous rearrangement has been achieved by treatment with certain Lewis acids. Thus heating of aryl 2-chlorocarbonylphenyl tellurides **123** in the presence of $ZnCl_2$ results in their rearrangement to 2-aroylbenzenetellanyl chlorides **124**,[111,113] which are probably stabilised by the formation of the intermediates **125**.



Ar = Ph, 4-MeC$_6$H$_4$, 2-C$_4$H$_3$S.

The selenium analogues of compound **123** undero a similar rearrangement, whilst the corresponding sulfur and oxygen analogues cyclise the thioxanthones and xanthones.

Another similar example illustrating the influence of the nature of the chalcogen atoms on the mode of reaction is the cyclisation of β-arylchalcogenopropenoyl chlorides **126** [51,54,115] or the corresponding acids.[115] The electrophilic cyclisation of these compounds can be achieved either by *ortho*-acylation, which leads to six-membered heterocycles — chalcogenochromones (flavones) **127**, or via *ipso*-acylation accompanied by the formation of five-membered heterocycles — 1,2-oxachalcogenolium chlorides **34**.



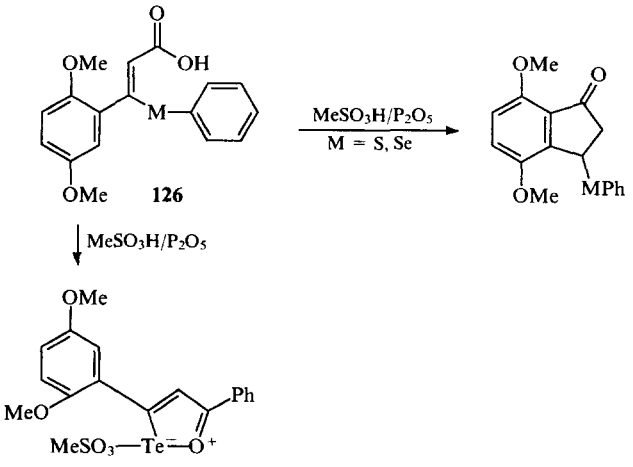
X = Cl, OH; M = S, Se, Te.

Regardless of the nature of substituents in the arene ring, the sulfur derivatives **126** (M = S) are only *o*-acylated, which leads to the thiochromones **127** (M = S).[115,395–398] Only *ipso*-acylation and the formation of the heterocycles **34** (M = Te) is characteristic of the *para*-substituted β-aryltelluropropenoyl chlorides **126** (M = Te).[51,54,115] This is probably due to both the increased polarisability of the tellurium atom and to its relatively low electronegativity compared with other chalcogenes. Depending on the nature of the substituents in the selenoaryl rings, the selenium compounds **126** (M = Se) can cyclise either to the heterocycles **127** (M = Se)[399–401] or to 1,2-oxaselenolium chlorides **34** (M = Se).[115] Mixtures of the two heterocycles are formed in some cases.

However, one should note that, by varying the nature and positions of the substituents in telluroaryl rings of compound **126** (M = Te), it is possible to activate the *ortho*-positions in these rings to electrophilic attack, i.e. to drive the interaction towards the preferential formation of tellurochromones (flavones).[54,115]

Furthermore, whereas the cyclisation of β-thio(seleno)arylcinnamic acids **126** (M = S, Se) on treatment with the $MeSO_3H-P_2O_5$ system leads to benzocyclopentenones,[401] the analogous reaction with the tellurium analogues affords 1,2-oxatellurolium methanesulfonates[54] (Scheme 3).

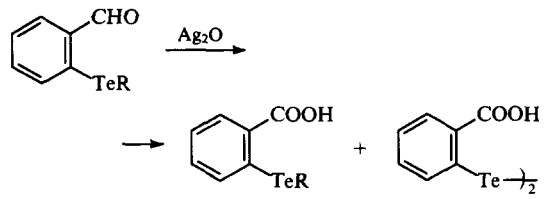
Scheme 3



The dissociation of the C–Te bond in diorganyl tellurides can also take place in the presence of other than halogen-containing ($SOCl_2$, SO_2Cl_2) oxidants. Thus, according to Balfe and coworkers,[169,170] on reaction with O_2 or H_2O_2 dialkyl tellurides

are converted into complexes of different compositions, one of the components of which is tellurinic acids RTe(O)OH. These old data probably require additional confirmation. Incidentally, the formation of alkanetellurinic acids, the structure of which has been established by spectroscopic methods, has also been noted in the oxidation of 1-alkyltellurobut-3-en-1-ynes of type **50**.[402] The C(*sp*)–Te bonds are dissociated during the reaction and vinylethyne is formed together with the trimers.

The oxidation of 2-alkyltellurobenzaldehydes by Ag_2O in an alkaline medium affords, apart from the expected 2-alkyltellurobenzoic acid **128**, the product of the cleavage of the C(sp^3)–Te bond — ditellurosalicylic acid.[190] In the case of *o*-methyltellurobenzaldehyde, the acid **128** is obtained in a yield of about 60%.



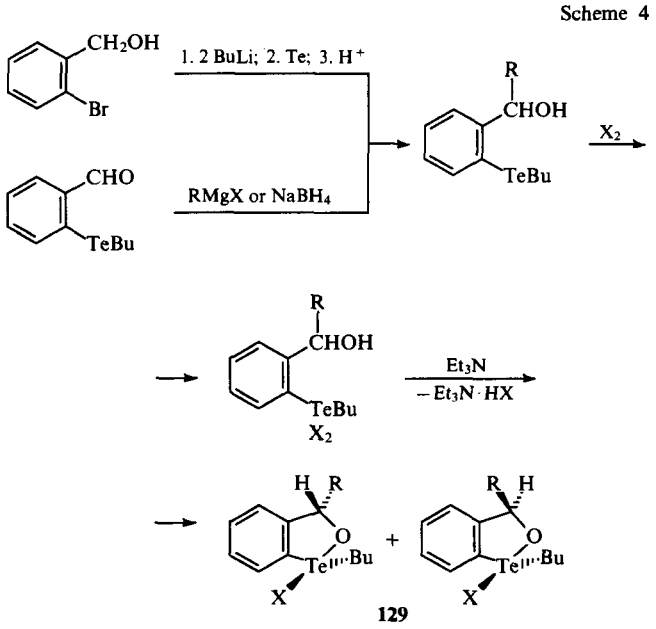
128

R = Me, Bu.

On the other hand, the oxidation of aryl benzyl tellurides by atmospheric oxygen gives rise to the corresponding benzaldehydes.[81,364,366,394]

The ready dissociation of the C–Te bonds under the influence of oxidants is the reason why some of the usual oxidation reactions in organic chemistry cannot be employed for the synthesis of organotellurium compounds. Thus the oxidation of the secondary alcohol 1-(2-methyltellurophenyl)ethanol (in order to obtain 2-methyltelluroacetophenone) by DMSO in acetic acid [109] or of the methyl group in 2-methyltellurotoluene (in order to synthesis 2-methyltellurobenzaldehyde) [190] is accompanied by the elimination of the tellurium atom. The recently developed method of synthesis of tellurium-containing carbonyl compounds from 3*H*-2,1-benzoxatelluroles **129**, the synthesis of which is illustrated in Scheme 4, is of definite interest in the chemistry of such tellurium-containing carbonyl compounds.[403,404]

Scheme 4

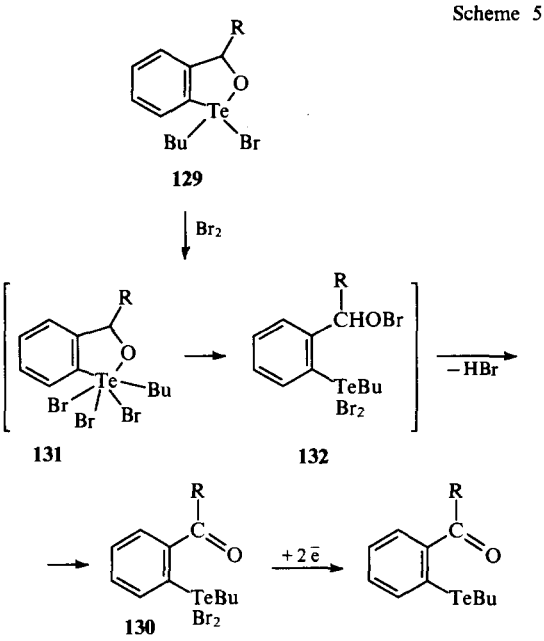


129

X = Cl, Br, I; R = H, Me, Ph, 4-MeC$_6$H$_4$.

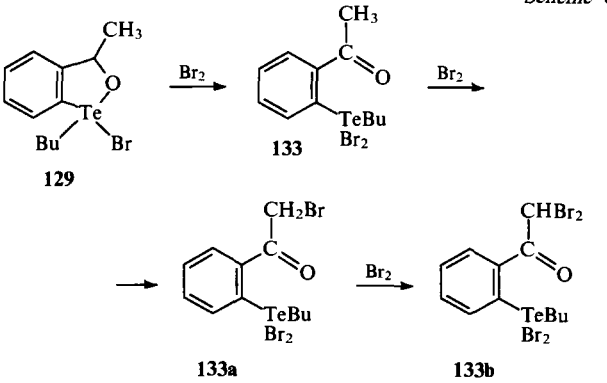
On treatment with bromine, the O–Te bond in the heterocycles **129** is cleaved, giving rise to aldehydes or ketones **130**, depending on the nature of the substituents in the 3-position in the heterocycle, with the Te(Bu)Br_2 group in the *o*-position. The reaction probably proceeds via intermediate **131** with a hexacoordinate tellurium atom, which rearranges to compound **132**. Yields of the carbonyl derivatives **130** are 70%–90% (Scheme 5).

Scheme 5

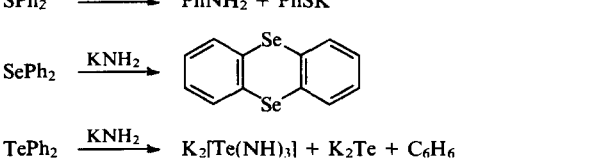


Bearing in mind that 3-R benzoxatelluroles **129** can be obtained from 2-butyltellurobenzaldehyde, the above sequence of reactions can be regarded as a new method for the conversion of *o*-alkyltellurobenzaldehyde into ketones and of *o*-alkyltellurobenzyl alcohols into aldehydes, which is specific to organotellurium compounds. In the case of the 3-methyl derivative **129** (R = Me), the acetophenone derivative **133** formed initially is brominated at the methyl group with formation of compounds **133a** and **133b** (Scheme 6).[404]

Scheme 6



Finally, the cleavage of the Te–C bonds by various nucleophiles is possible. Thus the nature of the chalcogen atoms in diphenyl chalcogenides determines the different results of their reactions with potassium amide in liquid ammonia presented below.[405] The reaction with Ph_2Te is accompanied by the complete dissociation of the C_{Ar}–Te bonds.



On treatment with lithium in liquid NH_3 or with $LiNH_2$, the bonds between the chalcogens and the unsaturated groups in the alkylseleno(telluro)alkenynes of type **50** are ruptured, whereas in their thio-analogues both these bonds and the C(sp^3)–S bonds are cleaved.[406]

$$CH_2{=}CHC{\equiv}CLi + RMLi$$

$LiNH_2$; M = S, Se, Te; R = Me, Bu

$$CH_2{=}CHC{\equiv}CMR \xrightarrow[M = S,\ R = Me]{LiNH_2} CH_2{=}CHC{\equiv}CSLi + RLi$$

50

On the other hand, in contrast to the sulfur and selenium derivatives **50**, which combine with RMgX at the triple bond[407] with formation of chalcogen-containing allenes, their tellurium analogues react with dissociation of the C(sp)–Te bond and the formation of dialkyl tellurides. The cleavage of the C–Te bonds in compound **50** (M = Te) is also observed in the reaction with EtSH.[408]

Lithium in liquid NH_3 also ruptures the C(sp^2)–Te bonds; on subsequent alkylation of ethynetellurolate by alkyl halides, alkyl vinyl tellurides are formed.[409]

$$(CH_2{=}CH)_2Te \xrightarrow[2.\ RX]{1.\ Li/NH_3} CH_2{=}CHTeR$$

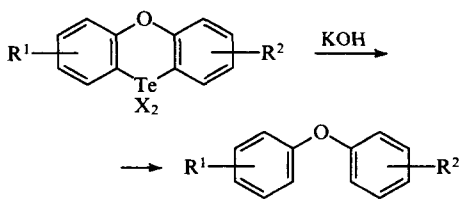
R = Me, Et, Pr.

On the other hand, the cleavage of the Te–C bonds in bis(perfluoroalkyl)tellurides by aqueous solutions of alkalies takes place at room temperature and leads to perfluoroalkanes.[410]

$$(R_F)_2Te \xrightarrow{KOH} R_FH$$

$R_F = CF_3, C_2F_5$.

Eimination of the tellurium atom is also observed on heating phenoxatelluranes, 10,10-dichlorophenoxatelluranes, and 10,10-dinitratophenoxatelluranes in aqueous K_2CO_3 or KOH solutions;[18,21] diaryl ethers are then formed in high yields. These reactions have been used to identify the products of electrophilic substitution of phenoxatellurane (nitration, bromination).



X = Cl, ONO_2.

Much attention has been devoted in recent years to the reactions of diorganyl tellurides with organolithium compounds. Like the Grignard reagents, these compounds cleave the C–Te bond in dialkyl,[411–413] alkyl aryl,[411,413–416] and even diaryl tellurides.[411,417–420] The reactions of butyllithium with organyl vinyl and divinyl telluride are accompanied by the dissociation of the C(sp^2)–Te bonds and lead to vinyllithium derivatives,[58,411,413,421] the latter being formed with retention of the configuration. The C(sp)–Te bonds are ruptured just as readily by organolithium and organomagnesium compounds [the C(sp)–Te bonds[411,413,422,423] are also cleaved by $NaBH_4$].[422,424] It has been shown by ^{13}C NMR spectroscopy that the reactions of organolithium compounds with diorganyl tellurides proceed via the intermediate formation of complexes **134** containing a tricoordinate Te atom. The latter decompose with formation of the thermodynamically more stable organolithium derivative (for example, R^1Li) and a new diorganyl telluride.

$$R^1TeR^2 + R^3Li \longrightarrow \left[R^1{-}\underset{\displaystyle R^3}{\overset{|}{Te}}{-}R^2\right]^- Li^+ \longrightarrow$$

134

$$\longrightarrow R^1Li + R^2TeR^3$$

The comparatively readily available diorganyl tellurides have therefore been used as effective sources of alkyl-, alkenyl-, alkynyl-, aryl-, acyl(aroyl)-,[425] and carbamoyl-lithium compounds.[426] They can be synthesised from organyl halides without the preliminary isolation of the telluride, in accordance with the following scheme:

$$R^1X + R^2TeLi \xrightarrow[-LiX]{} R^1TeR^2 \xrightarrow[-R^2TeR^3]{R^3Li} R^1Li$$

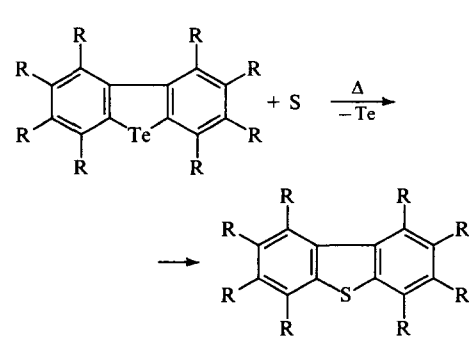
The interaction of diaryl and alkyl aryl tellurides with Grignard reagents (for alkyl aryltellurides the group R in RMgX must be the same as one of the groups in ArTeR) in the presence of catalytic amounts of nickel or cobalt compounds [$NiCl_2(PPh_3)_2$, $NiCl_2(Ph_2PCH_2CH_2PPh_2)_2$, $CoCl_2(PPh_3)_2$] also takes place with dissociation of the C–Te bonds. This leads to the formation of a mixture of cross- and homo-coupling products.[50,52]

$$ArTeR + RMgBr \xrightarrow{Cat} Ar{-}R + Ar{-}Ar + R{-}R$$

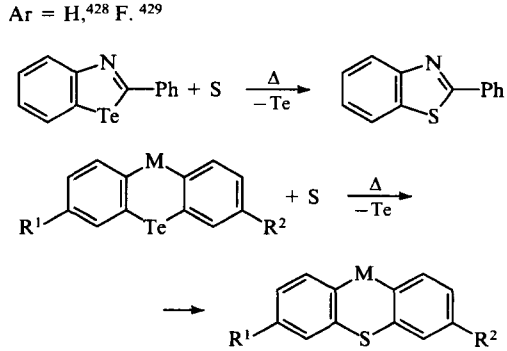
On heating with elemental sulfur, the tellurium atom in certain organotellurium compounds is substituted by a sulfur atom. These reactions are undergone both by diaryl tellurides[336,427] and by tellurium-containing heterocycles: dibenzotellurophenes,[428,429] 2-phenylbenzotellurazole,[178] phenoxatelluranes,[177,321–324,430] phenothiatellurane,[196] and phenotellurazines.[431] The only example of the substitution of the tellurium atom by selenium involves the formation of phenoxaselenane on heating phenoxatellurane with powdered selenium.[430]

$$Ar_2Te + S \xrightarrow[-Te]{\Delta} Ar_2S$$

Ar = Ph,[427] C_6F_5.[336]



Ar = H,[428] F.[429]

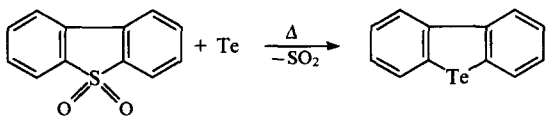


M = O; $R^1 = R^2$ = H,[430] Me,[321] Cl,[322] F;[323]

R^1 = F, R^2 = Me,[177] Cl;[324]

M = S; $R^1 = R^2$ = H;[196] M = NEt; $R^1 = R^2$ = H, Me[431].

This property of organic tellurium derivatives is evidently due both to the higher C–S bond energy compared with that of C–Te and the more pronounced aromaticity of the sulfur heterocycles compared with their tellurium analogues.[15] On the other hand, the greater aromaticity of tellurium-containing heterocycles compared with heterocyclic sulfones leads to the possibility of the substitution of the SO_2 group by a Te atom.[432]



X. Intramolecular Te←N(O) coordination and the reactivity of organotellurium compounds

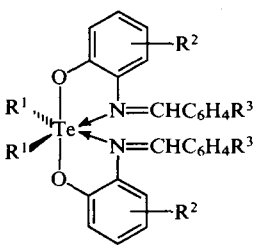
Intramolecular Te←N and Te←O coordinate bonds are one of the principal factors ensuring the stability of certain classes of organotellurium compounds (see Section IV) and exerting a significant influence on the reactivity and structure of organic tellurium derivatives.[104–106] Data concerning the influence of intramolecular coordination on reactivity are qualitative; one of the examples of the influence of the N→Te coordination on the halogenolysis of 2-butyltellurobenzylideneanilines was examined previously (see Section IX).

1. Reduction of C=N bonds

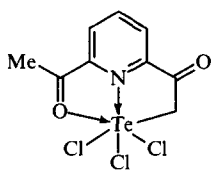
In contrast to the C=N bonds of the tellurium-free aromatic azomethines, which are readily reduced by $NaBH_4$ in ethanol, 2-butyltellurobenzylidene-4′-methylaniline does not change even after prolonged refluxing with this reductant.[126] On the other hand, both the C=N bond and the $TeBr_3$ group are reduced (the latter to TeBr) in 2-tribromotellurobenzylidene-4′-methylaniline on treatment with $NaBH_4$, leading to a secondary amine.[127] Replacement of the 4-methyl group by the more bulky *tert*-butyl groups in the 2-, 4-, and 6-positions inhibits both these reactions.

2. Reactions of σ-telluranes

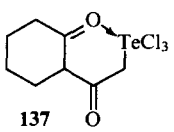
The presence of the Te←N and Te←O coordinate bonds in the molecules of σ-telluranes increases significantly their hydrolytic stability. The diorganyl (diaryloxy)telluranes **135** with Te←N bonds are not hydrolysed on prolonged contact with water,[433,434] whereas diaryl(dialkoxy)telluranes which do not contain such bonds are rapidly hydrolysed even by atmospheric moisture.[351] A similar behaviour is characteristic also of the tellurium trichlorides **136–138**,[435] which are inert to water [the usual trichlorides are rapidly hydrolysed by water with formation of the tellurium oxide chlorides RTe(O)Cl].[2,3]



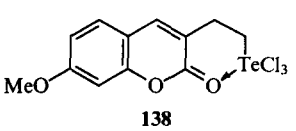
135



136



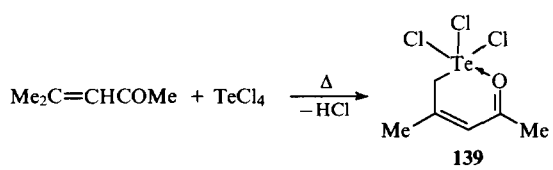
137



138

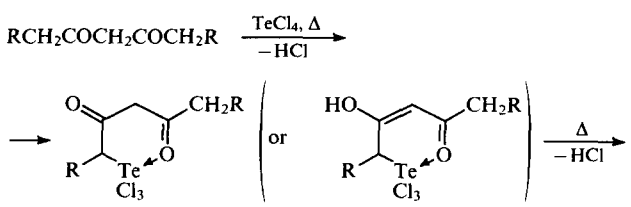
The electrophilic nature of the $TeCl_3$ groups coordinated to N and O atoms is less pronounced than that of noncoordinated trichlorotelluro-groups. Thus, whereas acetophenone and its derivatives afford σ-telluranes of the type $(ArCOCH_2)_2TeCl_2$ on interaction with $TeCl_4$,[436–439] the reactions of 2,6-diacetylpyridine, 2-acetylcyclohexanone, and 3-acetyl-7-methoxycoumarin with $TeCl_4$ give rise to only σ-telluranes of the type $RTeCl_3$ (compounds **136–138**) even in the presence of a twofold molar excess of the carbonyl component.[435]

The reaction of mesityl oxide with $TeCl_4$ in $CHCl_3$ is also instructive. It leads to 2-methylpent-2-en-4-onetellurium trichloride **139**,[440,441] i.e. involves the methyl group adjoining the double bond and not that linked to the carbonyl group, as happens in the analogous reactions of acetophenones and other methyl ketones.[436–439] The possible reaction mechanism involves the initial electrophilic attack by $TeCl_4$ on the COMe group with the subsequent rearrangement of the resulting tellurium trichloride to compound **139**. The driving force of the reaction is the marked stabilisation of the trichloride **139** with the Te←O coordinate bond (the bond length is 2.44 Å).[441]

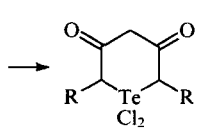


139

This is probably the reason[440] why in the reactions of 1,3-diketones with $TeCl_4$ the latter attacks the terminal carbon atom, which results in the formation of 1-telluracyclohexane-3,5-dione 1,1-dichlorides **140**.[18,21] When the hydrogen atoms at the terminal carbon atoms are substituted, there is a possibility of the formation of the tellurium trichlorides **141**, which are stabilised by the Te←O coordination.

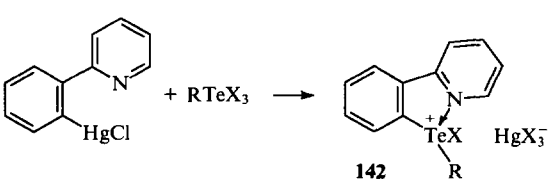


141



140

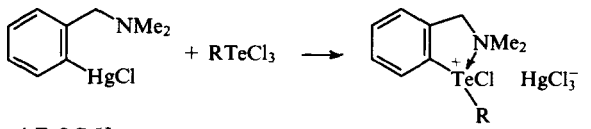
The interaction of organyltellurium dichlorides and tribromides $RTeHal_3$ with RHgHal leads readily to diorganyltellurium dihalides R_2TeHal_2 and $HgHal_2$.[2,3] However, when the formation of coordinate bonds involving the Te atom becomes possible in the final product, the reactions of $RTeHal_3$ with ArHgCl lead to 2-(2-pyridyl)phenylhalo-tellurium trihalomercurates **142**.[129,442]



142

X = Cl, Br; R = 4-$EtOC_6H_4$.

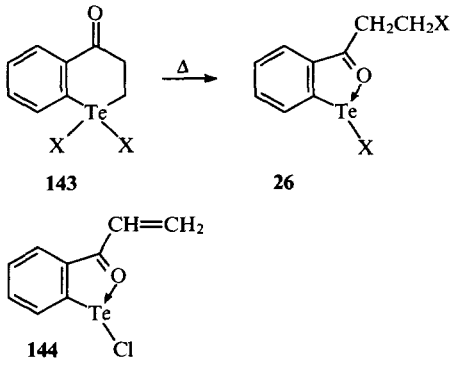
The products of the interaction of 2-chloromercuriobenzyldimethylamine with $ArTeCl_3$ have an analogous structure.[131]



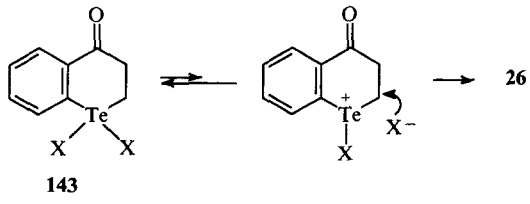
R = 4-EtOC$_6$H$_4$.

3. Rearrangement of dihalotellurochromanones

Dihalotellurochromanones **143** undergo on heating a rearrangement, not described previously, which involves the dissociation of the C(sp^3)–Te bond and the formation of 2-(β-halopropionyl)benzenetellurenyl halides **26**.[118] In the case of the chloro-derivative **143** (X = Cl), the ketone **144** was isolated as the final product, evidently as a consequence of the elimination of HCl from compound **26** (X = Cl) formed initially. The rearrangement is achieved by heating solutions of dihalotellurochromanones in $CHCl_3$, C_6H_5Br, or $C_6H_5NO_2$ for 20–30 h.

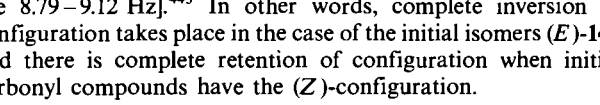


As in the series of reactions considered above, the driving force of the rearrangement is the marked stabilisation of the tellanyl halides **26** with the Te←O coordinate bonds [the length of the bond in 2-(β-iodopropionyl)benzenetellanyl iodide **26** (X = I) is 2.368 Å][118] and the possible mechanism involves the predissociation of the Te–X bond with subsequent attack by the halide anion on the β-carbon atom.



4. Stereochemistry of reactions involving the substitution of chlorine atoms in β-chlorovinylcarbonyl compounds by arenetellurolate anions

The reactions involving the nucleophilic substitution of chlorine atoms in β-chlorovinylcarbonyl compounds **145** by arenetellurolate anions leads in all cases to the formation of only (*Z*)-isomers by β-aryltellurovinylcarbonyl compounds **146** [the spin–spin coupling constants for the ketones **146** ($R^1 = R^2 = H$) are 8.79–9.12 Hz].[443] In other words, complete inversion of configuration takes place in the case of the initial isomers (*E*)-**145** and there is complete retention of configuration when initial carbonyl compounds have the (*Z*)-configuration.

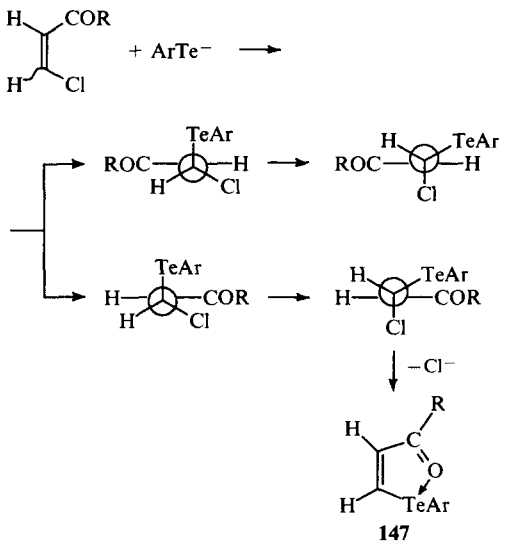


$R^1 = R^2 = H$; R^3 = Ph, 4-MeC$_6$H$_4$, 4-MeOC$_6$H$_4$, 4-BrC$_6$H$_4$;

R^1 = Ph, $R^2 = R^3 = H$; $R^1 + R^2 = -(CH_2)_4-$, $R^3 = H$;

Ar = Ph, 4-MeC$_6$H$_4$, 4-EtOC$_6$H$_4$.

The stereochemical result obtained may be interpreted in terms of a 2-stage nucleophilic substitution mechanism (addition–elimination).[444] The first stage of the process is the addition of the arenetellurolate anions to the double bond activated by the strongly electron-accepting carbonyl group. Among the possible conformers arising on rotation of the C–C single bond in the carbanion formed, the most stable is evidently the conformer stabilised by the intramolecular Te←O coordinate bond. In the second stage, the elimination of the chloride ions from this conformer leads to the formation of the (*Z*)-isomers **147** which are additionally stabilised by the formation of the Te←O coordinate bonds.[443]



Apparently 2-(4′-ethoxyphenyltelluro)-1-formylcyclohexene **146** [Ar = Ph; $R^1 + R^2 = -(CH_2)_4-$, $R^3 = H$], which is a cyclohexene derivative, is also a (*Z*)-isomer with an intramolecular Te←O coordination bond. Judging from the ^{1}H NMR spectrum, the aldehyde **146** (Ar = R^1 = Ph, $R^2 = R^3 = H$) exists in solution in only one form. On the basis of the mechanism proposed above and the marked stabilisation of tellurium(II) derivatives by intramolecular coordinate bonds, the hypothesis that this form has the (*Z*)-structure in which the Te and O atoms are coordinated is evident.

* * *

The specific features of the chemical behaviour of organotellurium compounds considered in the present review give rise to interesting additional possibilities for a rapidly developing aspect of organic synthesis — the methodology of the use of organoelement synthons incorporating heavy elements of the main groups of the Periodic Table. The organoiodine[233] and organoselenium[445] methodologies, based on the extensive possibilities for the introduction, modification, and elimination of the corresponding groups accompanied by the formation of new carbon–carbon bonds, have come to be widely used.

The possible employment of phenyl derivatives of bismuth(V) for the *C*- and *O*-phenylation of various organic compounds is being developed.[446] It is so far too early to speak of an organotellurium methodology, but the foundations for its establishment have already been laid in the specific reactions of organotellurium compounds which have been presented.

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The vinyl ethers of aminoalcohols and their derivatives

B F Kukharev, V K Stankevich, G R Klimenko

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Abstract. The results of studies on the methods of synthesis and properties of the vinyl ethers of aminoalcohols are surveyed and described systematically. Their practical applications are considered. The bibliography includes 265 references.

I. Introduction

The vinyl ethers of aminoalcohols (VE AA) occupy a notable place among the vinyl derivatives of nitrogen- and oxygen-containing compounds which are widely used in organic synthesis.

By virtue of the presence of amino- and vinyloxy-groups, these compounds combine the very extensive synthetic possibilities of both amines and vinyl ethers. Here one should note that, although these groups do not exert a mutual influence on one another in the classical sense of this concept, nevertheless in many reactions the VE AA behave differently from both amines and the vinyl ethers of alcohols. This difference is manifested primarily by the competition between the amino- and vinyloxy-groups in reactions with electrophiles and also by the occurrence of secondary processes with participation of the group which is not involved in the main reaction.

As a result of the lower dissociation energy of the C – N bond compared with the C – O and C – C bonds, the conditions in the main method for synthesis of vinyl ethers — vinylation of alcohols by ethyne — frequently prove to be somewhat too severe for the vinylation of aminoalcohols and leads to the elimination of the amino-group. Furthermore, the reaction is complicated by *N*-vinylation and cyclisation processes.

Thus specific methods, differing significantly from those known for aliphatic amines and vinyl ethers, are frequently needed to increase the selectivity and yields both in the synthesis of the VE AA and in their chemical reactions.

Individual questions associated with the synthesis and chemical properties of the VE AA have been considered hitherto in monographs[1–5] and reviews[6–8] devoted to the chemistry of ethyne and its derivatives. However, the range of problems discussed there is extremely narrow because of the specific nature of the publications and, furthermore, these compounds are considered mainly as a special case of the vinyl ethers of alcohols.

In the present review, an attempt is made to represent as fully as possible the available literature data on the synthesis and chemical properties of the VE AA, the aim being also to demonstrate and assess the position occupied by these compounds in organic synthesis. The prospects for their practical application are also considered.

B F Kukharev, V K Stankevich, G R Klimenko Irkutsk Institute of Organic Chemistry of the Siberian Branch of the Russian Academy of Sciences, ul. Favorskogo 1, 664033 Irkutsk, Russian Federation. Fax (7-395) 246 03 31 Tel. (7-395) 246 24 45 (B F Kukharev)

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II. Methods of synthesis of the vinyl ethers of aminoalcohols

1. Interaction of aminoalcohols with ethyne

Among the methods of synthesis of the VE AA known hitherto, the commonest and most universal is the base-catalysed addition of aminoalcohols to ethyne.

$$RR^1NCR^2R^3(CH_2)_nCR^4R^5OH \xrightarrow{CH\equiv CH} RR^1NCR^2R^3(CH_2)_nCR^4R^5OCH{=}CH_2$$

$n = 0–8$; $R–R^5$ = H, Alk, Ar, Het;

R = $Me_3Si(CH_2)_3$, CH_2CH_2OH, $CH_2CH_2NH_2$;

$R + R^1 = -CH_2CH_2OCH_2CH_2-$;

$R + R^1$, $R + R^2$, $R + R^4$, $R^2 + R^4 = -(CH_2)_{2-5}-$.

Since the 1930's, this reaction has been used to obtain a wide range of VE AA with various structures.[9–50]

The potassium or sodium alkoxides derived from the aminoalcohols to be vinylated[9–29] or the hydroxides of the corresponding metals were used (in an amount corresponding to 5% – 20% of the weight of the aminoalcohol) as the catalyst.

Lithium, sodium, potassium, rubidium, and caesium oxides, hydroxides, alkoxides, phenoxides, naphthoxides, cyanides, zincates, and sulfides have been proposed as the catalysts in a series of patents.[30–32]

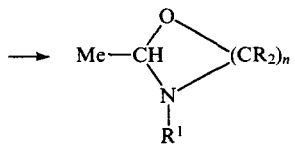
The interaction of the aminoalcohols **1** with ethyne in the absence of catalysts[9,51,52] and also in the reaction catalysed by cadmium acetate[33,53] results in the formation either of polymerisation products[9,53] or of 2-methyl-1,3-oxazacycloalkanes **2**.[33,51,52]

It has been suggested that the formation of the cyclic product **2** is associated with the occurrence under these conditions of the *N*-vinylation and subsequent cyclisation of the unstable intermediate enamines.[51] It is noteworthy that the *N*-vinylation, especially in the case of aminoalcohols with a secondary

hydroxy-group which is difficult to vinylate, is possible also under the conditions of base catalysis. Thus it has been reported that only 3-aryl-5-aryloxymethyl-2-methyl-1,3-oxazolidines were obtained from 3-arylamino-1-aryloxypropan-2-ols and ethyne.[54]

$$HO(CR_2)_nNHR^1 \xrightarrow[100-200\,^\circ C]{CH\equiv CH,\ 2-4\ MPa}$$

1 (conversion 10% – 30%)



2 5% – 75%

n = 2, 3; R = H, Me, Et;

R^1 = H, Me, Ph, CHMePh, CH_2CH_2OH, $CH_2CH_2NH_2$.

The vinylation of aminoalcohols at atmospheric pressure of ethyne is usually carried out without solvents.[10-17,34-36] On the other hand, when the reaction is carried out in autoclaves, solvents are usually employed, for example benzene,[9,18-26,37] dioxane,[21,38,39] *tert*-butyl alcohol,[27] n-butyl alcohol,[33] ethers and polyethers,[30] and dimethyl sulfoxide.[40] This greatly increases the amount of ethyne introduced into the reaction, accelerates the process, and makes it possible to raise the yield of the products. The use of water as the solvent lowers the yield of the products and hinders their isolation.[9,22]

The reaction temperature and ethyne pressure are varied within wide limits depending on the structure of the aminoalcohol and the method used for carrying out the reaction. Thus the vinylation of ethanolamines in the vapour phase,[31,32,41] (temperature 250 – 300 °C) and in a gas – liquid emulsion[10,12-14,16,17] in flow-type[11,36] and bubble-type[34,35] reactors has been carried out at atmospheric pressure (temperature 100 – 150 °C, yield of the VE AA 54% – 86%), while the reaction in the liquid phase[30] has been performed at 11.2 MPa and a temperature of 120 – 180 °C with a yield of 75% – 95%. In the vinylation in periodic-action autoclaves, which is commonest, the initial ethyne pressure is usually 1 – 2.5 MPa and the temperature is 100 – 180 °C.

A detailed analysis of various methods for the vinylation of ethanolamines and an assessment of the prospects for their industrial application on the basis of literature data published up to 1972 have been presented in a monograph.[2] The monograph deals with problems concerning the optimisation of the process and its kinetics and discusses the ways in which the side products of the reaction are formed and the methods for the analytical monitoring, isolation, and purification of the vinyl ethers.

From the standpoint of practical application, the vinyl ether of monoethanolamine **3** is undoubtedly of greatest interest. However, in the series of ethanolamines the vinylation of monoethanolamine actually involves the greatest difficulties.[9,11,23] It has been shown recently that the main reason for this is the ready decomposition at a temperature above 100 °C of the ether **3** by alkali.[55,56] In the presence of potassium hydroxide at 110 – 115 °C, it decomposed to the extent of 70% after 5 h, affording a 45% yield of the azomethine **4** and other extensive degradation products. Under the same conditions but in the presence of sodium hydroxide, the degree of decomposition of the ether **3** did not exceed 2%.

In this connection, it is clear that, in the synthesis of the vinyl ether **3**, its continuous removal from the reaction zone is necessary and that preference should be given to sodium hydroxide as the catalyst. Taking into account these refinements, a method has been developed for the vinylation of monoethanolamine at atmospheric pressure in which the yield of the ether **3** is 93% – 96%.[53,57]

$$\underset{\mathbf{3}}{CH_2{=}CHOCH_2CH_2NH_2} \xrightarrow{MOH}$$

$$\longrightarrow \underset{\mathbf{4}}{CH_2{=}CHOCH_2CH_2N{=}CHCH_3} + NH_3$$

$$+ H_2 + H_2O + EtOH + MeCOOM + M_2CO_3$$

M = K, Na.

2. Interaction of aminoalcohols with substituted ethynes

There are very few literature data on the synthesis of VE AA having substituents in the vinyl group by the addition of aminoalcohols to substituted ethynes.

It has been shown that the addition of one molecule of 2-diethylaminoethanol to diethyne in the 1,2-positions with formation of the *cis*-isomer **5** takes place exothermically without catalysts. The addition of a second molecule requires a catalyst (potassium alkoxide or hydroxide) and heating. This results in the formation of both regioisomers **6** and **7** in an overall yield of 55% – 60%.[25,58-60]

$$CH{\equiv}C{-}C{\equiv}CH \xrightarrow{Et_2N(CH_2)_2OH}$$

$$\longrightarrow \underset{\mathbf{5}\ 80\%-90\%}{Et_2N(CH_2)_2OCH{=}CH{-}C{\equiv}CH} \xrightarrow{Et_2N(CH_2)_2OH}$$

$$\longrightarrow \underset{\mathbf{6}}{Et_2N(CH_2)_2OCH{=}CH{-}\overset{\displaystyle O(CH_2)_2NEt_2}{\overset{|}{C}}{=}CH_2} +$$

$$+ \underset{\mathbf{7}}{Et_2N(CH_2)_2OCH{=}CH{-}CH{=}CHO(CH_2)_2NEt_2}$$

The study of the reactions of diethyne alcohols **8** with aminoalcohols established that, at 105 – 110 °C in the presence of potassium hydroxide, acetone is split off from the alcohols **8** and the resulting diethynes **9** combine with aminoalcohols, affording the vinylethyne derivatives **10** in yields up to 52%.[61]

$$\underset{\mathbf{8}}{R{-}C{\equiv}C{-}C{\equiv}C{-}CMe_2OH} \xrightarrow[-Me_2CO]{}$$

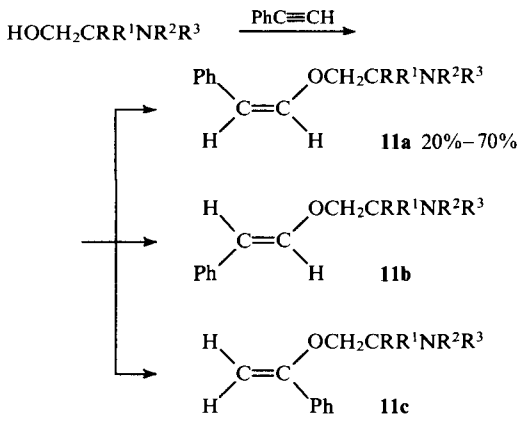
$$\longrightarrow \underset{\mathbf{9}}{R{-}C{\equiv}C{-}C{\equiv}CH} \xrightarrow{HO(CH_2)_2NR^1_2}$$

$$\longrightarrow \underset{\mathbf{10}}{R{-}C{\equiv}C{-}CH{=}CHO(CH_2)_2NR^1_2}$$

R = Me, Ph; R^1 = Et, Bu.

The use of diethyne as well as other substituted ethynes with an activated triple bond is probably limited to the synthesis of vinyl ethers with a tertiary amino-group, since aminoalcohols with primary or secondary amino-groups add to such ethynes as typical amines with formation of enamines.[62-64]

The study of the reactions of aminoalcohols with phenylethyne showed that, at 120 – 130 °C in the absence of solvents, the products **11a** of the *trans*-addition to the β-carbon atom in phenylethyne are formed preferentially on treatment with alkali metal hydroxides. The amount of the products **11b** of the *cis*-addition is between 3% and 15%, while that of the products **11c** of the addition to the α-carbon atom in phenylethyne is 2% – 5% relative to the amount of the *trans*-isomer **11a**. When the reaction is carried out in dimethyl sulfoxide (DMSO), its stereoselectivity diminishes (the ratio of the *trans*- and *cis*-adducts **11a** and **11b** is 1 : 0.6), but their regiospecificity is unaffected.[65,66]

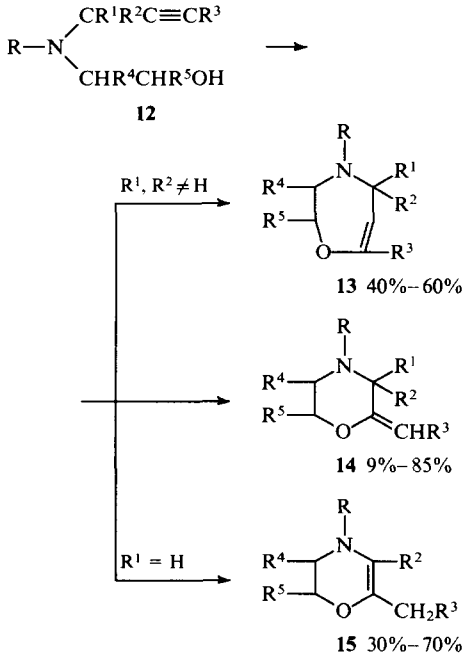


R, R^1 = H, Me, Et; $R^2+R^3 = -CH_2CH_2OCH_2CH_2-$;

R^2, R^3 = H, Me, Et, CH_2Ph, Ph, 2-MeC_6H_4, 4-MeC_6H_4, Ac.

The base (KOH, $NaNH_2$)-catalysed intramolecular cyclisation of *N*-propargylethanolamines **12** to the oxazepines **13**[67,68] or the morpholine derivatives **14** and **15** (Scheme 1)[1,39,69–72] is a special case of the reaction under consideration.

Scheme 1



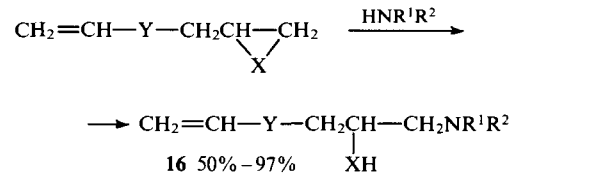
R = H, Me, Et, Bu^t, CH_2CH_2OH; $R^1 = R^2 = H$, Me;

$R^1+R^2 = -(CH_2)_5-$;

R^3, R^4, R^5 = H, Me, $CH_2CH=CH_2$, Ph, $PhCH_2CH_2$, 2-$MeOC_6H_4$, 4-$MeOC_6H_4$, CH_2OMe, $CH_2OCH=CH_2$, CH_2NEt_2.

3. Other methods of synthesis of the vinyl ethers of aminoalcohols

A series of procedures for the synthesis of VE AA based on the reactions of amines with reactants containing the vinyl group have been described. For example, the vinyl ethers **16** have been obtained by the reaction of amines with the vinyl derivatives of oxiranes[73–79] and thiiranes.[80]

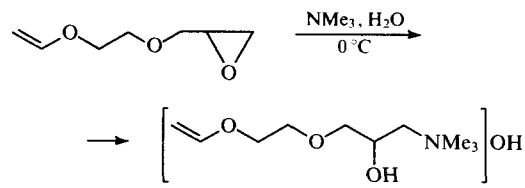


X = O, S; Y = O, $O(CH_2)_2O$, $O(CH_2)_3O$, $OCHMeCH_2CH_2O$, $O(CH_2)_2O(CH_2)_2O$, $O(CH_2)_2O(CH_2)_2O(CH_2)_2O$;

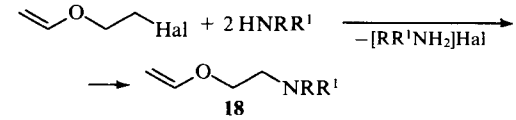
R^1, R^2 = H, Et, Pr, Bu, Bu^t, $CH_2CH=CH_2$, CH_2Ph, CH_2CH_2OH, $CH_2CH(OH)CH_2OCH_2CH_2OCH=CH_2$;

$R^1+R^2 = -(CH_2)_5-$, $-CH_2CH_2OCH_2CH_2-$.

The quaternary base **17** has been obtained from trimethylamine and the glycidyl vinyl ether of ethylene glycol.[75]



Methods have been developed for the synthesis of the vinyl ethers of the aminoethanols **18**[18,81–84] and their quaternary salts **19**[85] by the nucleophilic substitution of the halogen in 2-haloethyl vinyl ethers by amines.



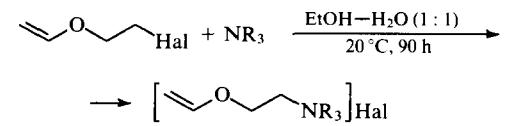
Hal = Cl, Br;

R = R^1 = Bu (30%), $CH_2CH=CH_2$ (26%), $CH_2=C(Me)CH_2$ (29%);

R = H, R^1 = CH_2Ph (61%); R = H, R^1 = $Me_3Si(CH_2)_3$ (70%);

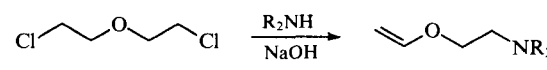
R = Bu, R^1 = $CH_2CH=CH_2$ (57%);

$R+R^1 = -(CH_2)_5-$ (55%), $-CH_2CH_2OCH_2CH_2-$ (90%).



Hal = Br, R = Me (82%); Hal = I, R = Me (67%).

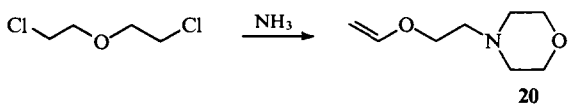
The vinyl ethers of aminoalcohols have also been obtained by the reaction of secondary aliphatic and aromatic amines with di(2-chloroethyl) ether at 50–200 °C with subsequent treatment of the reaction mixture with an aqueous solution of sodium hydroxide.[86]



R = Et, Bu, C_6H_{13};

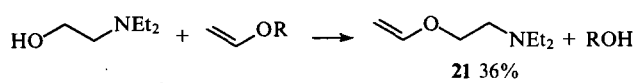
R_2 = $-(CH_2)_5-$, $-CH_2CH_2OCH_2CH_2-$, $-CH=CH-CH=CH-$

The vinyl ether of 2-morpholinylethanol **20** has been obtained from an aqueous solution of ammonia and di(2-chloroethyl)ether under similar conditions.[87]



20

Attempts have been made to synthesise VE AA by the mercury acetate-catalysed transvinylation reaction. It was then possible to obtain only the vinyl ether of 2-diethylaminoethanol **21**.[88]



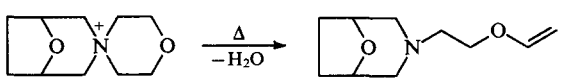
21 36%

R = Et, CH_2CH_2OBu.

Only 2-methyl-1,3-oxazacycloalkanes **2** have been obtained from the amino-alcohols **1** with primary and secondary aminogroups under the conditions of this reaction.[89,90]

The addition of amines,[91–94] alcohols,[93,95] thioalcohols,[93,96] urea,[97] and carboxylic acids[98] to 2-vinyloxyalkyl isocyanates[94,97] and to 2-vinyloxyethyl isothiocyanate (Scheme 2) may be regarded as a method of synthesis of the vinyl ethers of *N*-acyl- and *N*-thioacyl-ethanolamines.

The Hofmann degradation of the morpholine bases can also lead to vinyl ethers. However, the only example is the synthesis of the vinyl ether **23** from the spirocyclic morpholine base **22**.[99]



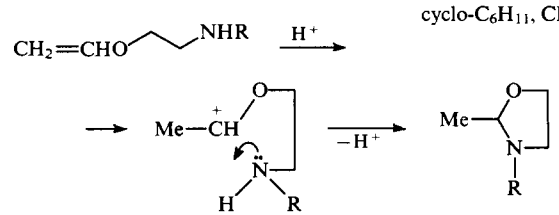
22 **23** 57%

III. Chemical properties of the vinyl ethers of aminoalcohols

1. Reactions of the vinyl ethers of aminoalcohols with acids

In contrast to aliphatic amines, the VE AA contain several basicity centres of different nature: hard centres (nitrogen and oxygen atoms) and a soft centre (the sp^2-carbon atom). This is the reason for their more complex, compared with aliphatic amines, behaviour in relation to acids. Thus, there is only isolated evidence that the salts of vinyloxyethylamines and protic acids, for example the substituted benzoates[100] and the oleate[101] of the amine **3**, as well as the picrates of *N*,*N*-bis(2-vinyloxyethyl)-amines[102] and vinyloxyethylmorpholine **23**[99] can be obtained in solution in benzene.

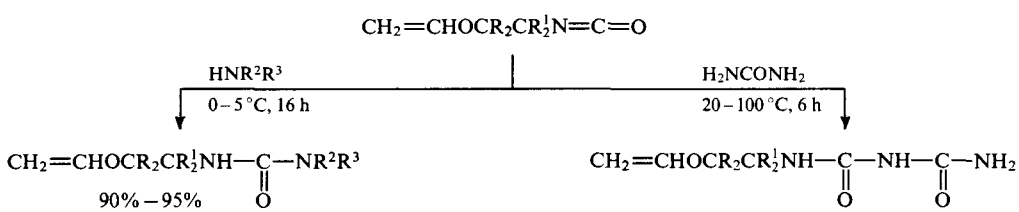
As a result of the reduction of the basicity of the nitrogen atom due to the electronic effect of the substituents, the protonation of the soft basicity centre becomes competitive. Thus the vinyl ether of *N*-phenylethanolamine is cleaved by traces of hydrochloric acid to phenylaminoethanol and products of unknown structure. At the same time, it cyclises to 2-methyl-3-phenyloxazolidine in 13% yield.[22] The even more weakly basic vinyl ethers of *N*-acylethanolamines cyclise quantitatively[91,103–107] in the presence of catalytic amounts of protic acids.



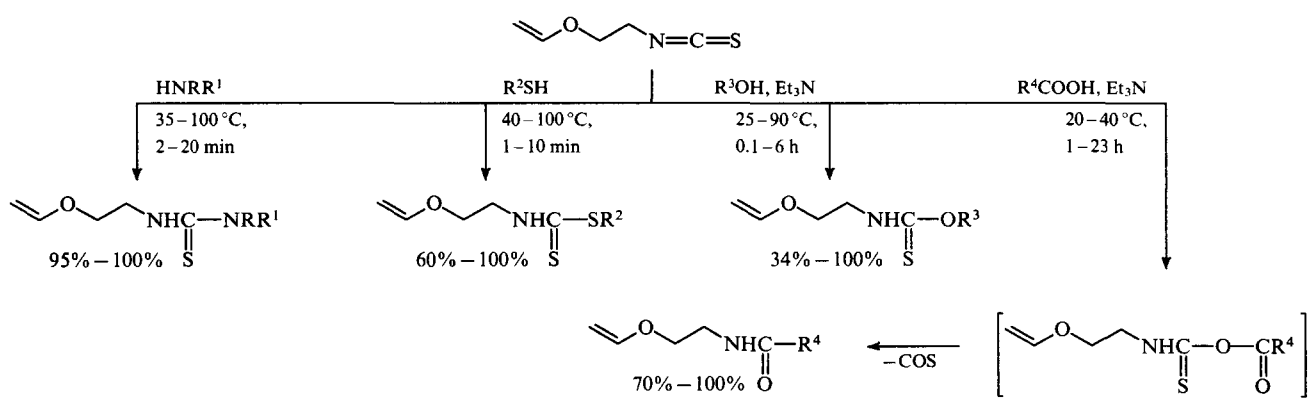
R = Ph (13%), Ac (100%), C(S)SAlk (100%),

Alk = Me, Et, Pr, Bu, Bu^i, Bu^t, $CH_2CH{=}CH_2$, cyclo-C_6H_{11}, CH_2Ph

Scheme 2



R, R^1, R^2, R^3 = H, Me, Et, C_8H_{17}, $C_{12}H_{25}$.



R, R^1 = H, Me, Et, Bu, Bu^i, $CH_2CH{=}CH_2$, cyclo-C_6H_{11}, CH_2CH_2OH, CH_2CH_2SH, $CH_2CH_2OCH_2CH_2SBu$, Ph, 2,4-$Me_2C_6H_3$, 3,4-$Cl_2C_6H_3$, 3-ClC_6H_4, 2-$MeCOC_6H_4$, 2-$C_{10}H_7$, 3-Me-2-C_5H_3N;

R+R^1 = $-(CH_2)_5-$, $-CH_2CH_2OCH_2CH_2-$; R^2 = Et, Pr, Bu, C_5H_{11}, C_6H_{13}, C_7H_{15}, CH_2Ph;

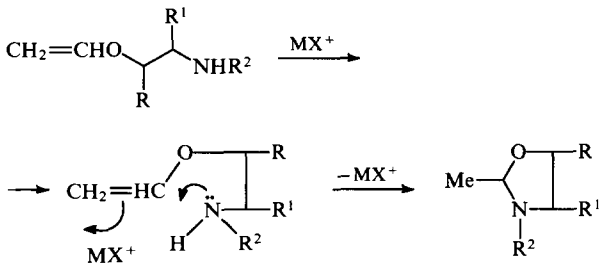
R^3 = $CH_2(CF_2)_nH$, n = 2, 4, 6, 8, 10; R^4 = Me, Et, Pr^i, Bu, Bu^i, C_7H_{15}, Ph, (3-Ind)CH_2 (Ind = indolyl).

When cyclisation is impossible due to structural factors, as happens, for example, in the case of the weakly basic vinyl ether of *N,N*-diphenylethanolamine[19] or quaternary vinyloxyethylammonium salts,[83] polymerisation involving the vinyl group, catalysed by strong acids (H^+, Fe^{3+}, BF_3), takes place readily.

The highly basic vinyl ethers, for example the vinyl ethers of *N*-monoalkylethanolamines and *N,N*-dialkylethanolamines, as well as the vinyl ethers **16** (X = O) neither cyclise nor polymerise on treatment with catalytic amounts of HCl, $FeCl_3$, and $BF_3.Et_2O$.[19,22,26,75]

However, on treatment with more than an equimolar amount of BF_3 [108,109] or $BF_3.Et_2O$, [40] the VE AA polymerise regardless of the structure of the amino-group, since in this case the complex of the vinyl ether with BF_3 actually polymerises and not the ether itself.

Soft acids (for example, Hg^{2+} and Pd^{2+}) coordinating to the soft π-basic centre induce the cyclisation of the VE AA regardless of the basicity of their amino-group.[110–112]



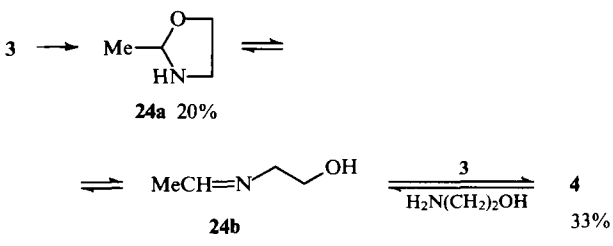
76%–99%

R, R^1 = H, Me, $MeOCH_2$;

R^2 = H, Me, Et, CH_2Ph, Ph, Ac, CH_2CH_2OH, CH_2CH_2CN, $CH_2CH_2OCH{=}CH_2$;

M = Hg, Pd; X = Cl, AcO.

The reaction is complicated by the occurrence of an exchange process with formation of the azomethine **4** only in the case of the simplest vinyl ether **3** owing to the ability of the oxazolidine **24a** to undergo a tautomeric transformation into the azomethine alcohol **24b**.



24a 20%

24b 33%

The available data on the interaction of VE AA with acids belonging to the class intermediate between hard and soft acids are limited to only one example of the formation of a chelate complex of the vinyl ether of monoethanolamine $[(CH_2{=}CHO(CH_2)_2NH_2)_2Cu]Cl_2$, in which the copper atom is coordinated simultaneously to the ether oxygen and the amino-group.[113]

2. Alkylation

The alkylation of VE AA with a tertiary amino-group usually leads to the formation of monomeric quaternary salts.[25,83,85,114–177] As in the quaternisation of aliphatic amines, in this case the yields of the salts and the reaction time depend greatly on the structure of the amino-group and of the alkylating agent and also on the reaction conditions. For example, in the interaction of the vinyl ether of diethylaminoethanol with ethyl bromide in the absence of a solvent at 20 °C, the yield of the quaternary salt is only 15% after 21 days.[116] The alkylation of 4-(2-vinyloxyethyl)-1,4-perhydrotriazine 1-oxide by benzyl chloride, allyl bromide, or methyl iodide at 20 °C in nitromethane is completed by the formation of the corresponding salts in 93%–97% yields after only 10–12 h.[115]

$$CH_2{=}CHO(CH_2)_nNRR^1 + R^2X \longrightarrow [CH_2{=}CHO(CH_2)_nNRR^1R^2]X$$

R = Bu, R^1 = $CH_2CH{=}CH_2$;

R = R^1 = Et, Bu, $CH_2CH{=}CH_2$, $CH_2C(Me){=}CH_2$;

R + R^1 = $-(CH_2)_5-$, $-CH_2CH_2OCH_2CH_2-$, $-CH_2CH_2S(O)CH_2CH_2-$;

R^2 = Me, Et, $CH_2CH{=}CH_2$, $CH_2C{\equiv}CH$, CH_2Ph, CH^2COCH_3, CH_2COPh; X = Cl, Br, I, $MeSO_4$, 4-$MeC_6H_4SO_3$.

Only polymeric quaternary salts have been obtained in the alkylation of the trivinyl ether of triethanolamine[19] and also of the vinyl ether **16** (X = O)[75] by methyl iodide. Partial polymerisation is observed when amines of the type $(CH_2{=}CHOCH_2CH_2)_2NCH_2XAlk$ (where X = O, S) are treated with alkyl halides.[102]

The alkylation of the vinyl ethers of aminoalcohols with primary[84,118] and secondary amino-groups by alkyl halides, methyl monochloroacetate,[19] and chloro- or bromo-cyanogen[119] in the presence of KOH,[38,69,84,118,120,121] NaOH,[19] Na_2CO_3,[117] and K_2CO_3,[40,119] leads to the formation of the corresponding secondary and tertiary amines in 50%–95% yields without any complications.

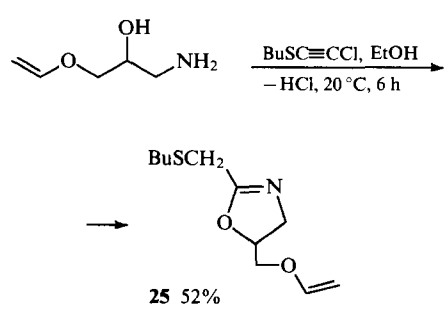
$$RNHCR^1_2CHR^2OCH{=}CH_2 + R^3Hal \longrightarrow RR^3NCR^1_2CHR^2OCH{=}CH_2$$

R = H, Me, Et, Ph, CH_2Ph, $CH_2C{\equiv}CH$, CH_2CH_2OH, $CH_2CH_2OCH{=}CH_2$

R^1, R^2 = H, Me; $RNHCR^1_2CHR^2 = \overline{CH_2CMe_2NHCMe_2CH_2CH}$;

R^3 = Me, $CH_2CH{=}CH_2$, $CH_2C{\equiv}CH$, CH_2Ph, CH_2COOMe, CH_2COOEt, CN; Hal = Cl, Br, I.

In the interaction of the monovinyl ether of 3-aminopropane-1,2-diol with butylthiochloroethyne, the hydroxyl adds to the triple bond with formation of the oxazoline **25** in addition to the chlorine-substitution reaction.[122]

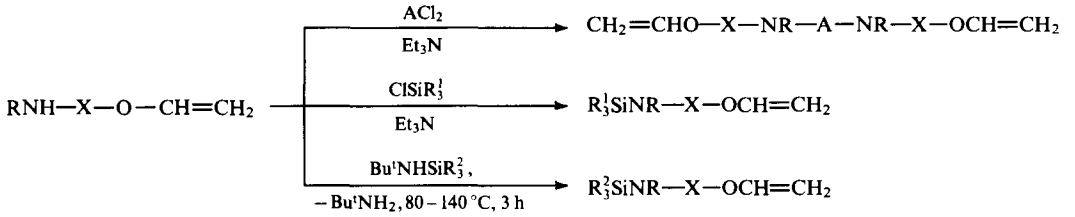


25 52%

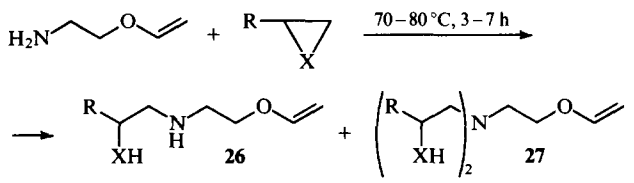
Both the products **26** and **27** with alkoxy- and alkylthio-substituents and the vinyl ethers of epoxyaminoalcohols **28** have been obtained[123] by the interaction of VE AA with epoxy-compounds[76] and thiiranes.[80]

Together with alkylation, also the silylation of VE AA, for example by α-ω-dichloropolysiloxanes,[124] alkyl(aryl)chlorosilanes, and silylamines, has been described (Scheme 3).[125]

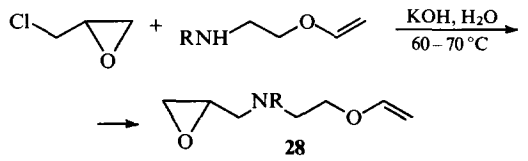
Scheme 3



X = $(CH_2)_2$, CMe_2CH_2, $CMe_2(CH_2)_3CHMeCH_2CH_2$; A = $(SiMe_2O)_nSiMe_2$; R = H, Alk; R^1 = Alk, Ph, Cl; R^2 = Alk, Ph.



X = O, S; R = $CH_2OCH_2CH_2OCH{=}CH_2$,

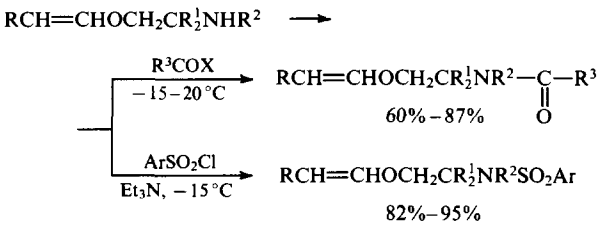


R = $CH_2CH{=}CH_2$ (82%); $CH_2CH_2OCH{=}CH_2$ (75%)

3. Acylation

The acylation of VE AA by the anhydrides[65,126,127] and chlorides of carboxylic acids[128–130] and sulfonic acids[84] usually takes place without complications of any kind.

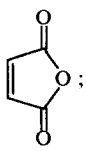
The reaction is carried out in the presence of organic bases



R = H, Ph; R^1 = H, Me;

R^2 = H, CH_2Ph, 4-$Me_2NC_6H_4CH_2$, 4-$MeOC_6H_4CH_2$, $CH_2CH_2OCH{=}CH_2$, $\overline{OCH{=}CH{-}CH{=}CCH_2}$, CH_2CH_2COOBu, $CH_2CHMeCOOMe$;

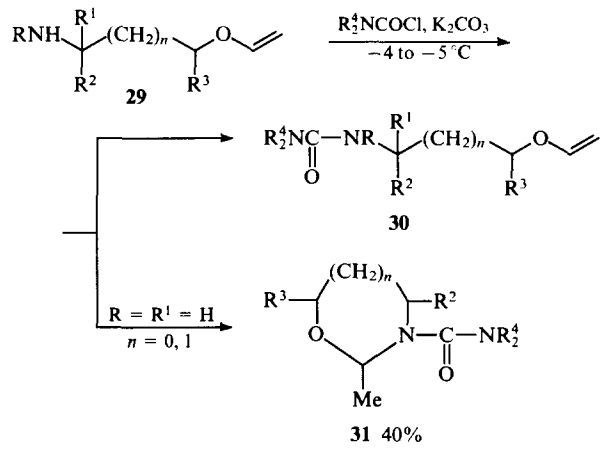
R^3 = Me, Ph, 2,4-$Cl_2C_6H_3OCH_2$, EtO; X = Cl, AcO;

R^3COX =  ; Ar = Ph, 4-MeC_6H_4.

(pyridine,[128] triethylamine[84,129]) or inorganic bases[65] as acid acceptors. An excess of the vinyloxyalkylamine is more rarely employed.[127,130]

Both linear carbamides **30**[94] and cyclic carbamides **31**[131] have been obtained as a result of the acylation of the VE AA **29** by *N,N*-dialkylcarbamoyl chlorides.

The carbamides **30** are formed from the amines **29** with a secondary amino-group and also from the same amines with a primary amino-group, for which there is steric hindrance to cyclisation ($n > 2$ or the amino-group is attached to a tertiary carbon atom). Only the carbamides **31** have been obtained in all other cases.



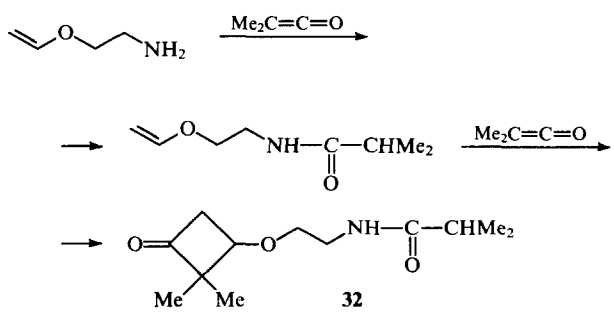
n = 0–3, 4, 8;

R, R^1, R^2, R^3 = H, Me, Bu, $C_{12}H_{25}$, $C_{18}H_{37}$, CH_2Ph, cyclo-C_6H_{11};

R^4 = Me, Et, Bu, $C_{12}H_{25}$, $C_{18}H_{37}$, cyclo-C_6H_{11};

R^4_2 = $-(CH_2)_5-$, $-CH_2CH_2OCH_2CH_2-$.

In the interaction of diethylketene with the vinyl ether of monoethanolamine, the latter is initially acylated, after which cycloaddition takes place and leads to the formation of the cyclobutanone **32** in 80% yield.[132]



The acylation of VE AA by esters is carried out by keeping the reactant mixture for 2–7 days at room temperature or for 5–40 h at 60–95 °C.[18,97,133,134]

$$RNH(CH_2)_nOCH{=}CH_2 \xrightarrow[-R^2OH]{R^1COOR^2} \rightarrow R^1CONR(CH_2)_nOCH{=}CH_2$$

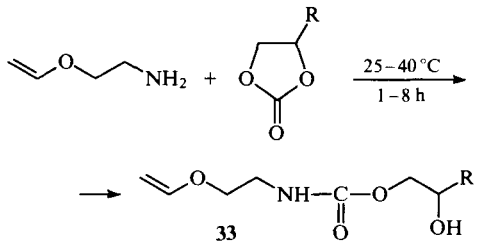
30%–75%

R = H, Me, Ph, CH_2Ph, $CH_2CH_2OCH{=}CH_2$, $Et_3Si(CH_2)_3$;

R^1 = Me, CH_2OH, CH(OH)Me, $CH_3(CH_2)_5CH(OH)CH_2CH{=}CH(CH_2)_7$, $NH_2C(O)NH$;

R^2 = Me, $CH{=}CH_2$; n = 2, 3.

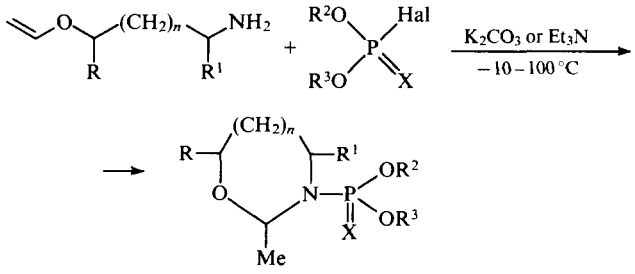
Cyclic carbonates interact with vinyloxyethylamine much more readily, affording high yields of the carbamates **33**.[135–138]



33

R = H (70%), CH_2Cl (100%).

The reactions of dialkyl phosphorothiohalidates or phosphorohalidates with the vinyl ethers of ethanol- and propanolamines lead to the cyclic phosphoramidate derivatives **34**.[139]

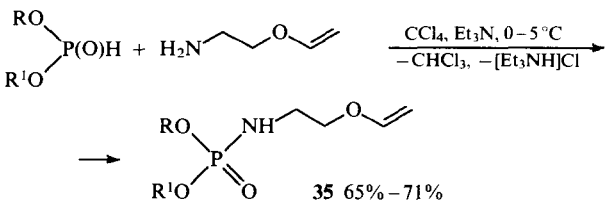


34 70%–80%

n = 0, 1; R = H, Me, $C_{16}H_{33}$, Ph; R^1 = H; X = O, S;

$R^2 = R^3$ = Et, $C_{12}H_{25}$, Ph; $R^2 + R^3 = -(CH_2)_2-$; Hal = F, Cl, Br.

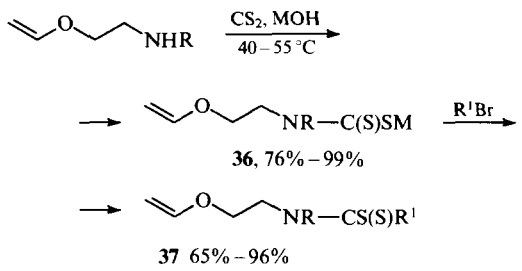
The acyclic phosphoramidates **35** have been obtained by the reaction of dialkyl phosphites with the vinyl ether of monoethanolamine in the presence of carbon tetrachloride and triethylamine.[140]



35 65%–71%

R, R^1 = Et, Pr, Pr^i, Bu, Bu^i, C_5H_{11}.

The dithiocarbamic acid salts **36** have been obtained by the reaction of the vinyl ethers of mono- and di-ethanolamines with carbon disulfide in the presence of alkali metal hydroxides.[141–143] Subsequent alkylation of the salts gave rise to the dithiocarbamates **37**.[141,144]



36, 76%–99%

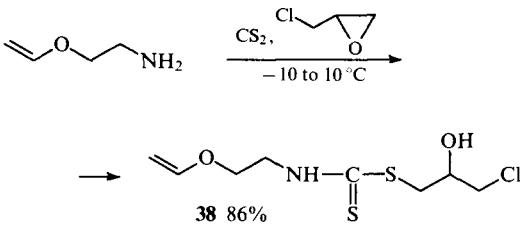
37 65%–96%

R = H, $CH_2CH_2OCH{=}CH_2$;

R^1 = Me, Et, Bu, Bu^i, CH_2Ph, $CH_2CH{=}CH_2$, $CH_2C{\equiv}CH$;

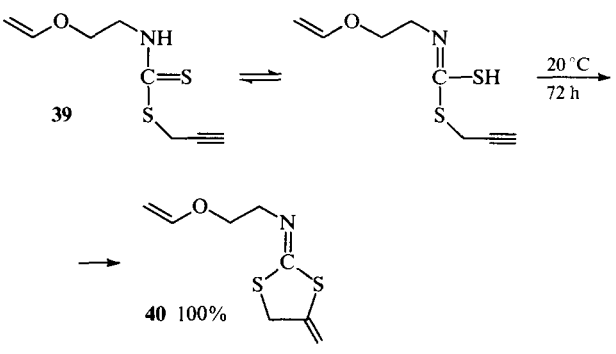
M = Na, K.

The joint treatment of 2-vinyloxyethylamine with carbon disulfide and epichlorohydrin leads to the dithiocarbamate **38**.[145]



38 86%

The thione–thiol tautomerism of dithiocarbamates leads to the possibility of the existence of derivatives of the isomeric dithiocarbamic acid. This type of cyclic derivative **40** has been obtained from the dithiocarbamate **39** at room temperature in a quantitative yield.[144]



40 100%

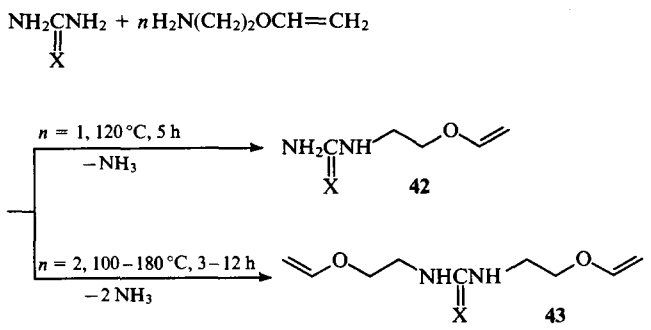
Carbon dioxide and carbon disulfide react readily with VE AA, but the stable carbamic acid salts **41** have been obtained only for the vinyl ethers of 2-amino-ethanol and 3-aminopropanol.[146]

$$2\,CH_2{=}CHO(CH_2)_nNH_2 \xrightarrow{CO_2} [CH_2{=}CHO(CH_2)_nNHC(O)O]NH_3(CH_2)_nOCH{=}CH_2$$

41 99%

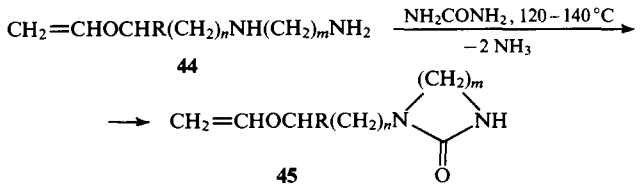
n = 2, 3.

The amide exchange reaction has also been used to acylate vinyloxyalkylamines. For example, when urea or thiourea is fused together with the vinyl ether of ethanolamine high yields of *N*-mono(2-vinyloxyethyl)urea and *N*,*N*-bis(2-vinyloxyethyl)-urea, as well as the corresponding thiourea derivatives (compounds **42** and **43**) were obtained depending on the reactant ratio.[42,147]



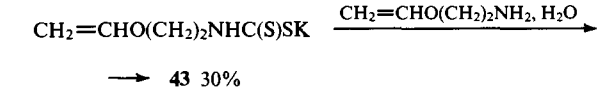
X = O, S.

The cyclic ureas **45** have been obtained from the vinyl ethers **44** and urea under similar conditions.[43]



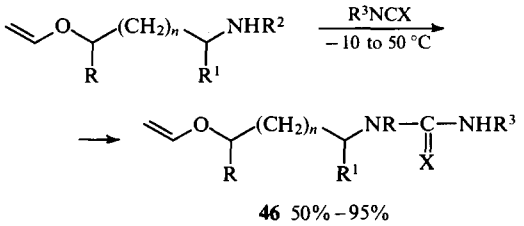
n = 1, 2; m = 2, 3; R = H, cyclo-C_6H_{11}, Ph.

The substituted thiourea **43** has also been synthesised by the interaction of an aqueous solution of a potassium carbamate derivative with vinyloxyethylamine.[148]



Isocyanates,[84,94,129,149,150] isothiocyanates,[91,150–152] and isocyanic acid, obtained in situ from KOCN and inorganic acids at pH 6.8,[153,154] readily combine with vinyloxyalkylamines, giving rise to the corresponding urea and thiourea derivatives **46** (Scheme 4).

Scheme 4



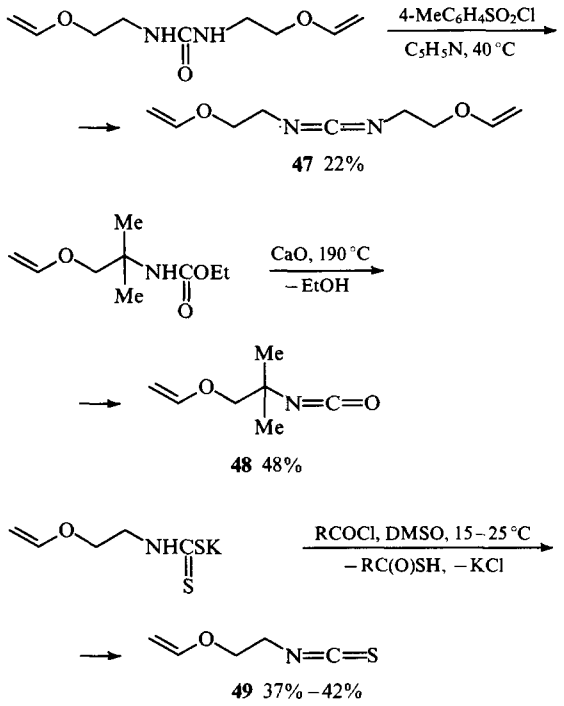
n = 2–5; R, R^1 = Me, Et, $C_{16}H_{33}$, Ph;

R^2 = H, Me, Et, Bu, cyclo-C_6H_{11}, CH_2Ph, $CH_2CH_2OCH{=}CH_2$, CH_2CH_2CN, 4-$Me_2NC_6H_3CH_2$, 4-$MeOC_6H_4CH_2$, $\overline{OCH{=}CH{-}CH{=}CCH_2}$, CMe=CHC(O)Me, $\overline{CH_2CH_2OCHMeCH}$, $\overline{CH_2(CH_2)_3CHMeCH}$;

R^3 = H, Me, Et, Bu, $MeOCH_2$, $BuOCH_2$, Ph, 2-ClC_6H_4; X = O, S.

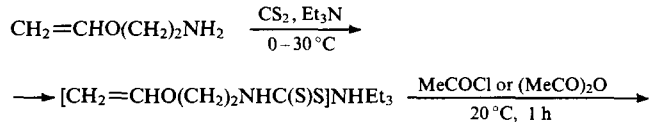
Some of the vinyl derivatives of urea and carbamic and dithiocarbamic acids described above have been used to synthesise vinyl-containing carbodiimide (compound **47**),[155] isocyanate (compound **48**),[130] and isothiocyanate (compound **49**)[104,106,156] derivatives (Scheme 5).

Scheme 5



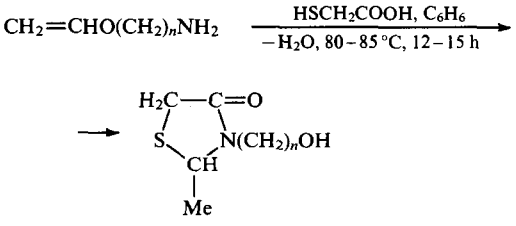
R = Me, Ph.

It was shown that the method of synthesis of the isothiocyanates **49** can be greatly improved by combining the synthesis of the carbamic acid salt from vinyloxyethylamine and carbon disulfide with the subsequent treatment with acid anhydrides. This single-reactor synthesis makes it possible to raise the yield of the isothiocyanate **49** to 95%.[157,158]



The replacement of carboxylic acid anhydrides by $POCl_3$ lowers the yield of compound **49** to 21%.[159]

Carboxylic acids are unsuitable for the acylation of VE AA owing to the instability of the latter in an acid medium already mentioned. The not altogether unusual result of the reactions of vinyloxyethyl- and vinyloxypropyl-amines with thioglycolic acid may serve as confirmation of this.[160]

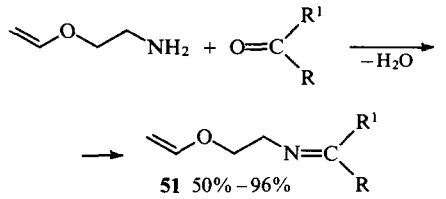


n = 2, 3.

Here there is also a possibility of the intermediate formation of the azomethine alcohol **24b**, which subsequently reacts with thioglycolic acid, affording the thiazolidinone **50**.[161]

4. Reactions with carbonyl compounds

As a typical primary amine, the vinyl ether of monoethanolamine readily condenses with aldehydes[162–164] and ketones,[165–169] giving rise to the Schiff bases **51**.

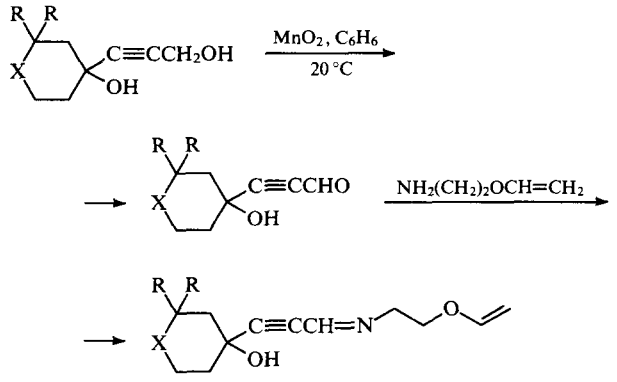


51 50%–96%

R, R^1 = H, Me, Ph, 2-HOC$_6$H$_4$, 4-MeOC$_6$H$_4$, 4-NO$_2$C$_6$H$_4$, 3-NO$_2$C$_6$H$_4$, 4-ClC$_6$H$_4$, 3-CF$_3$C$_6$H$_4$, 4-Me$_2$NC$_6$H$_4$, 3,4-(MeO)$_2$C$_6$H$_3$, OCH=CH—CH=C;

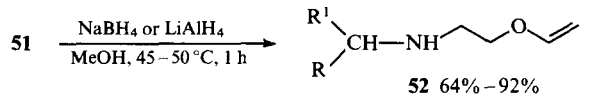
R + R^1 = –(CH$_2$)$_{4-5}$–, –CHMe(CH$_2$)$_4$–, –CHMeCH$_2$NMeCHMeCH$_2$–, –CH$_2$CH$_2$OCMe$_2$CH$_2$–.

The condensation of the vinyl ether of monoethanolamine with aldehydes proceeds so smoothly that it is possible to obtain the Schiff bases of unstable ethynealdehydes by oxidising ethyne glycols with active manganese dioxide in the presence of the above amine.[170,171]



X = O, R = Me (49%); X = CH$_2$, R = H (61%).

The hydrogenation of the vinyl derivatives of Schiff bases by hydrogen on Raney nickel even at room temperature and atmospheric pressure proceeds with reduction of the C=N and C=C bonds.[162] The selective reduction of the C=N bond alone with formation of the ether **52** is achieved with the aid of metal hydrides.[84,121,166–169]

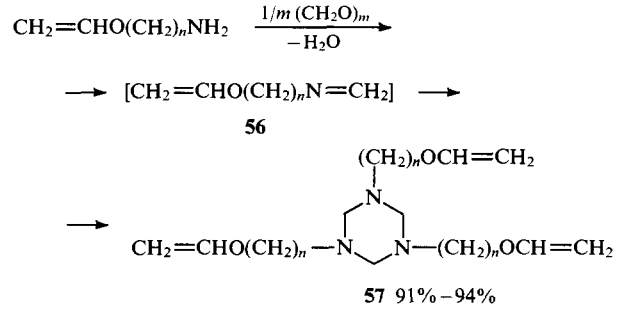


52 64%–92%

The amides **54** have been obtained by acylating the Schiff bases **53**,[166,167,172,173] while the urea derivatives **55** have been synthesised by condensing the bases **53** with phenyl isocyanate (Scheme 6).[149]

The reaction proceeds selectively with formation of the type A enamine structure only for X = CH$_2$, whilst in all the remaining cases equal amounts of the isomers A and B are obtained.

The condensation of the vinyl ethers of ethanolamine and propanolamine with paraformaldehyde leads to the products of the trimerisation of the azomethines **56** — the trivinyl ethers of 1,3,5-tris(2-hydroxyalkyl)hexahydrotriazine **57**.[162,174]

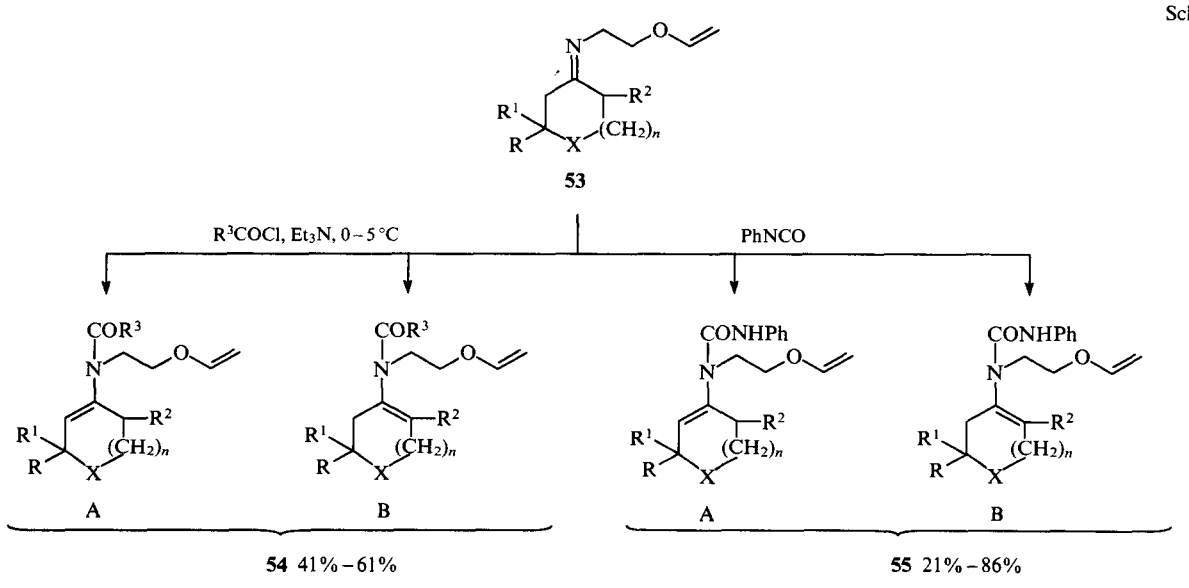


57 91%–94%

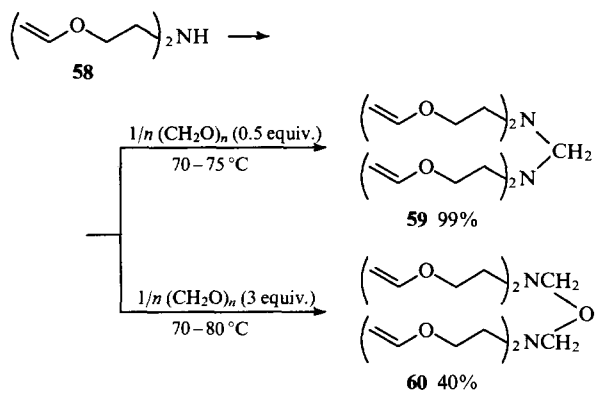
n = 2, 3.

N,N,N',N'-(2-Vinyloxyethyl)methylenediamine **59** has been obtained by the reaction of the divinyl ether of diethanolamine **58** with a stoichiometric amount of paraformaldehyde,[128,175] while in the presence of an excess of paraformaldehyde the product was the tetravinyl ether **60**.[102]

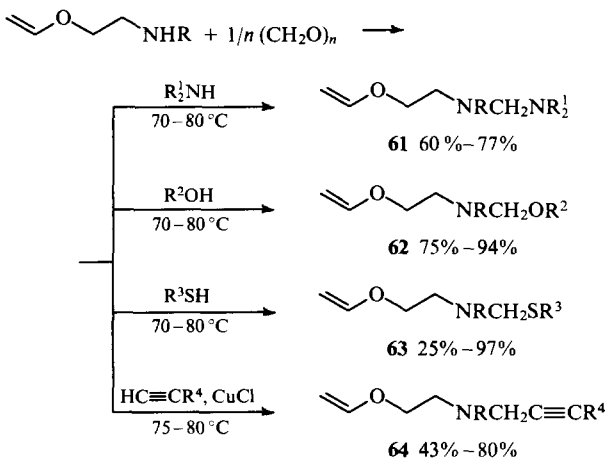
Scheme 6



n = 0, 1; R, R^1, R^2 = H, Me; R^3 = Me, Et, Pr, Ph; X = O, NMe, CH$_2$.



The vinyl ethers of aminoalcohols with a secondary amino-group and paraformaldehyde have been used for the amino-methylation of amines,[102] alcohols,[102,128] thioalcohols,[102] and ethynes[38,121,176-178] in the synthesis of the vinyl ethers of *N,N*-disubstituted aminoethanols **61**–**64**.



R = $CH_2CH_2OCH{=}CH_2$, CH_2CH_2COOEt, CH_2CH_2COOBu, $CH_2CHMeCOOMe$; R^1 = Et, $CH_2CH{=}CH_2$;

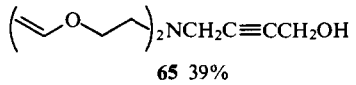
R_2^1 = $-CH_2CH_2OCH_2CH_2-$;

R^2 = Bu, $CH_2CH{=}CH_2$, $CH_2C{\equiv}CH$, $CMe_2C{\equiv}CCH{=}CH_2$, $CH_2CH_2OCH{=}CH_2$; R^3 = Bu, $CH_2CH{=}CH_2$, Ph;

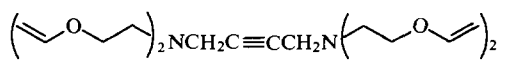
R^4 = H, Ph, $C{\equiv}CCH_2OH$, $C{\equiv}CCMe_2OH$

In the absence of catalysts, ethynyl alcohols are amino-methylated only at the hydroxy-group,[102] but in the presence of copper monochloride the aminomethylation takes place exclusively at the ethynyl group.[177]

The aminomethylation of ethyne by paraformaldehyde and the amine **58** gives rise to the formation of the aminoalcohol **65** and the diaminobutyne **66** together with propargylamine **64** (yield 18%).[177]

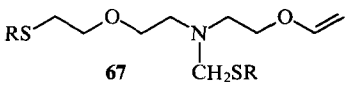


65 39%



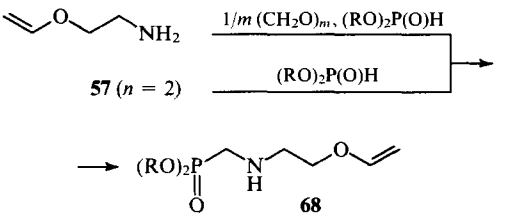
66 24%

The aminomethylation of thioalcohols is complicated by the side reaction involving the addition of the thioalcohols to the vinyl-oxy-group, as a result of which the sulfides **67** are obtained in yields up to 20% from the amine **58**, in addition to the sulfides **63**.[102]



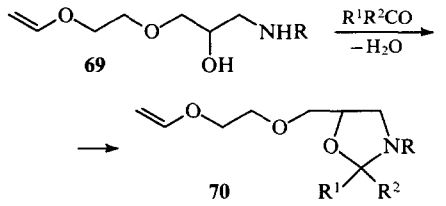
R = Bu, $CH_2CH{=}CH_2$.

When the vinyl ether of monoethanolamine and para-formaldehyde are used for the aminomethylation of dialkyl phosphites, the yields of the phosphonates **68** is significantly reduced. These compounds are obtained in satisfactory yields by the interaction of dialkyl phosphites with the triazine **57** (n = 2).[179]



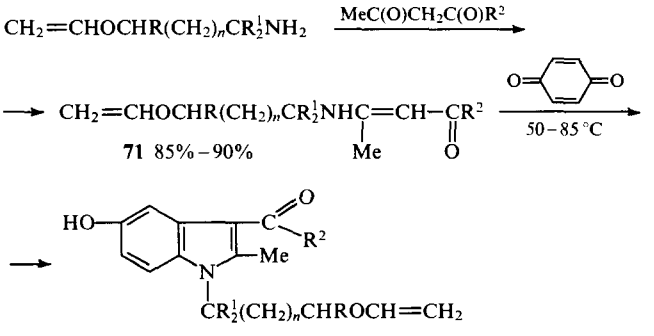
R = Et (43%), R = Bu (36%).

The vinyl ethers **69**, containing a hydroxy-group, condense with carbonyl compounds, affording the oxazolidines **70** in yields up to 91%.[180]



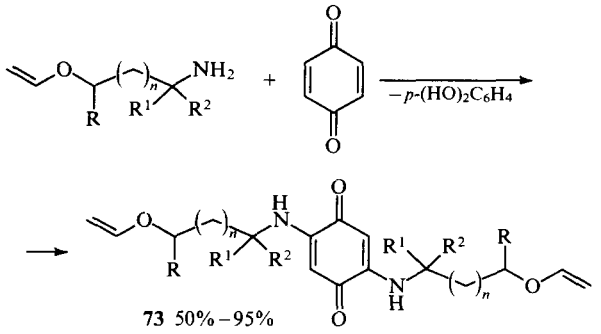
R, R^1, R^2 = H, Me, Et, Pr, Bu; $R^1 + R^2 = -(CH_2)_5-$.

Dicarbonyl compounds such as acetylacetone and aceto-acetic ester condense with VE AA, forming the enamines **71**,[149,167,181-183] the subsequent reaction of which with 1,4-benzoquinone leads to the indoles **72**.[182,183]



R, R^1 = H, Me, Et; R^2 = Me, OEt; n = 0–2.

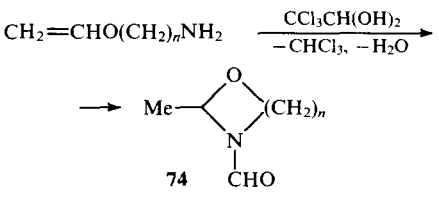
The interaction of 1,4-benzoquinone with VE AA, like that with primary amines,[184] involves an oxidation–reduction process, which results in the formation of the diaminobenzo-quinones **73**.[185,186]



73 50%–95%

R = R¹ = R² = H, Me, Et; *n* = 0–2.

The reaction of chloral hydrate with aliphatic amines is known to be accompanied by the formylation of the latter.[187] In the case of VE AA, not only their formylation but also their cyclisation to the 1,3-oxazacycloalkanes **74** take place.[188]

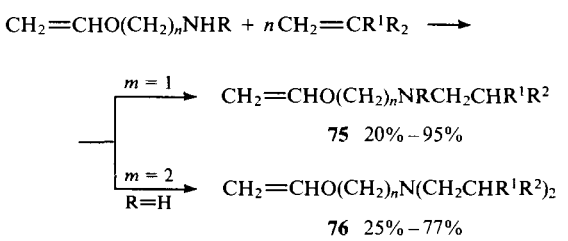


74

n = 2 (69%), *n* = 3 (56%).

5. Addition to carbon – carbon multiple bonds

Like the usual aliphatic amines, the vinyl ethers of aminoalcohols add to the activated C=C and C≡C bonds. For example, their addition to acrylonitrile,[189] acrylamide,[190] and the esters of acrylic[19,117,127] and methacrylic[127,191] acids has been described. Depending on the reactant ratio, the vinyl ethers with a primary amino-group can give rise to both the monoadducts **75** and the diadducts **76**.[117,127]



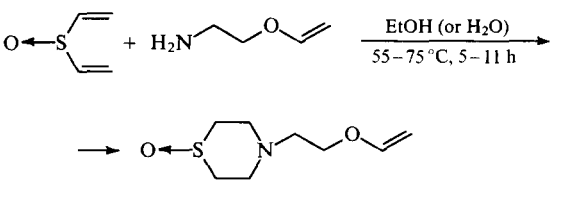
75 20%–95%

76 25%–77%

n = 2, 3; R = H, Me, $CH_2CH_2OCH{=}CH_2$; R^1 = H, Me;

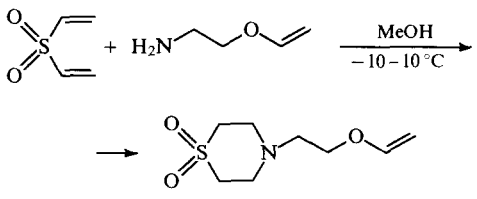
R^2 = CN, $CONH_2$, COOMe, COOEt, COOBu.

At a temperature above 50 °C, divinyl sulfoxide readily combines with the vinyl ether of monoethanolamine, affording 4-(2-vinyloxyethyl)-1,4-perhydrothiazine 1-oxide **77**.[114,115,192,193]



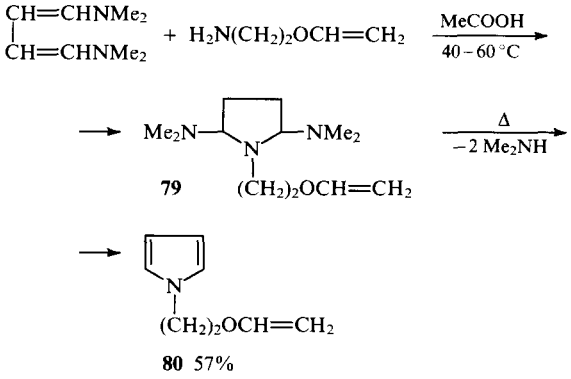
77 75%–85%

The reaction with divinyl sulfone takes place even on cooling, whereupon the sulfone **78** is formed.[194]



78 82%

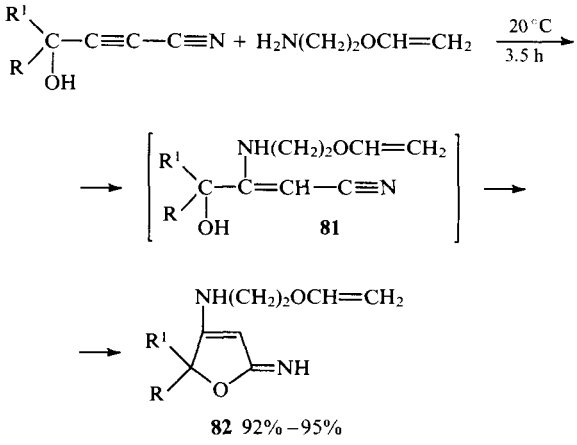
The interaction of the vinyl ether of monoethanolamine with 1,4-bis(dimethylamino)buta-1,3-diene is exothermic in the presence of catalytic amounts of acetic acid. The pyrrolidine **79** formed is converted into 1-(2-vinyloxyethyl)pyrrole **80** during distillation.[195]



79

80 57%

When the vinyl ether of monoethanolamine is added to the triple bonds of tertiary cyanoethynyl alcohols, the intermediate unstable nitriles **81** are formed initially and then cyclise to the furan derivatives **82**.[196]

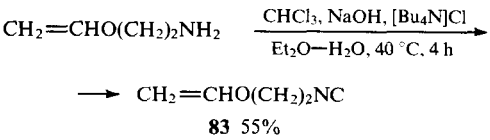


81

82 92%–95%

R = R¹ = Me; R + R¹ = –$(CH_2)_4$–.

Under the conditions of phase transfer catalysis by tetrabutylammonium chloride, the interaction of the vinyl ether of monoethanolamine and the dichlorocarbene generated from chloroform results in the formation of 2-vinyloxyethyl isocyanide **83**.[197]

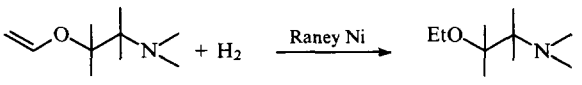


83 55%

6. Reactions involving addition to the vinyl group

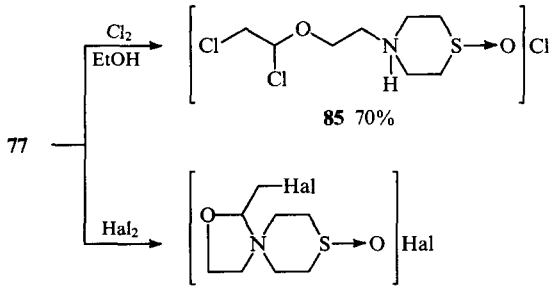
One of the reactions involving only the vinyl group is the hydrogenation of VE AA. The reaction is carried out on Raney nickel at temperatures in the range 20–150 °C and hydrogen pressures from atmospheric to 5 MPa. The yields of the ethyl ethers of aminoalcohols **84** are 65%–100%.[20,21,26,44,162,191,194,198–200]

The study of the hydrogenation of the vinyl ether of monoethanolamine on Raney nickel showed that the reaction is of zero order with respect to the vinyl ether and that its rate diminishes in the series of solvents ethanol > 1:1 ethanol–water > 1:1 dioxane–water > water.[199]



84

When chlorine adds to the vinyl ether **77** in ethanol, the hydrochloride of the dichloroether **85** is formed, whereas in aprotic solvents the product is the spiro-cyclic salt **86**. Regardless of the type of solvent, the interaction of iodine with compound **44** leads to the salt **86**.[114,201]

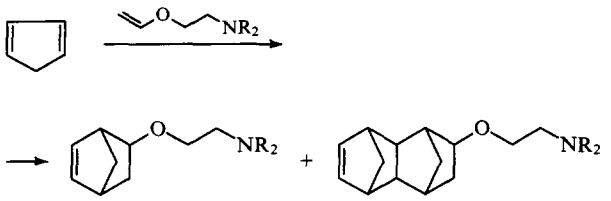


85 70%

86 95%–98%

Hal = Cl, I.

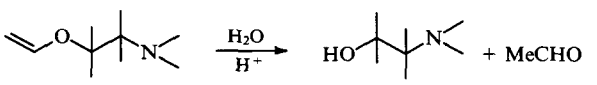
When the vinyl ethers of ethanolamines are used as dienophiles in the reaction with cyclopentadiene, the mono- and di-adducts **87** and **88** are formed in low yields.[202]



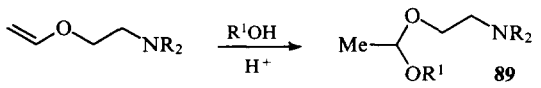
87 10%–17% **88** 6%–28%

R = H, Me, Et.

In acid aqueous solutions, VE AA are quantitatively hydrolysed to the aminoalcohols and acetaldehyde, but detailed studies of the hydrolysis have not been carried out. In the main, this reaction has been used to demonstrate the structure of the vinyl ethers.[18,20,21,26,44,99,191]



The vinyl ethers of aminoalcohols, which are stable in the presence of protic acids, are capable of combining with alcohols with formation of the acetals **89** when the reaction is catalysed by these acids.[20,21,24,203]



89

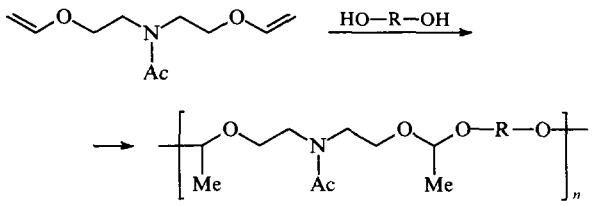
R = Et, R^1 = Bu (13%); R = Me, R^1 = $CH_2CH_2NMe_2$ (5%),

R = Et, R^1 = $CH_2CH_2NEt_2$ (6%); R = Ph,

R^1 = CH_2CH_2NHPh (62%); R = H, R^1 = $(AlkO)_2P(O)CH_2$ (70–82%).

Alk = Et, Pr^i, Bu.

When glycols are used as the alcohols, the reaction affords the oligoacetals **90**.[204]

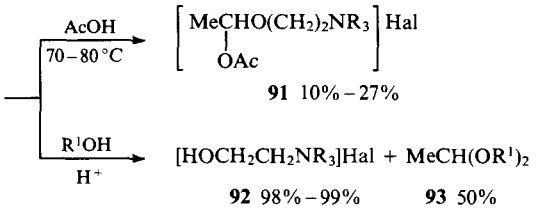


90 98%–99%

n = 4–7; R = $(CH_2)_2$, $(CH_2)_2O(CH_2)_2$, $(CH_2)_2O(CH_2)_2O(CH_2)_2$.

Quaternary vinyloxyethylammonium salts give rise to the adducts **91** with acetic acid, but are cleaved by alcohols when the reaction is catalysed by hydrochloric or sulfuric acids to the aminoalcohol salts **92** and the acetals **93**.[116]

$[CH_2{=}CHO(CH_2)_2NR_3]Hal$ ⟶



91 10%–27%

92 98%–99% **93** 50%

R = Me, Et; R^1 = Me, Et, Bu; Hal = Br, I.

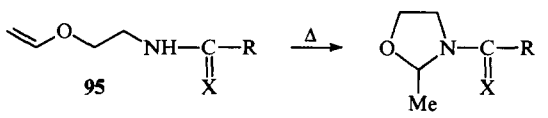
The addition of thioalcohols to the vinyloxy-group in VE AA proceeds, as in the case of alkyl vinyl ethers,[205] contrary to the Markovnikov rule with formation of the sulfides **94**.[67,102,124,141]

$CH_2{=}CHO(CH_2)_2NH_2 + EtSH \xrightarrow{100\,^\circ C,\ 6\ h}$

⟶ $EtS(CH_2)_2O(CH_2)_2NH_2$

94 20%–32%

Apart from the acid-catalysed cyclisation of vinyloxyalkylamines and vinyloxyalkylamides discussed above, it has been frequently noted that the cyclisation of certain amides **95** to the oxazolidines **96** can take place in the absence of acid catalysts. Thermal cyclisation has been observed at a temperature higher by 80–120 °C than in the acid-catalysed process.[95,96,104,105,137,138,156,206,207]

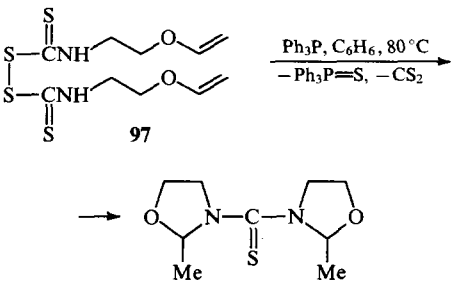


95 **96** 70%–100%

X = S, R = SBu, SCH_2Ph, $O(CF_2)_{6-10}H$;

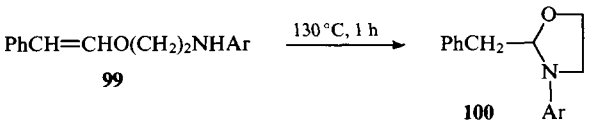
X = O, R = $OCH_2CH(OH)CH_2Cl$.

The unusual, not acid-catalysed, cyclisation of thiuram disulfide **97** to the thione **98** takes place when compound **97** interacts with triphenylphosphine.[208]



97 **98** 39%

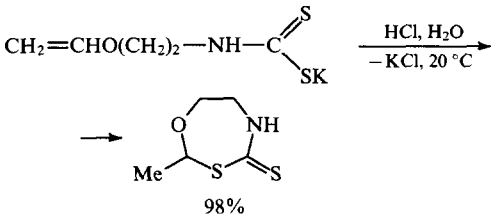
It has been shown recently[209] that the interaction of an aromatic substituent in the 2-position in the vinyloxy-group imparts to the ethers **99** the capacity for cyclisation to the oxazolidines **100** on treatment with bases. The thermal cyclisation of compound **99** does not occur.[65]



99 **100**

Ar = Ph (87%), 4-MeC_6H_4 (91%).

In the case of *N*-(2-vinyloxyethyl)dithiocarbamic acid, formed in situ from an aqueous solution of potassium carbamate and hydrochloric acid, the cyclisation takes place at the more acid SH group and not the amide group.[210]



98%

7. Polymerisation

In contrast to alkyl vinyl ethers for which cationic polymerisation is the main polymerisation reaction,[205] the vinyl ethers of aminoalcohols polymerise as a rule via a radical mechanism. This is associated with the deactivation of the cationic catalyst by the reaction forming a complex with the amino-group. Rare examples of the successful cationic polymerisation were examined above in the discussion of the reactions of vinyl ethers with acids.

2,2'-Azobisisobutyronitrile[19,21,26,211–225] or other azo-compounds[42,108,124,125] are usually employed to initiate the radical polymerisation. In the case of homopolymerisation, the reaction is carried out at 60–80 °C with 2%–5% of the initiator for 20–100 h. The yield of the polymers, which are viscous liquids with a low molecular mass (1000–2000), is usually low and ranges from 5% to 20%. Solid polymers with a three-dimensional structure are obtained under analogous conditions from certain divinyl ethers of diethanolamines and the trivinyl ether of triethanolamine in 40%–70% yields.[19,26,133,211,213]

The attempts to initiate the homopolymerisation of the vinyl ethers of ethanolamines by benzoyl peroxide were unsuccessful.[19,108,219] On the other hand, this initiator induces the polymerisation of quaternary vinyloxyalkylammonium salts.[83]

There are data on the initiation of the polymerisation of the vinyl ether **3** by γ-radiation.[226–229] It has been noted that in this case the degree of conversion of compound **3** into water-soluble polymers with quantitative retention of the amino-groups does not exceed 30%. For higher degrees of conversion of compound **3**, water-insoluble products are formed.

The use of elemental sulfur as the initiator of the polymerisation of the ether **3** has been described.[224,230] The polymer formed under these conditions contains up to 4.4% of sulfur and has a molecular mass of about 1000.

In order to investigate the reactivities of VE AA, they were copolymerised with other vinyl monomers, for example with methyl methacrylate,[125,191,212–214,219,231,232] acrylamide,[225,233,234] hexamethylenedimethacrylamide,[223] acrylonitrile,[42,225,231,232] divinylbenzene,[42] styrene,[150,225,232] vinyl chloride[150,153,231] *N*-vinylpyrrolidinone,[215,216,221,227,233–235] 4-vinylpyridine and 2-methyl-5-vinylpyridine,[216,235] 1-vinyl-4,5,6,7-tetrahydroindole,[236] the glycidyl vinyl diether of ethylene glycol,[217,218] the monovinyl ether of ethylene glycol,[154,237] and other vinyl ethers.[42,150,225,232,234,238]

The presence of the highly reactive amino-groups in the VE AA homopolymers makes it possible to achieve readily polymer-analogue reactions and to obtain in this way graft copolymers which are difficult to obtain by other procedures. For this purpose, the homopolymers were alkylated by alkyl halides and alkyl sulfates,[225,239–244] acylated by acid halides,[245] hydroxyalkylated by oxiranes,[243] and cyanoethylated by acrylonitrile.[246,247] The homopolymers were modified by condensing them with formaldehyde and acetylacetone,[97,243,248,249] by making them undergo the amide exchange reaction with urea,[250,251] and by their addition to isocyanates.[42,245]

IV. Practical applications

Although it is at present still impossible to say that the VE AA are employed as widely as, for example, vinyl ethers and esters, nevertheless the available literature data indicate considerable prospects for their use in industry, agriculture, and medicine.

In the study of their physiological activity, it was established that the vinyl ethers **16** (X = O) and the quaternary salts **19** exhibit hypotensive and spasmolytic activities.[75,85] Compound **77** and its salts may be used to correct the haemostasis in antithrombic therapy.[114,115,193] 2-Aryl-1-methyl-*N*-(2-vinyloxyethyl)-ethylamines reduce the appetite and are recommended for the treatment of obesity.[168,169] *N*,*N*-Bis(2-vinyloxyethyl)-*S*-(acylvinyl)dithiocarbamate and its salts possess a tuberculostatic activity.[252]

Effective fungicides,[42,119,150,152,238] insecticides[42,119,130,142,150,232] acaricides,[143,152] bactericides,[152] and bacteriostatic agents[94,152] have been found among VE AA derivatives.

The technical applications of VE AA are frequently associated with the solution of ecological problems. Thus they are employed for the detoxication of industrial waste by the elimination of heavy metals[163] and cyanides,[174,253] for the flotation purification of water by the elimination of organic suspensions (silt,[190] lignin[101,254]), and also for combating ore dust.[126] The employment of these compounds for the enrichment of muscovite[255,256] and polymetallic ores[146,257] not only increases efficiency but also makes it possible to reduce the amount of highly toxic reagents employed in these processes.

VE AA are used as intermediates in the synthesis of substances with analgesic, psychotropic,[258,259] and radio-protecting[141] properties. They are also employed to obtain corrosion

inhibitors,[42,139,152,154] plasticisers,[42,97,139,154] photostabilisers for plastics,[154] antioxidants for lubricating oils,[42,139] as fire-proofing reagents,[139] and as reagents imparting hydrophobic properties to materials of plant and animal origin.[97,231]

The polymers and copolymers obtained from VE AA are used as anion-exchange resins,[42,125,211] water-soluble complex-forming agents,[233,260] sorbents for transition and polyvalent metals,[42,223,233–235,243,248,261] flotation agents for the enrichment of polymetallic ores,[237,247,249,251,262,263] reagents for the removal of aldehydes, epoxides, and isocyanates,[42] as well as organic and mineral suspensions[239–243,246,250,264,265] from water, hardening agents for epoxide resins,[222,230] self-hardening epoxide resins,[217,218] adhesives,[109,130,150,217,218,238] plasticising[97,109,231,245] and antistatic[42,225] additives to plastics, coatings, and films,[42,97,125,150,152] auxiliary materials in the textile and cellulose-paper industries,[94,97,117,130,134,150,153,154,244,245] lubricating and hydraulic liquids or additives to them,[42,124] and fungicides and bactericides.[220,225]

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Ozonolysis of unsaturated compounds in the synthesis of insect pheromones and juvenoids

G Yu Ishmuratov, R Ya Kharisov, V N Odinokov, G A Tolstikov

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Abstract. The review surveys data on the use of the ozonolysis of cyclic and acyclic monoenes, dienes, and trienes in various stages of the total synthesis of insect pheromones and juvenoids. The bibliography includes 178 references.

I. Introduction

In a review published in 1981,[1] we presented the results of studies on the structures of peroxide ozonolysis products and the path followed in their transformation into the final oxygen-containing compounds without a peroxide fragment. As a result of progress in this field, the ozonolysis of alkenes has become not only a recognised analytical method for the determination of the structures of the initial unsaturated compounds but also a procedure for the highly selective introduction of oxygen-containing functional groups into organic molecules. The development of the ozone generation technique and of the control over ozonolysis have reached a level such that this reaction has advanced sufficiently to be included in the class of modern methods which are not only of preparative value but also of interest for industry.

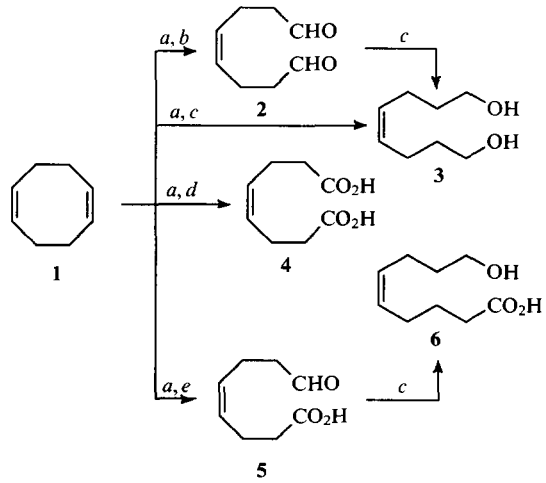
During the last decade, a considerable number of studies have been published on the use of ozonolysis of unsaturated compounds in the synthesis of insect pheromones and juvenoids. The present review is devoted to a survey of the results of these investigations.

II. Use of selective ozonolysis of cyclic and acyclic dienes and trienes in the synthesis of pheromones and juvenoids

The problems arising in the intensification of agricultural production and in the expansion and improvement of measures for the protection of nature and human health may be solved only with the aid of integrated systems for the protection of cultivated plants, forests, and agricultural and forestry produce. An indissoluble component of these measures in the fight against insect pests is the partial or complete replacement of the traditional chemical poisons by ecologically clean new generation insecticides, which include pheromones and juvenile hormones regulating arthropod behaviour and development.

The primary tasks in the synthesis of insect pheromones, juvenile hormones, and their analogues include the development of preparatively convenient methods of synthesis of the key intermediates, such as the α,ω-bifunctional compounds capable of undergoing selective chemical transformations. One of the promising ways of synthesising such compounds is the ozonolysis of alkenes.[1-57] The study of the oxidative cleavage of alkenes has become especially timely in connection with advances in metal complex catalysis, by virtue of which cyclic and acyclic oligomers and cooligomers of 1,3-dienes have become available.

The products of ring opening of cyclic butadiene oligomers are widely used in the synthesis of pheromones and other natural products. Thus the partial ozonolysis of one of the most readily available butadiene oligomers — (1*Z*, 5*Z*)-cyclo-octadiene **1** — as well as other cyclic butadiene oligomers and cooligomers provides a simple and effective path to bifunctional unsaturated compounds containing terminal functional groups which are of the same or different nature depending on the procedure used in the treatment of the peroxide ozonolysis product.[1,58-64]

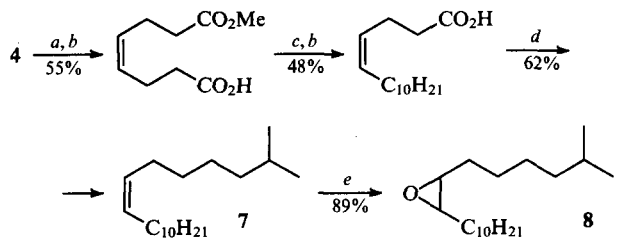


(*a*) O_3; (*b*) H_2–Pd–$CaCO_3$–PbO; (*c*) $NaBH_4$; (*d*) H_2CrO_4; (*e*) AcONa–AcOH–Ac_2O.

G Yu Ishmuratov, R Ya Kharisov Insect Bioregulators Laboratory, Institute of Organic Chemistry, Ufa Scientific Centre of the Russian Academy of Sciences, prosp. Oktyabrya 71, 450054 Ufa, Russian Federation. Fax (7-347) 235 60 66
V N Odinokov Biologically Active Substances Laboratory, Institute of Petrochemistry and Catalysis, Academy of Sciences of the Bashkortostan Republic, prosp. Oktyabrya 141, 450075 Ufa, Russian Federation.
G A Tolstikov Novosibirsk Institute of Organic Chemistry, Siberian Division of the Russian Academy of Sciences, prosp. Akad. Lavrent'eva 9, 630090 Novosibirsk, Russian Federation. Fax (7-383) 335 47 52.

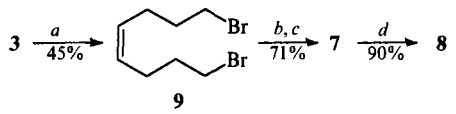
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A whole series of Lepidoptera pheromones have been obtained from α,ω-bifunctional alkenes **2–6**. Disparlure **8**—the pheromone of the gypsy moth (*Porthetria dispar*)—has been synthesised from (*Z*)-oct-4-ene-1,8-dioic acid **4**. The Kolbe condensation was used in two stages of this process (*c*, *d*).[65,66]



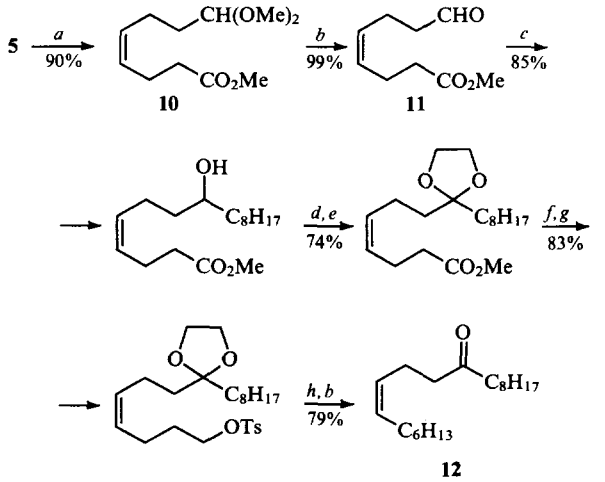
(*a*) MeOH–H$^+$; (*b*) KOH–MeOH;
(*c*) $Me(CH_2)_7CO_2H$–Pt/anode–MeOH;
(*d*) $Me_2CHCH_2CH_2CO_2H$–Pt/anode–MeOH;
(*e*) MCPBA (*m*-chloroperbenzoic acid)–CH_2Cl_2.

The simpler synthesis of disparlure from (*Z*)-oct-4-ene-1,8-diol **3** involves its transformation into the dibromo-derivative **9** and two successive stages in which it is coupled with n-heptyl- and isobutyl-magnesium bromides.[67–69]



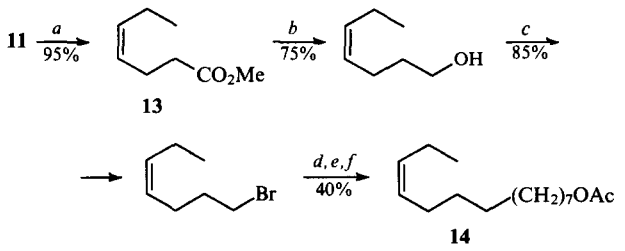
(*a*) PBr_3–Py; (*b*) n-$C_7H_{15}MgBr$; (*c*) Bu^iMgBr; (*d*) $ArCO_3H$ (Ar = 3-ClC_6H_4, 2-$HO_2CC_6H_4$).

The aldehydoacid **5** can be converted into the acetal-ester **10**, which has served as a convenient reagent for the synthesis of certain insect pheromones. For example, the synthesis of the sex pheromone **12** of the peach fruit moth (*Carposina niponensis Walsingham*) is based on the selective hydrolysis of the acetal **10** to the aldehydoester **11** and its interaction with n-octylmagnesium bromide.[70]



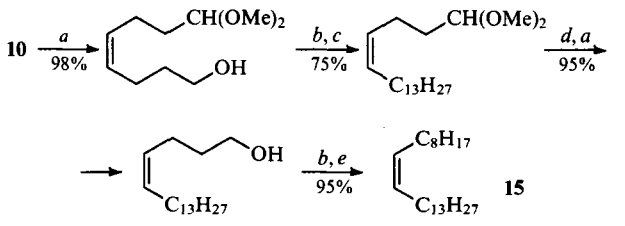
(*a*) MeOH–H$^+$; (*b*) H_3O^+; (*c*) n-$C_8H_{17}MgBr$; (*d*) PCC (Py·$HCrO_3Cl$, pyridinium chlorochromate); (*e*) $(CH_2OH)_2$–TsOH; (*f*) DIBALH (Bu^i_2AlH); (*g*) TsCl–Py; (*h*) PrMgBr–Li_2CuCl_4.

Yet another variant of the transformation of the aldehydoester **11** leads to the sex pheromone **14** of the oak moth (*Tortrix viridana*). The decarbonylation of compound **11** by treatment with tris(triphenylphosphine)rhodium chloride takes place under mild conditions, affording a high yield of the methyl ester of the (4*Z*)-heptenoic acid **13**, which determines the subsequent success of the entire synthesis.[71]



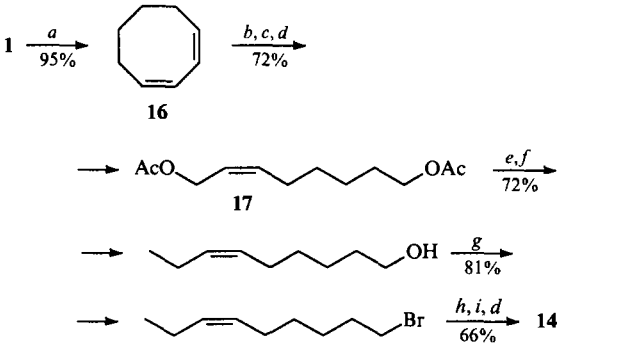
(*a*) $(Ph_3P)_3RhCl$; (*b*) DIBALH; (*c*) $Br_2·PPh_3$;
(*d*) $EtOCH(Me)O(CH_2)_7MgBr$–CuI–2,2′-Bipy;
(*e*) TsOH–MeOH–H_2O; (*f*) Ac_2O–Py.

The stereospecific syntheses of (9*Z*)-tricosene **15** [a component of the sex pheromone of the housefly (*Musca domestica*)[72,73]] and of (9*Z*)-tetradec-1-enyl acetate and (9*Z*)-hexadecenal[74] [the components of the sex pheromones of the pine moth (*Panolis flammea*) and the cotton bollworm (*Heliothis armigera*) respectively] have been achieved by the successive transformations of the acetal-ester **10** involving the ester and acetal groups and two cross-couplings with the corresponding organomagnesium and organolithium reagents catalysed by copper salts.



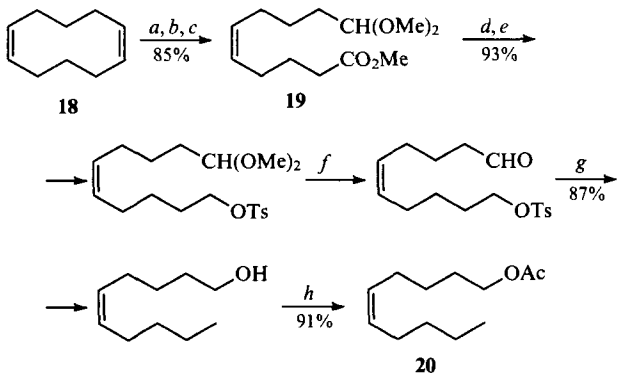
(*a*) DIBALH; (*b*) TsCl–Py; (*c*) n-$C_{10}H_{21}MgBr$–Li_2CuCl_4;
(*d*) H_3O^+; (*e*) n-$C_5H_{11}MgBr$–Li_2CuCl_4.

After reduction and acetylation, the product of the partial ozonolysis of cycloocta-1,3-diene **16** gave rise to (2*Z*)-1,8-diacetoxyoct-2-ene **17**, capable of regio- and stereo-selective coupling with Grignard reagents via the allylacetoxy-groups, which has been used in the regio- and stereo-selective synthesis of the oak moth pheromone **14**.[71]



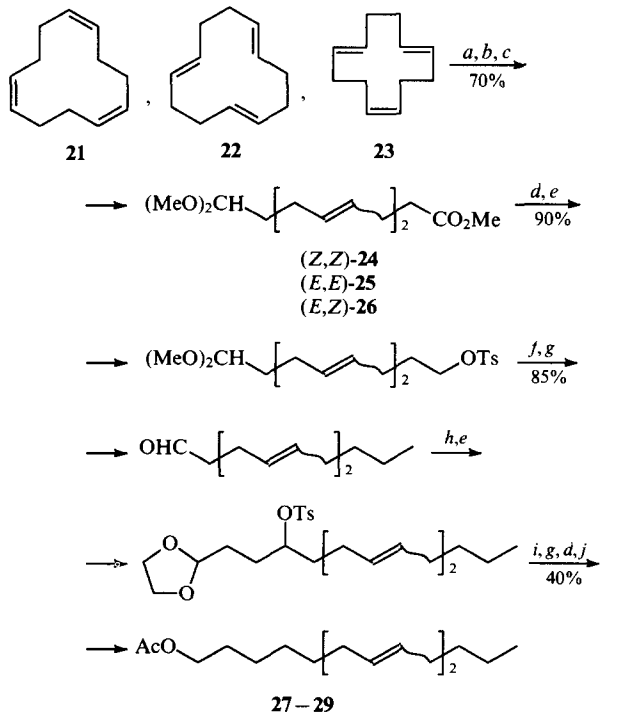
(*a*) Bu^tOK–DMSO; (*b*) O_3–cyclo-C_6H_{12}–MeOH;
(*c*) $NaBH_4$–MeOH; (*d*) Ac_2O–Py; (*e*) MeMgI–Li_2CuCl_4;
(*f*) DIBALH; (*g*) $Br_2·PPh_3$;
(*h*) $EtOCH(Me)O(CH_2)_5MgBr$–CuI–2,2′-Bipy;
(*i*) TsOH–MeOH–H_2O.

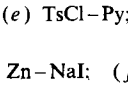
The carbon skeleton of the (*Z*)-C_{10} block **19**, obtained from the products of the selective ozonolysis of (1*Z*,6*Z*)-cyclodecadiene **18**, is identical to the skeleton of the component of the pheromone of the turnip moth (*Agrotis segetum*)—(5*Z*)-dec-1-enyl acetate **20**; the latter was therefore synthesised via chemoselective transformations of the functional groups.[75,76]



(*a*) O_3–cyclo-C_6H_{12}–AcOH; (*b*) AcONa–AcOH–Ac_2O; (*c*) TsOH–MeOH; (*d*) DIBALH; (*e*) TsCl–Py; (*f*) H_2O–PPTS (Py·HOTs, pyridinium *p*-toluenesulfonate); (*g*) $LiAlH_4$; (*h*) Ac_2O–Py.

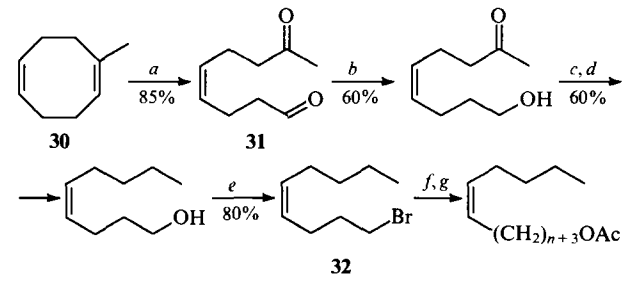
The C_{12} α,ω-bifunctional compounds **24**–**26**, obtained by the selective ozonolysis of (1*Z*,5*Z*,9*Z*)-cyclododecatriene **21**, (1*E*,5*E*,9*E*)-cyclododecatriene **22**, and (1*E*,5*E*,9*Z*)-cyclododecatriene **23**, are of evident interest for the synthesis of the diene components **27**–**29** of the pheromone of the pink bollworm (*Pectinophora gossypiella*).[77,78]



(*a*) O_3–cyclo-C_6H_{12}–AcOH; (*b*) AcONa–AcOH–Ac_2O; (*c*) TsOH–MeOH; (*d*) DIBALH; (*e*) TsCl–Py; (*f*) Me_2CuLi; (*g*) HCl; (*h*)  ; (*i*) Zn–NaI; (*j*) Ac_2O–Py.

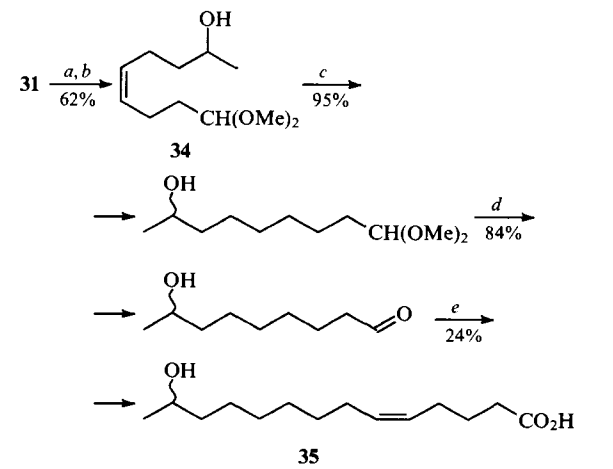
One of the approaches to the solution of the problem of the synthesis of pheromones with a terpenoid structure and a trisubstituted double bond involves the use as the starting compounds of regularly constructed oligomers, cooligomers, and telomers of isoprene, the methods of synthesis of which have now been thoroughly worked out, as well as natural terpenoids with trisubstituted double bonds. When this approach is employed, the task reduces to the choice of selective methods for the necessary transformation of the initial compound for the subsequent construction from the resulting functional block-synthon of the required carbon skeleton of the pheromone. The transformation of the initial cyclic isoprenoid into the α,ω-bifunctional synthon is achieved by opening its ring[79–81] and, in the case of an acyclic initial compound with a specified geometry of the double bond, a suitable method is chosen for its conversion into an intermediate which is suitable for subsequent employment in the formation of the target pheromone.[82–86]

A series of pheromones have been synthesised from 1-methyl-(1*Z*,5*Z*)-cyclooctadiene **30**. The partial ozonolysis of this isoprene—butadiene codimer proceeds selectively via the trisubstituted double bond, which makes it possible to obtain (*Z*)-alk-1-enyl acetates—the pheromones of the order Lepidoptera.[87,88] (*Z*)-Non-4-enyl bromide **32** was obtained by successive transformations of the functional groups of the ozonolysis products of compound **31**. Compound **32** was converted into the corresponding Grignard reagent and the latter was subsequently coupled with the acetoxybromo-derivatives **33**.



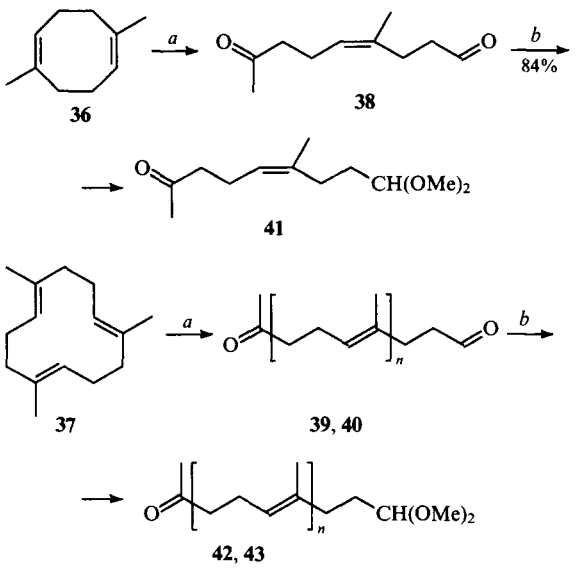
(*a*) O_3–cyclo-C_6H_{12}–MeOH; H_2–Pd–$CaCO_3$–PbO; (*b*) $KBH(OAc)_3$; (*c*) $TsNHNH_2$; (*d*) $NaBH_3CN$; (*e*) PBr_3–Py; (*f*) Mg; (*g*) $AcO(CH_2)_nBr$ (**33**).

After a two-stage reaction (selective protection of the aldehyde functional group and subsequent reduction of the keto-group to give the hydroxyacetal **34**), the ketoaldehyde **31** affords the key intermediate for the synthesis of (13*RS*)-hydroxy-(*Z*)-tetradec-5-enoic acid **35**—the acyclic precursor of the racemic form of the macrolide component of the aggregation pheromone of the flat grain beetle (*Cryptolestes pusillus*).[89]



(*a*) MeOH–NH_4Cl; (*b*) $NaBH_4$–MeOH; (*c*) H_2–Raney Ni; (*d*) PPTS–H_2O; (*e*) $HO_2C(CH_2)_4PPh_3Br$, $NaN(SiMe_3)_2$.

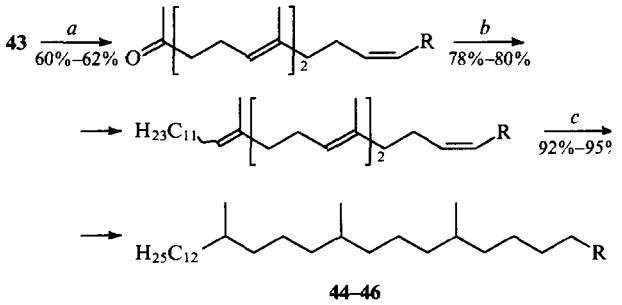
The most readily available cyclooligomers of isoprene are its (1*Z*,5*Z*)-dimer **36** and the (1*E*,5*E*,9*E*)-trimer **37**. The products of their selective ozonolysis have been used widely in the synthesis of pheromones.[59,60,79–81] The ozonolysis of (1*Z*,5*Z*)-1,5-dimethylcycloocta-1,5-diene **36** gives the monoterpene ketoaldehyde **38** with the (*Z*)-configuration, while ozonolysis of (1*E*,5*E*,9*E*)-1,5,9-trimethylcyclododeca-1,5,9-triene **37** affords the ketoaldehydes **39** and **40** with the (*E*)-configuration. The easily achieved selective protection of the aldehyde group in the ketoaldehydes **38**–**40** led to the corresponding monoacetals **41**–**43**, from which the target pheromones were synthesised.



n = 1 (**39**, **42**), 2 (**40**, **43**)

(*a*) O_3–cyclo-C_6H_{12}–MeOH, H_2–Pd–$CaCO_3$–PbO; (*b*) MeOH–NH_4Cl.

The subsequent conversion of compound **43** into an alkene via the aldehyde group and then the keto-group and subsequent hydrogenation led to the diastereoisomeric (±)-13,17,21-trimethyltriacontane and its homologues **44**–**46**.[90,91]

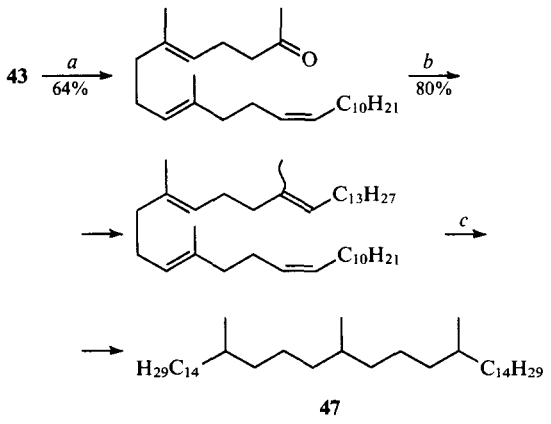


R = n-C_8H_{17} (**44**), n-$C_{10}H_{21}$ (**45**), n-$C_{12}H_{25}$ (**46**)

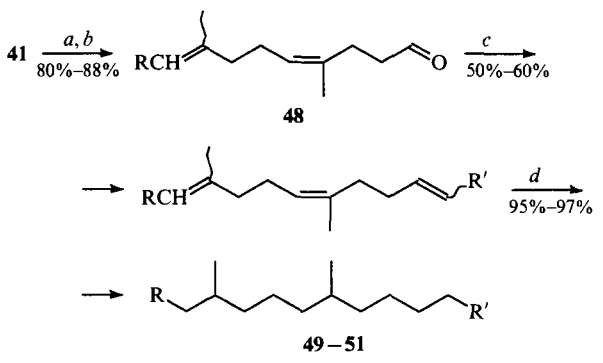
(*a*) RCH=PPh_3; (*b*) n-$C_{11}H_{23}CH$=PPh_3; (*c*) H_2–Pd/C.

A similar approach has been used in the synthesis of 15,19,23-trimethylheptatriacontane **47** — a component of the pheromone of the tsetse fly (*Glossina morsitans morsitans*).[92]

The carbon skeletons of the diastereoisomeric (±)-7,11-dimethyloctadecane **49**, (±)-15,19-dimethyltritriacontane **50**, and (±)-17,21-dimethylheptatriacontane **51** — the components of the egg-laying pheromones of the yellow-fever mosquito (*Aedes aegypti*), the stable fly (*Stomoxys calcitrans*), and the tsetse fly respectively, have been constructed by the introduction of double bonds into the unsaturated ketoacetal **41** with the (*Z*)-configuration via the keto-group and then the aldehyde-group (in compound **48**).[93–95]



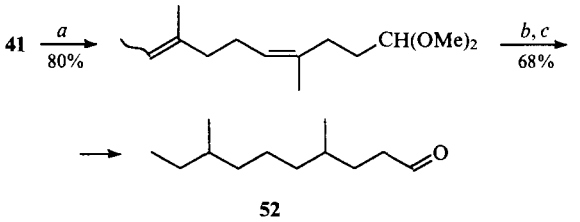
(*a*) n-$C_{10}H_{21}CH$=PPh_3; (*b*) n-$C_{13}H_{27}CH$=PPh_3; (*c*) H_2–Pd/C.



49: R = n-C_5H_{11}, R′ = n-C_3H_7;
50: R = n-$C_{13}H_{27}$, R′ = n-$C_{10}H_{21}$;
51: R = n-$C_{15}H_{31}$, R′ = n-$C_{12}H_{25}$.

(*a*) RCH=PPh_3; (*b*) H_3O^+; (*c*) R′CH=PPh_3; (*d*) H_2–Pd/C.

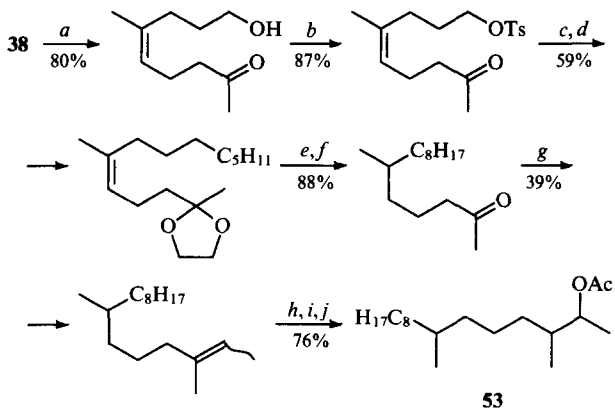
4,8-Dimethyldecanal **52** — the aggregation pheromone of the flour beetles (*Tribolium confusum* and *Tribolium castaneum*) — has been conveniently synthesised from the ketoacetal **41** by increasing its carbon chain length by two atoms via the keto-group with subsequent hydrogenation and hydrolysis.[96]



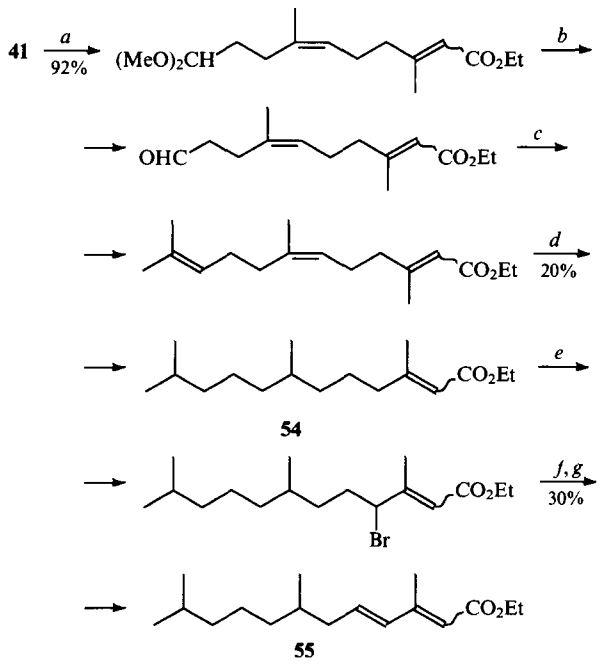
(*a*) MeCH=PPh_3; (*b*) H_2–Pd/C; (*c*) H_3O^+.

By use of the difference between the reactivities of the carbonyl groups of the ketoaldehyde **38**, it proved possible to achieve selective transformations leading to the racemic 3,7-dimethylpentadec-2-yl acetate **53** — the sex pheromone of the pine sawflies of the genera *Diprion* and *Neodiprion*.[97]

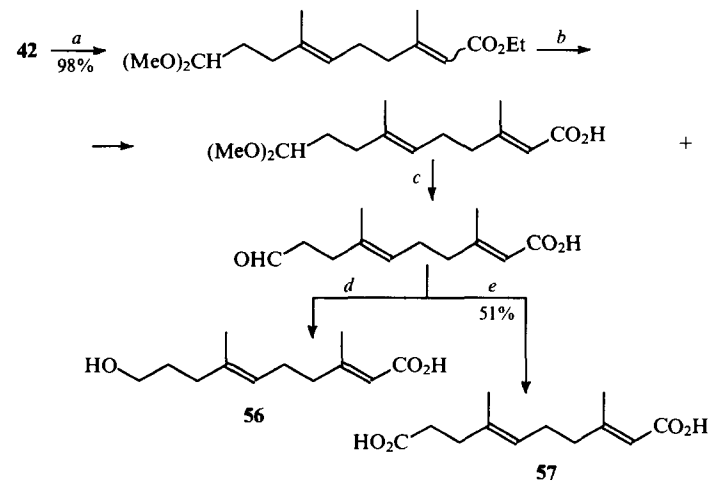
The synthesis of the ethyl ester of (2*E*,4*E*)-3,7,11-trimethyldodeca-2,4-dienoic acid (hydroprene) **55**, which has found extensive application as a juvenoid, is based on selective transformations of the unsaturated ketoacetal **41**, involving ethoxycarbonylmethylenation of the keto-group, conversion of the formyl group into an alkene by treatment with isopropylidenetriphenylphosphorane, ionic hydrogenation to the α,β-unsaturated ester **54**, and then transformation (via allylic bromination–dehydrobromination) into the target hydroprene.[98]



(*a*) $NaBH(OAc)_3$; (*b*) TsCl–Py; (*c*) $(CH_2OH)_2$–TsOH; (*d*) n-$C_5H_{11}MgBr$–Li_2CuCl_4; (*e*) H_2–Pd/C; (*f*) H_3O^+; (*g*) $MeCH{=}PPh_3$; (*h*) B_2H_6; (*i*) H_2O_2–NaOH; (*j*) Ac_2O–Py.



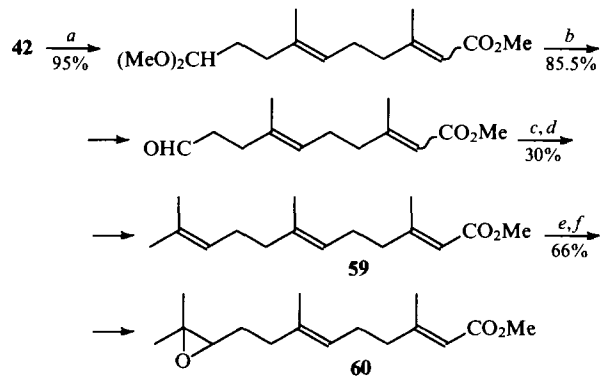
(*a*) $Me_3SiCH_2CO_2Et$–LDA ($LiNPr^i_2$); (*b*) PPTS–H_2O; (*c*) $Me_2C{=}PPh_3$; (*d*) Et_3SiH–CF_3CO_2H; (*e*) NBS (*N*-bromosuccinimide)–$(PhCO_2)_2$; (*f*) Li_2CO_3–LiBr; (*g*) HPLC.



(*a*) $Me_3SiCH_2CO_2Et$–LDA; (*b*) Pr^iONa–Pr^iOH; (*c*) H_3O^+; (*d*) $NaBH_4$; (*e*) H_2CrO_4; (*f*) $LiAl(OBu^i)H_2$.

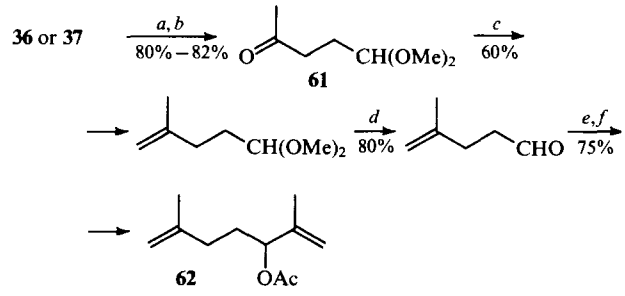
The ketoacetal **42** proved to be a convenient starting compound in the stereospecific synthesis of (2*E*,6*E*)-3,7-dimethyldeca-10-hydroxy-2,6-dienoic acid **56** and (2*E*,6*E*)-3,7-dimethyldeca-2,6-diene-1,10-dioic acid **57**, as well as the diol **58** — the terpenoid components of the pheromone of the danaid butterflies (*Danaus plexippus* and *Danaus chrysippus*) (Scheme 1).[99]

The racemic juvenile hormone YuG-III **60** has been synthesised stereospecifically from the ketoacetal **42** by means of its successive Petersen methoxycarbonylmethylenation, hydrolysis, coupling of the resulting aldehyde to isopropylidene-triphenylphosphorane, and the selective epoxidation of the intermediate triene ester **59** at the terminal double bond.[100]



(*a*) $Me_3SiCH_2CO_2Et$–LDA; (*b*) PPTS–H_2O; (*c*) $Me_2C{=}PPh_3$; (*d*) SiO_2–$AgNO_3$; (*e*) NBS; (*f*) K_2CO_3.

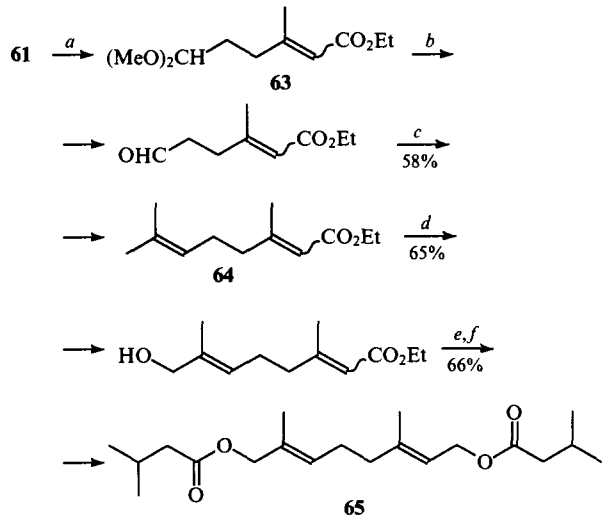
1,1-Dimethoxy-4-oxopentane **61**, obtained by the exhaustive ozonolysis of the isoprene oligomers **36** and **37** and the selective formation of acetal groups, has been used in the synthesis of 2,6-dimethylhepta-1,6-diene-3-yl acetate **62** — the attractant of the Comstock mealybug (*Pseudococcus comstoki*).[101]



(*a*) O_3–cyclo-C_6H_{12}–MeOH, H_2–Pd/$CaCO_3$–PbO; (*b*) MeOH–NH_4Cl; (*c*) $CH_2{=}PPh_3$; (*d*) H_3O^+; (*e*) $H_2C{=}C(Me)MgBr$; (*f*) AcCl.

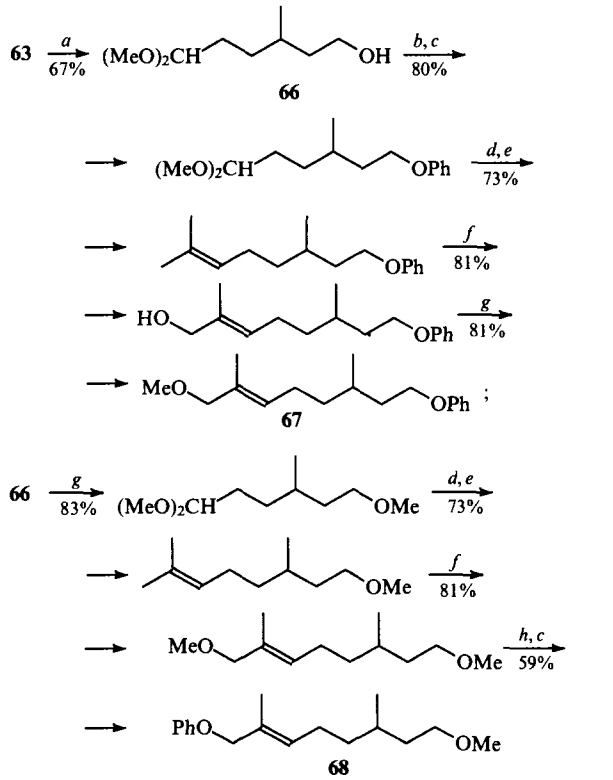
Scheme 1

(2*E*,6*E*)-2,6-Dimethylocta-2,6-diene-1,8-diyl diisovalerate **65**—the sex pheromone of the Crimean click beetle (*Agriotes tauricus*)—has been synthesised from the dimethyl acetal of levulinic aldehyde **61**.[102] The synthesis includes, among others, stages involving the epoxycarbonylmethylenation of the product and the introduction of double bonds into the latter to give the α,β-unsaturated ester **64** and subsequent allylic oxidation with a mixture of *tert*-butyl hydroperoxide and selenium dioxide.



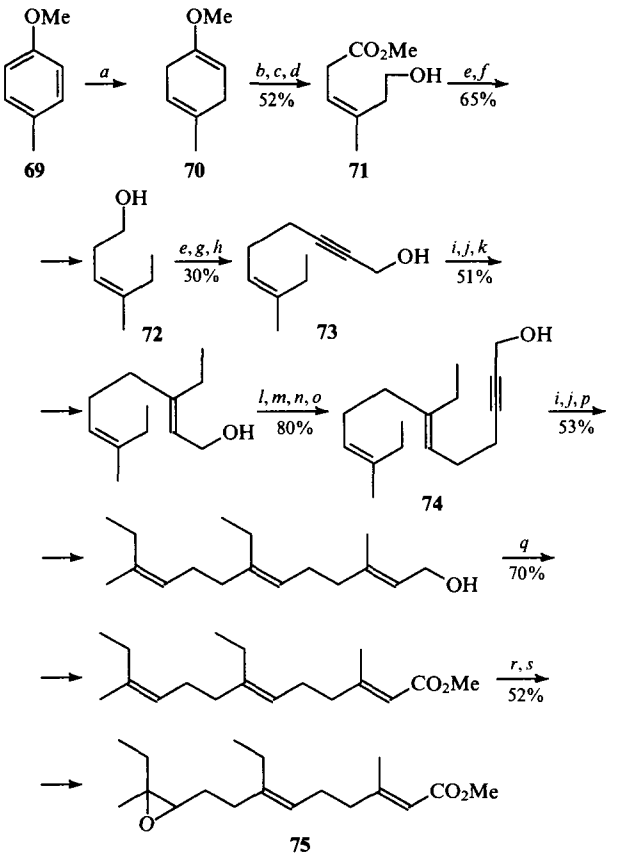
(*a*) $Me_3SiCH_2CO_2Et$–LDA; (*b*) H_3O^+; (*c*) $Me_2C{=}PPh_3$; (*d*) Bu^tOOH–SeO_2; (*e*) $LiAl(OBu^i)H_3$; (*f*) Me_2CHCH_2COCl–Et_3N.

The product of the Petersen ethoxycarbonylmethylenation of the ketoacetal **61**, namely the ester **63**, served as a convenient intermediate in the synthesis of (2*E*)-1-methoxy-8-phenoxy- and (2*E*)-1-phenoxy-8-methoxy-2,6-dimethyloct-2-enes **67** and **68**, which exhibit a juvenoid activity.[103]



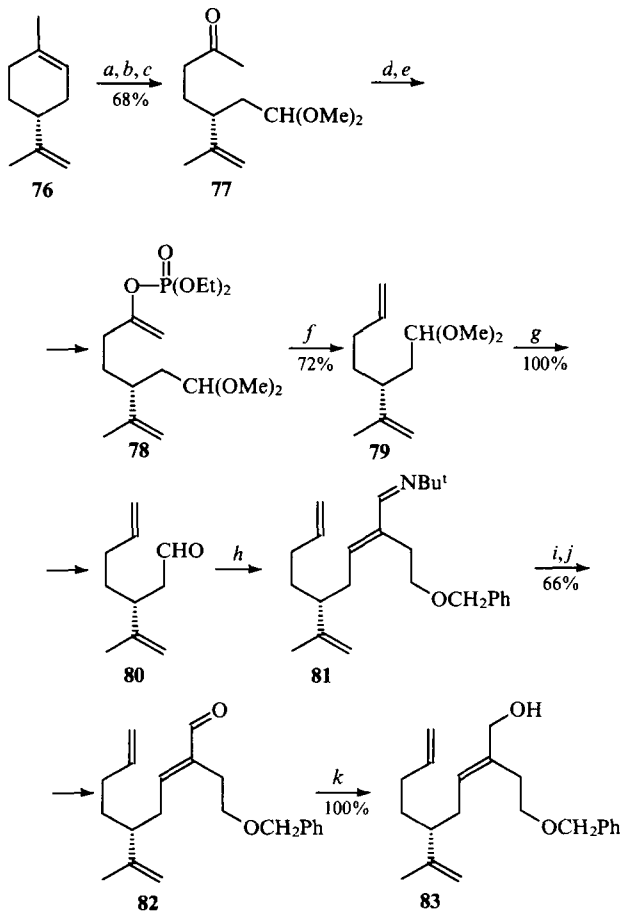
(*a*) Li–NH_3; (*b*) TsCl–Py; (*c*) PhONa; (*d*) PPTS–H_2O; (*e*) $Me_2C{=}PPh_3$; (*f*) Bu^tOOH–SeO_2; (*g*) NaH, MeI; (*h*) PBr_3–Py.

Ozonisation proved to be very effective in the conversion of the vinyl ether **70**—the readily available product of the Birch reduction of the methyl ether of *p*-cresol **69**—into the precursor for the synthesis of the juvenile hormone YuG-I **75**—the alcohol **72**.[104] The selectivity of the ozonolysis of compound **70** to give compound **71** is due to the significantly higher reactivity of the methoxy-substituted double bond. The illustrated sequence of stages in the conversion of compound **70** into compound **72** ensured automatically the required (*Z*)-configuration of the terminal unit of the chain of the juvenile hormone **75**. The transition from the C_7 block **72** to the target compound **75** is achieved by increasing the length of the carbon chain by means of the regio- and stereo-selective alkylation of the propargyl alcohols **73** and **74** via the corresponding vinyl iodides.

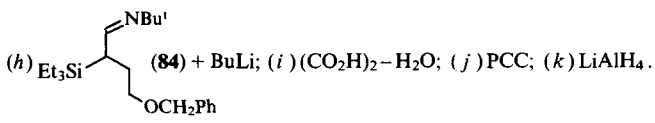


(*a*) Li–NH_3–$EtCMe_2OH$–THF; (*b*) O_3–MeOH; (*c*) Me_2S; (*d*) $NaBH_4$; (*e*) TsCl–Py; (*f*) $LiAlH_4$; (*g*) $LiC{\equiv}CCH_2OTHP$ (THP = tetrahydropyran-2-yl); (*h*) HCl; (*i*) $LiAlH_4$–NaOMe; (*j*) I_2; (*k*) Et_2CuLi; (*l*) PBr_3; (*m*) $LiCH_2C{\equiv}CSiMe_3$; (*n*) Ag^+, CN^-; (*o*) BuLi, CH_2O; (*p*) Me_2CuLi; (*q*) MnO_2, NaCN–MeOH; (*r*) HOBr; (*s*) Pr^iONa.

Limonene proved to be a convenient starting material for the synthesis of pheromones containing a chiral centre. (6*R*)-3-methyl-6-(2-propenyl)deca-3,9-dien-1-yl acetate (*R*)-**88**—the sex pheromone of the California red scale (*Aonidiella aurantii*)—has been synthesised from (*R*)-limonene **76**.[105] This was possible as a result of partial ozonolysis of limonene **76**, which takes place selectively and involves the endocyclic double bond. This gave ketoaldehyde **77**, in which the aldehyde group was protected selectively. The enolisation of the ketone **77** by a strong base and the fixation of the enolic form as the diethyl phosphate **78** followed by treatment with lithium in ammonia gave the diene acetal **79**. The deblocking and Petersen condensation of the aldehyde **80** with the silane **84** led to the imine **81**, from which the allyl alcohol **83** was obtained by successive hydrolysis and reduction.

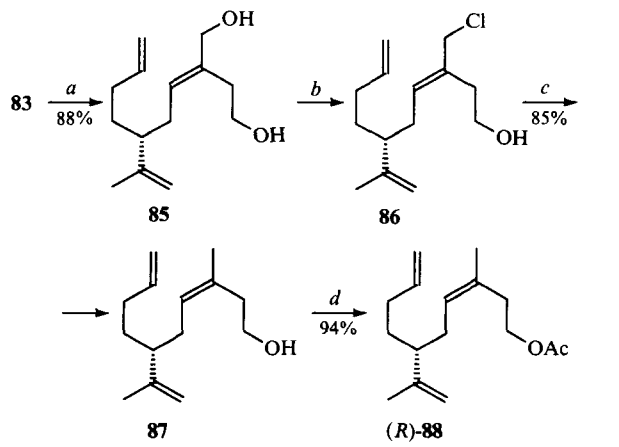


(*a*) O_3–MeOH; (*b*) $(H_2N)_2CS$; (*c*) $HC(OMe)_3$–$CeCl_3 \cdot 6H_2O$; (*d*) LDA; (*e*) $ClPO(OEt)_2$; (*f*) Li–NH_3; (*g*) $HClO_4$–H_2O–THF;



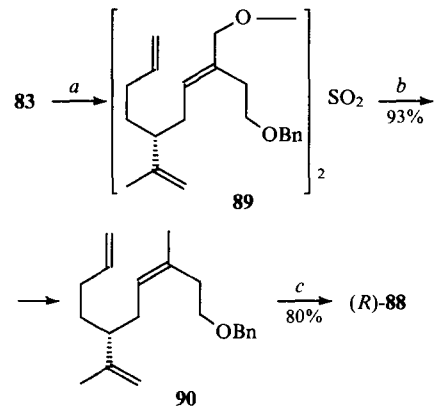
(*h*) **(84)** + BuLi; (*i*) $(CO_2H)_2$–H_2O; (*j*) PCC; (*k*) $LiAlH_4$.

The alcohol **83** was transformed into the target pheromone (*R*)-**88** in two ways. The first involved the removal of the benzyl protecting group under mild conditions (the conditions of the Birch reaction) and the subsequent substitution of the allylic OH group of the resulting diol **85** by chlorine. The hydrogenolysis of the chlorohydrin **86** afforded the pheromone precursor **87**, the acetylation of which completed the synthesis.



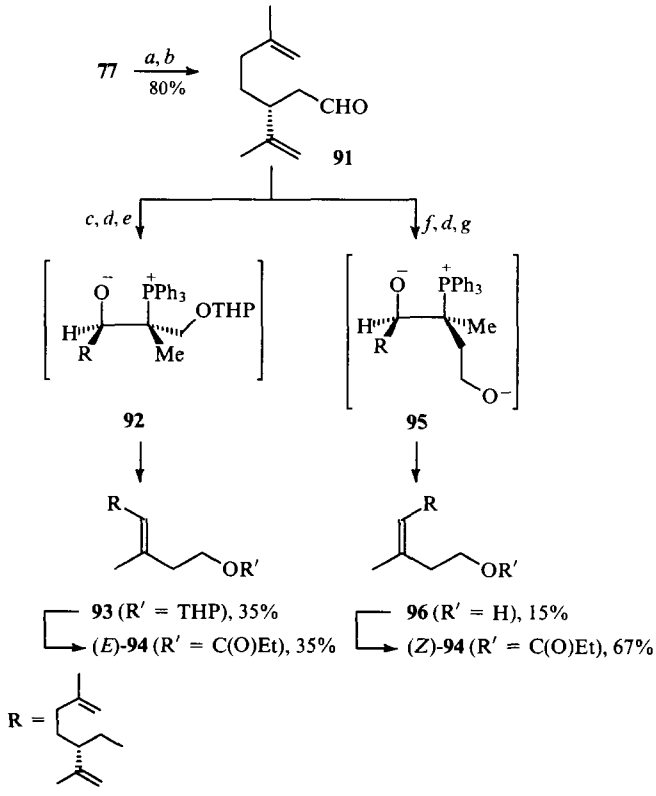
(*a*) Li–NH_3; (*b*) NCS (*N*-chlorosuccinimide)–Me_2S; (*c*) $LiAlH_4$; (*d*) Ac_2O–Py.

The alternative procedure for the transformation of compound **83** into the acetate **88** included the stage in which the sulfate **89** was formed and was subsequently reduced to the benzyl ether **90** and the benzyl group in the latter was replaced by the acetate group.



(*a*) SO_3–Py; (*b*) $LiAlH_4$; (*c*) Ac_2O–$HClO_4$.

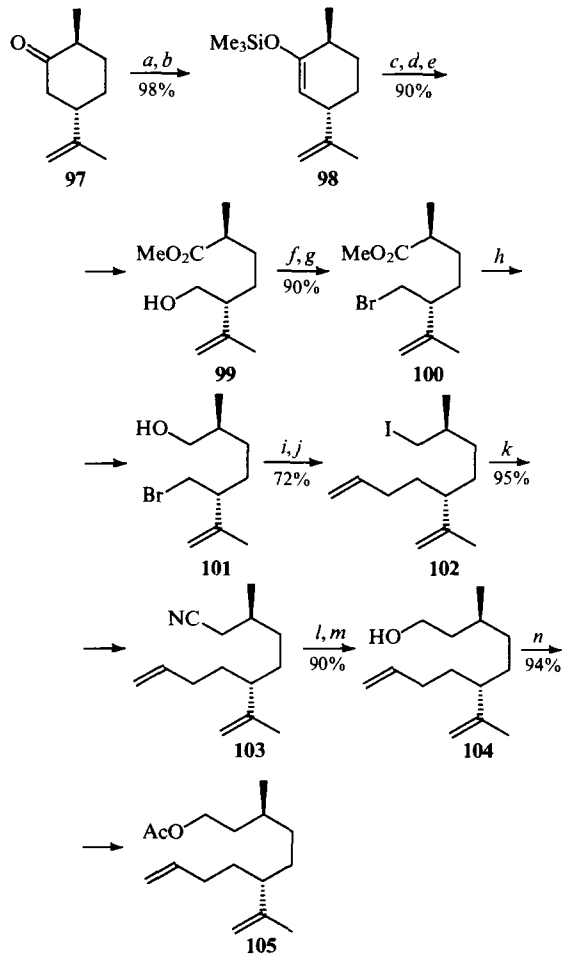
The optically active bifunctional reagent **77** has been used successfully in the stereospecific synthesis of the (*E*)- and (*Z*)-stereoisomers of (6*R*)-3,9-dimethyl-6-(2-propenyl)deca-3,9-dien-1-yl propionate **94** — the components of the sex pheromone of the white peach scale (*Pseudaulacaspis pentagona*).[106] In the synthesis of the pheromone component having the (*E*)-configuration (*E*)-**94**, the product of the methylenation of the ketoacetal **77** and subsequent hydrolysis (the dienal **91**) was converted by means of a modified Wittig reaction via the intermediate betaine **92** into the trisubstituted alkene pheromone precursor **93** (*E* ⩾ 97%). The deprotonation of the betaine **95**, generated from ethylidenetriphenylphosphorane and the chiral



(*a*) $CH_2{=}PPh_3$; (*b*) H_3O^+; (*c*) $THPO(CH_2)_2CH{=}PPh_3$; (*d*) BuLi; (*e*) MeI; (*f*) $MeCH{=}PPh_3$; (*g*)  ; (*h*) EtCOCl–Et_3N.

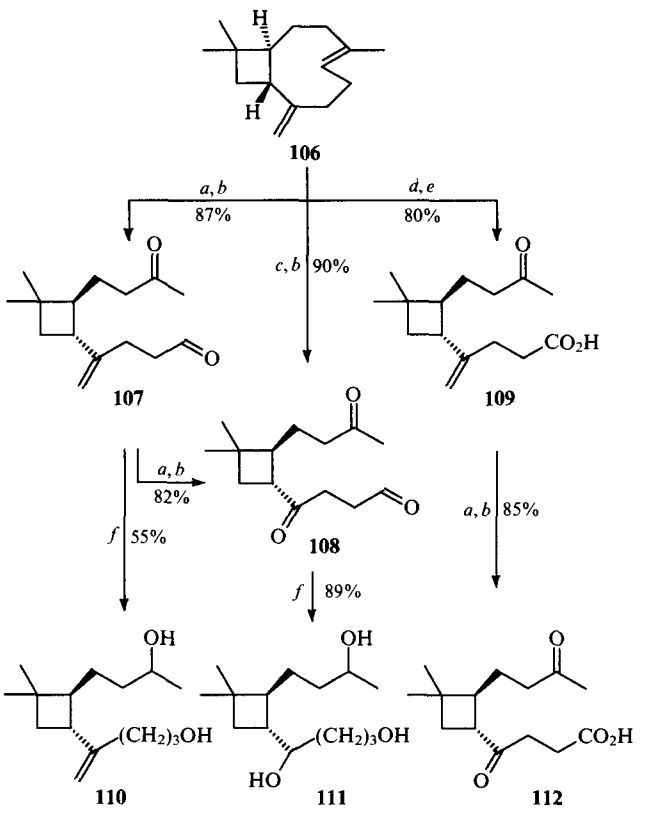
aldehyde **91**, and treatment of the resulting anion with epoxyethane led to the (*Z*)-homoallyl alcohol **96**, which was converted into the target pheromone component with the (*Z*)-configuration (*Z*)-**94**, in which the content of the principal stereoisomer was ⩾98%.

Dihydrocarvone **97** proved convenient for the synthesis of (3*S*,6*R*)-3-methyl-6-(2-propenyl)dec-9-en-1-yl acetate **105** — the sex pheromone of the California red scale (*Aonidiella aurantii*).[107] In order to open the ring in the cyclic ketone **97**, the latter was converted into the silyl enol ether **98**, the ozonolysis of which afforded the hydroxyester **99**. The iodo-derivative **102** was obtained via the bromoester **100** and bromohydrin **101** stages by coupling with allylmagnesium chloride and by the replacement of the alcoholic functional group by the halogen. Conversion into a higher homologue (by reaction with cyanide) and transformation of the functional group led to the target pheromone **105**.



(*a*) LDA; (*b*) Me_3SiCl; (*c*) O_3–MeOH–CH_2Cl_2; (*d*) $NaBH_4$; (*e*) CH_2N_2; (*f*) MsCl–Py; (*g*) Bu_4NBr; (*h*) DIBALH; (*i*) $H_2C{=}CHCH_2MgCl$–CuI; (*j*) $I_2 \cdot PPh_3$; (*k*) NaCN; (*l*) NaOH; (*m*) $LiAlH_4$; (*n*) Ac_2O–Py.

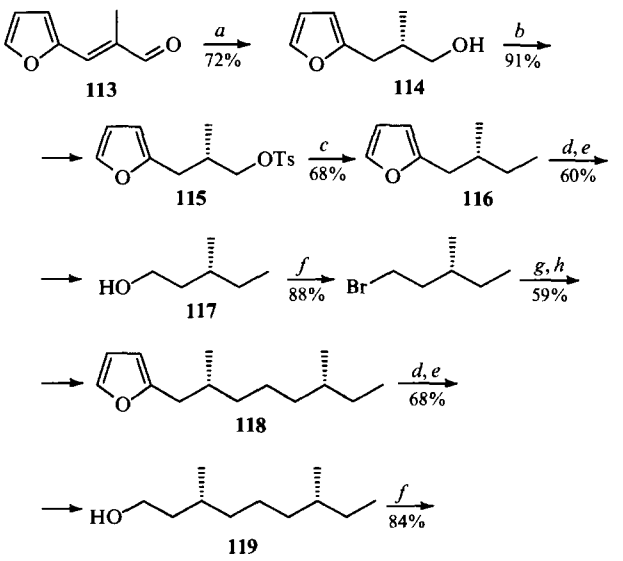
It has been established[108] that the ozonolysis of caryophyllene **106** takes place preferentially at the endocyclic double bond. On treatment with an equimolar amount of ozone and subsequent reduction of the peroxide ozonolysis products, the dicarbonyl derivative **107** was obtained, whereas exhaustive ozonolysis leads to the tricarbonylcyclobutane derivative **108**. The reduction of the keto- and diketoaldehydes **107** and **108** with sodium tetrahydroborate affords the di- and tri-hydroxy-*trans*-alkylcyclobutanes **110** and **111** respectively. The hydrolytic cleavage of the peroxide products of the partial ozonolysis of caryophyllene leads to the ketoacid **109**, the subsequent ozonolysis of which leads to the carboxylic deketoacid **112**.

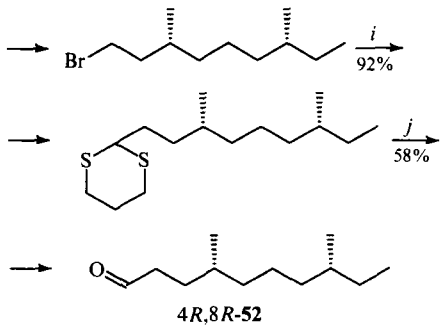


(*a*) O_3–MeOH; (*b*) H_2–Pd–$CaCO_3$–PbO; (*c*) excess O_3–MeOH; (*d*) O_3–cyclo-C_6H_{12}–AcOH; (*e*) AcONa–AcOH–Ac_2O; (*f*) $NaBH_4$.

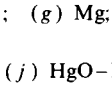
Laboratory biological tests on the cyclobutane derivatives synthesised demonstrated the likely usefulness of the search for analogues of juvenile hormones among compounds of this series.

The natural aggregation pheromone of the confused and red flour beetles (*Tribolium confusum* and *Tribolium castaneum*), namely (4*R*,8*R*)-4,8-dimethyldecanal **52**, has been synthesised from 3-(2-furyl)-2-methylacrolein **113** by means of enzymic reduction.[109] The optical purity of the resulting alcohol **114** was ⩾99%. Other key stages of this synthesis employed the ozonolysis of the 2-substituted furans **116** and **118** (obtained by alkylating the tosylate **115**), which led to the optically active alcohols **117** and **119** respectively.

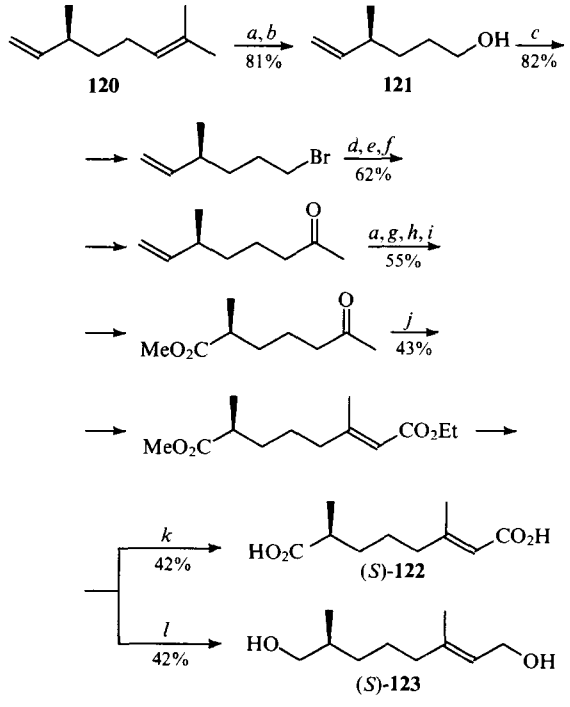




4*R*,8*R*-**52**

(*a*) baker's yeast; (*b*) TsCl–Py; (*c*) MeMgI–Li_2CuCl_4; (*d*) O_3; (*e*) $LiAlH_4$; (*f*) NBS–PPh_3; (*g*) Mg; (*h*) **115**–Li_2CuCl_4; (*i*)  –BuLi; (*j*) HgO–$BF_3 \cdot OEt_2$.

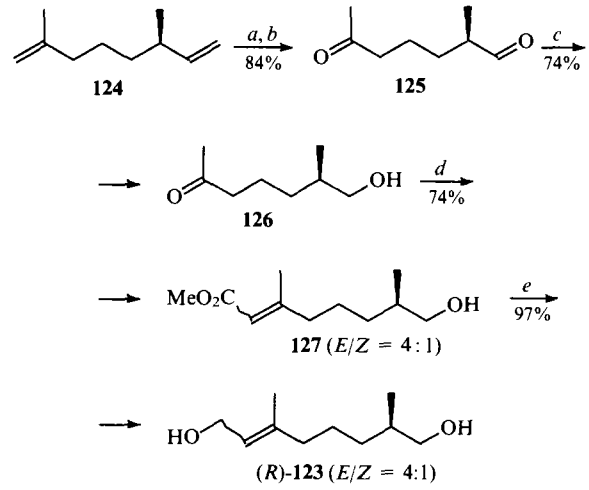
The enantiomerically enriched alcohol **121** has been synthesised from (*S*)-(+)-dihydromyrcene **120** by means of ozonolysis, which involves preferentially the trisubstituted double bond. The alcohol **121** was subjected to selective transformations leading to the unsaturated dicarboxylic acid **122** and the diol **123**—the pheromone components of the Chinese bean weevil (*Callosobruchus chinesis*) and the monarch butterfly respectively.[110]



120 **121** (*S*)-**122** (*S*)-**123**

(*a*) O_3–$NaHCO_3$–CH_2Cl_2–MeOH; (*b*) $NaBH_4$; (*c*) PBr_3–Py; (*d*) Mg; (*e*) MeCHO; (*f*) PCC; (*g*) H_2–Pd–$CaCO_3$–PbO; (*h*) Ag_2O; (*i*) CH_2N_2; (*j*) $(MeO)_2P(O)CH_2CO_2Et$–EtONa; (*k*) NaOH; (*l*) DIBALH.

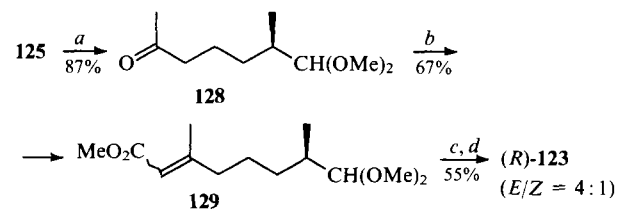
The initial chiral structural block in the syntheses of the (*R*)- and (*S*)-enantiomers of (2*E*)-3,7-dimethyloct-2-ene-1,8-diol **123** (the product secreted by the monarch butterfly) and (2*E*)-3,7-dimethyloct-2-ene-1,8-dicarboxylic acid **122** (the sex pheromone of *Callosobruchus chinesis*) is 2,6-dimethyloctadiene **124** (regioisomeric with respect to dihydromyrcene **120**) with the corresponding (*R*)- or (*S*)-configuration.[111] The schemes presented here indicate the transformations of the (*R*)-enantiomers of the diene **124**, the ozonolysis of which led to the chiral ketoaldehyde **125**. The carbonyl groups in the latter were differentiated (for the subsequent selective conversion into alkene groups) in two ways: by the selective hydride reduction of the aldehyde group, yielding the hydroxyketone **126**, or by blocking the aldehyde group, which leads to the ketoacetal **128**. The involvement of the hydroxyketone **126** in the Wittig–Horner reaction with trimethyl phosphonoacetate gave a mixture of the geometrical isomers of the hydroxyester **127** with respect to the Δ^2-double bond; reduction with lithium tetrahydroaluminate led to the corresponding mixture of the (*E*)- and (*Z*)-diols (*R*)-**123**.



124 **125** **126** **127** (*E*/*Z* = 4:1) (*R*)-**123** (*E*/*Z* = 4:1)

(*a*) O_3; (*b*) Me_2S; (*c*) $NaBH_4$; (*d*) $(MeO)_2P(O)CH_2CO_2Et$–NaH; (*e*) $LiAlH_4$.

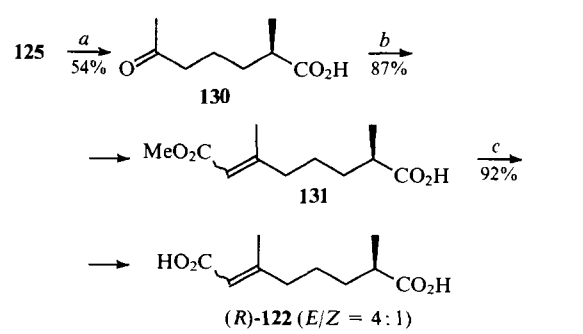
The transformation of the ketoacetal **128** into the diol (*R*)-**123** involved the Wittig–Horner reaction, which led to a mixture of the (*E*)- and (*Z*)-isomeric esters **129**. The deblocking of the aldehyde group and subsequent hydride reduction afforded a mixture of the (*E*)- and (*Z*)-isomers of the diol (*R*)-**123**.



128 **129**

(*a*) MeOH–TsOH; (*b*) $(MeO)_2P(O)CH_2CO_2Me$–NaH; (*c*) HCO_2H–H_2O; (*d*) $LiAlH_4$.

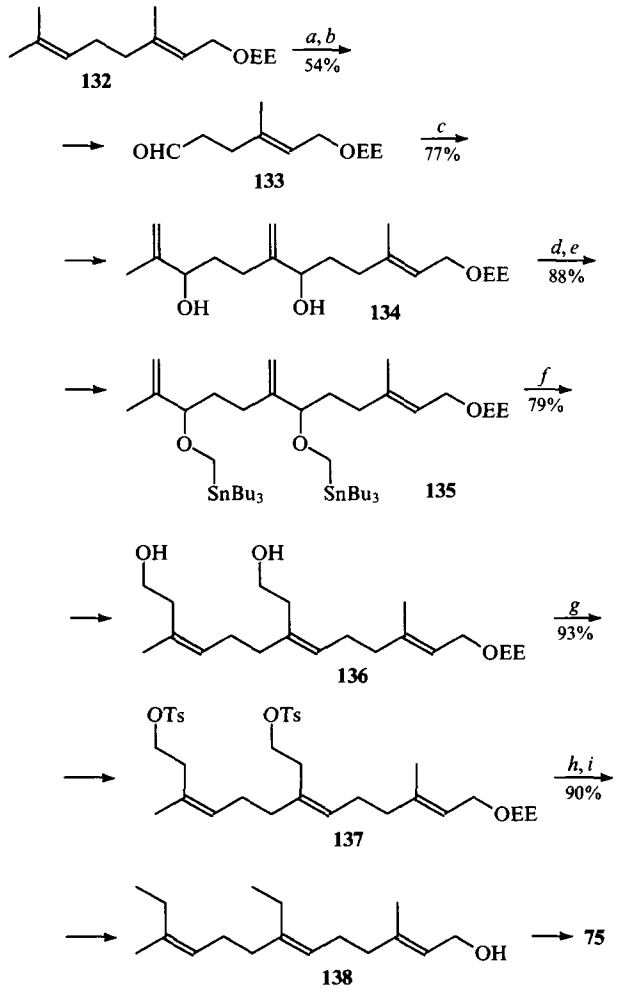
The synthesis of (*Z*,*E*)-(7*R*)-3,7-dimethyloct-2-ene-1,8-dioic acid (*R*)-**122** involves the oxidation of the aldehyde group in the ketoaldehyde **125** and the Wittig–Horner coupling of the ketoacid **130** with trimethyl phosphonoacetate, which leads to the monoester **131** in the form of a mixture of the (*E*)- and (*Z*)-isomers.[111]

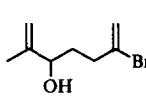


130 **131** (*R*)-**122** (*E*/*Z* = 4:1)

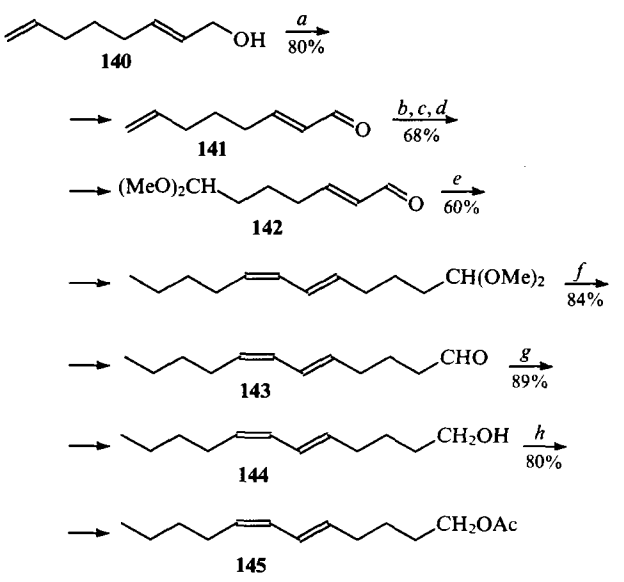
(*a*) $AgNO_3$–EtOH–H_2O; (*b*) $(MeO)_2P(O)CH_2CO_2Et$–NaH; (*c*) NaOH.

A highly stereoselective method of synthesis of bishomofarnesol **138** — an intermediate in the synthesis of the juvenile hormone YuG-1 **75** — has been achieved by means of the partial ozonolysis of the ethoxyethyl (EE) derivative of geraniol **132** at the isopropylidene group. The interaction of the resulting aldehyde **133** with the dianion derived from the diene bromohydrin **139** yields the monosubstituted trisallyl alcohol **134**; its distannyl derivative **135** is converted by means of a 2,3-sigmatropic rearrangement with high (*E*)-stereoselectivity into the bishomoallyl alcohol **136** and further, via the corresponding ditosylate **137**, into the target trienol **138**.[112]



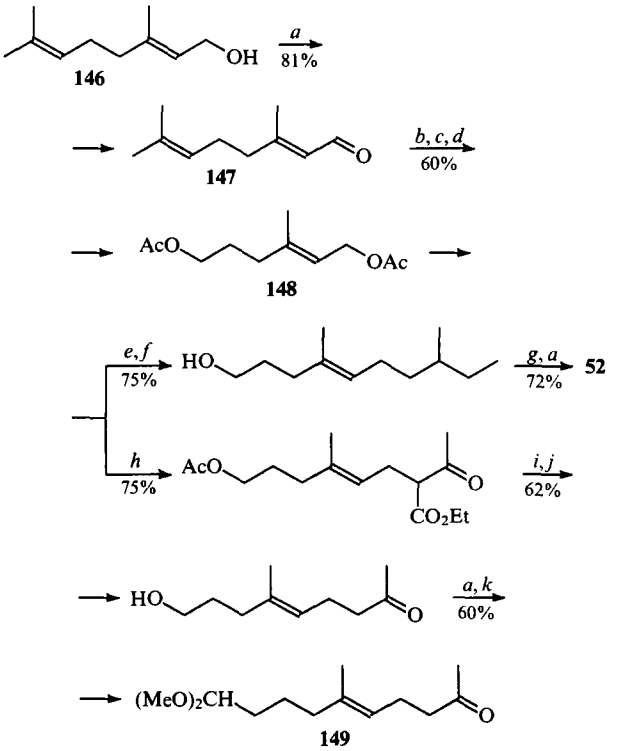
(*a*) O_3–CH_2Cl_2–Py; (*b*) Zn; (*c*)  Br (**139**) + BuLi;
(*d*) KH; (*e*) Bu_3SnCH_2I; (*f*) BuLi; (*g*) TsCl–Py; (*h*) $LiAlH_4$; (*i*) AcOH–H_2O.

An isolated double bond is known to have a reactivity an order of magnitude higher towards ozone than a double bond conjugated with the aldehyde group. This enabled us to expand the possibilities, discovered previously,[113] for the preparative application of the partial ozonolysis of acyclic polyenes as a method of synthesis of bifunctional unsaturated compounds. It was established[114] that (2*E*)-2,7-octadienal **141**, which can be readily obtained from the telomer **140** of butadiene and water, is converted into (2*E*)-7,7-dimethoxyhept-2-enal **142** in a satisfactory yield on interaction with ozone. The target compounds — (5*E*, 7*Z*)-5,7-dodecadienal **143** and the corresponding alcohol **144** and acetate **145** [the components of the sex pheromone of the lackey moth (*Malacosoma neustria* L.)] — were synthesised from compound **142**.



(*a*) PCC; (*b*) O_3–cyclo-C_6H_{12}–MeOH; (*c*) Me_2S; (*d*) MeOH–NH_4Cl; (*e*) $HO_2C(CH_2)_4PPh_3Br$, $NaN(SiMe_3)_2$; (*f*) H_2SO_4–MeOH; (*g*) $LiAlH_4$; (*h*) AcCl–Py.

(2*E*)-1,6-Diacetoxy-3-methylhex-2-ene **148** has been obtained by the partial ozonolysis of (2*E*)-3,7-dimethylocta-2,6-dienal **147** (the product of the oxidation of geraniol **146**) at the isopropylidene group. The aggregation pheromone **52** of the confused and red flour beetles and (4*E*)-1,1-dimethoxy-4-methylnon-4-en-8-one **149** — the intermediate for the synthesis of the components of the sex pheromone of the danaid butterflies (*Danaus plexippus* and *Danaus chrysippus*) — were synthesised from compound **148**.[114]

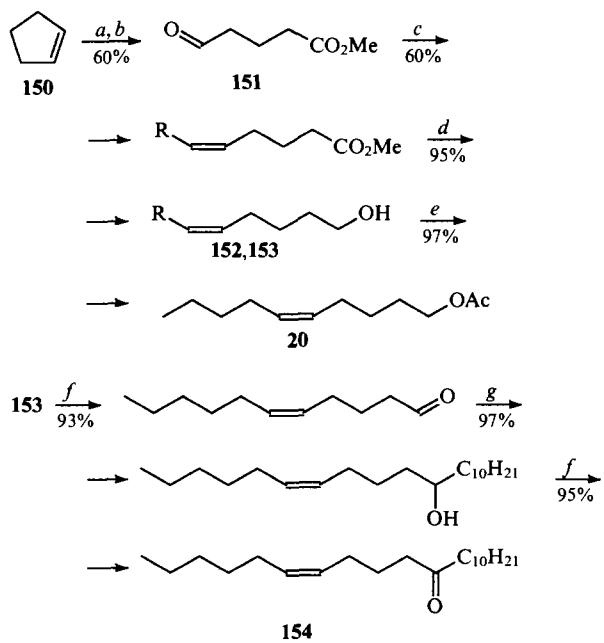


(*a*) PCC; (*b*) O_3–cyclo-C_6H_{12}–MeOH; (*c*) $NaBH_4$; (*d*) Ac_2O–Py; (*e*) EtCH(Me)CH_2Br–Mg–CuI; (*f*) KOH–MeOH; (*g*) H_2–Pd/C; (*h*) $MeCOCH_2CO_2Et$–NaH–$Pd(OAc)_2$–PPh_3; (*i*) NaOH; (*j*) H_2SO_4; (*k*) MeOH–NH_4Cl.

The decisive stages in these syntheses were the catalytic cross-coupling reactions between the diacetate **148** and the corresponding organomagnesium and organosodium reagents, which take place regio- and stereo-specifically with respect to the allylic acetoxy-group.

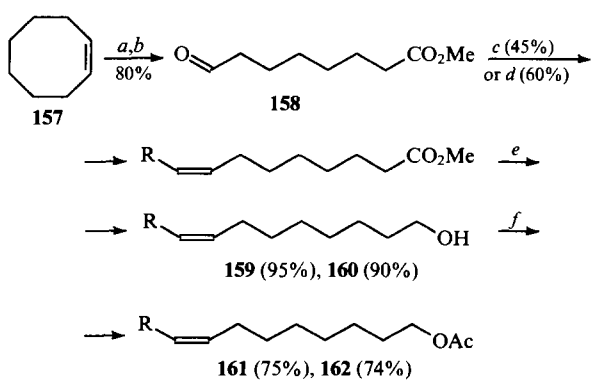
III. Synthesis of pheromones and juvenoids from the ozonolysis products of cyclic and acyclic alkenes

The ozonolysis of monoenes leads to saturated oxygen-containing compounds which are of interest for the synthesis of pheromones and juvenoids. Thus (5*Z*)-dec-5-enol **152** and (5*Z*)-undec-5-enol **153** have been synthesised from methyl 5-oxopentanoate **151** — the product of the functionally differentiated ozonolysis of cyclopentene **150**.[115] The acetate **20** of compound **151** is part of the composition of the pheromones of insects belonging to the genus *Agrotis*. (6*Z*)-Heneicos-6-en-11-one **154** — the sex pheromone of the tussock moth of the genus *Orgyia* which are pests on conifer forests — have been synthesised from compound **153**.



R = Bu (**152**, **155**), n-C_5H_{11} (**153**, **156**).

(*a*) O_3–$NaHCO_3$–CH_2Cl_2–MeOH; (*b*) Ac_2O–Et_3N; (*c*) RCH=PPh_3 (**155**, **156**); (*d*) DIBALH; (*e*) Ac_2O–Py; (*f*) PCC; (*g*) n-$C_{10}H_{21}MgBr$.

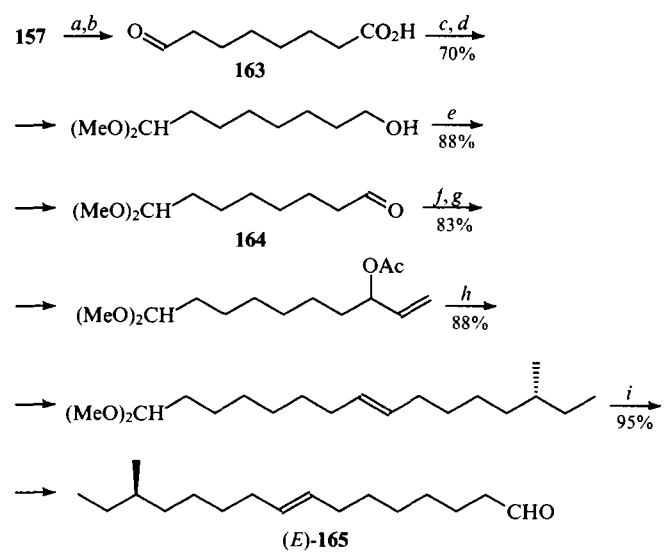


R = Pr (**159**, **161**), n-C_5H_{11} (**160**, **162**).

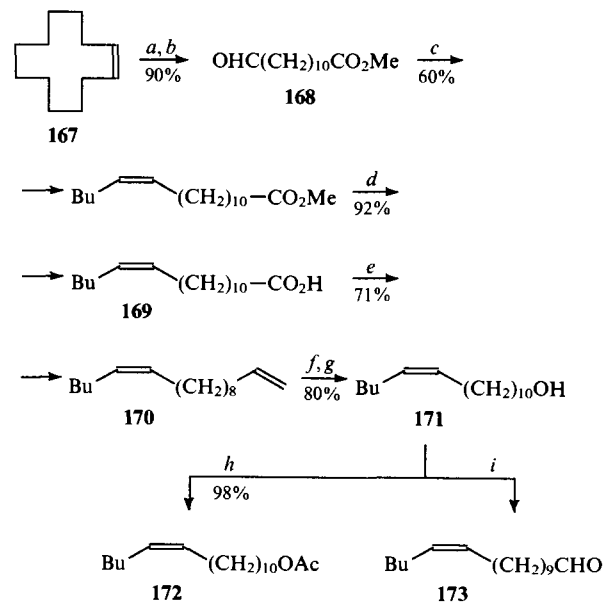
(*a*) O_3–$NaHCO_3$–CH_2Cl_2–MeOH; (*b*) Ac_2O–Py; (*c*) PrCH=PPh_3; (*d*) n-$C_5H_{11}CH$=PPh_3; (*e*) DIBALH; (*f*) Ac_2O–Py.

The ozonolysis of cyclooctane **157** under the conditions described by Odinokov et al.[115] led to a high yield of methyl 8-oxooctanoate **158**, which was used in the Wittig reaction with n-alkylidenetriphenylphosphoranes. This led to the discovery of a simple path to insect pheromones having the structure of (*Z*)-alk-8-enols **159** and **160** and their acetates **161** and **162**.[116]

In the synthesis of the optically active component (*E*)-**165** of the aggregation pheromone of the khapra beetle (*Trogoderma granarium*), the product of the ozonolysis of cyclooctene **157** and of the hydrolytic cleavage of the peroxide ozonolysis product — the aldehydoacid **163** — was converted in three stages into the monoacetal **164**, which reacted with the chiral bromo-derivative **166** obtained from dihydromyrcene **120**.[117]



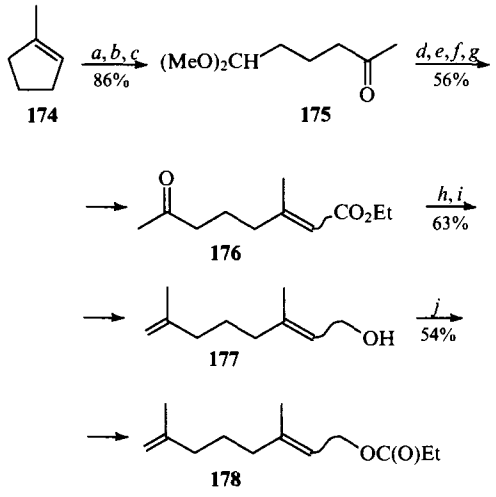
(*a*) O_3–cyclo-C_6H_{12}–AcOH; (*b*) AcONa–AcOH–Ac_2O; (*c*) TsOH–MeOH; (*d*) DIBALH; (*e*) PCC; (*f*) H_2C=CHMgBr; (*g*) Ac_2O; (*h*)  (**166**) + Mg + CuI; (*i*) PPTS–H_2O.



(*a*) O_3–$NaHCO_3$–CH_2Cl_2–MeOH; (*b*) Ac_2O–Et_3N; (*c*) BuCH=PPh_3; (*d*) KOH; (*e*) $Pb(OAc)_4$–$Cu(OAc)_2 \cdot H_2O$; (*f*) BBN {9-borabicyclo 3.3.1 nonane}; (*g*) H_2O_2–NaOH; (*h*) Ac_2O–Py; (*i*) PCC.

Methyl 12-oxododecanoate **168**, obtained by the ozonolysis of cyclododecene **167**, has been used to synthesise (11*Z*)-hexadec-11-en-1-ol **171**, its acetate **172**, and (11*Z*)-hexadec-11-enal **173** — the components of the sex pheromone of the noctuid moths belonging to the genera *Mamestra* and *Heliothis*. The key stages in this synthesis[118] are the Wittig conversion of the aldehyde **168** into an alkene, oxidative decarboxylation of the acid **169**, and selective hydroboration of the diene **170** at the terminal double bond.

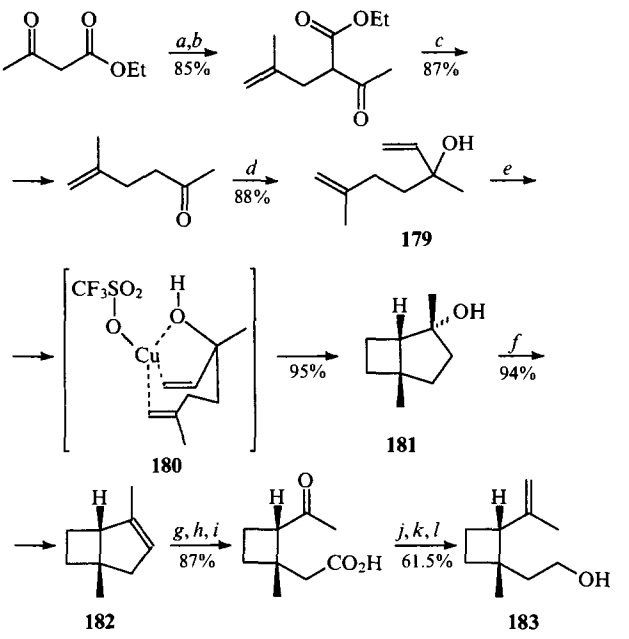
The ketoester **176** has been synthesised by the ozonolysis of 1-methylcyclopent-1-ene **174** and subsequent selective transformations of 1,1-dimethoxy-5-oxo-hexane **175**, including the conversion of the keto-group into an ethoxycarbonylalkene group and the alkylation of the formyl group by methylmagnesium iodide followed by oxidation. Compound **176** was converted in two stages into 3,7-dimethylocta-2,7-dien-1-ol **177** (isomer ratio $E/Z = 85 : 15$), the propionate **178** of which is a component of the sex pheromone of the San Jose scale *Quadraspidiotus perniciosus*.[119]



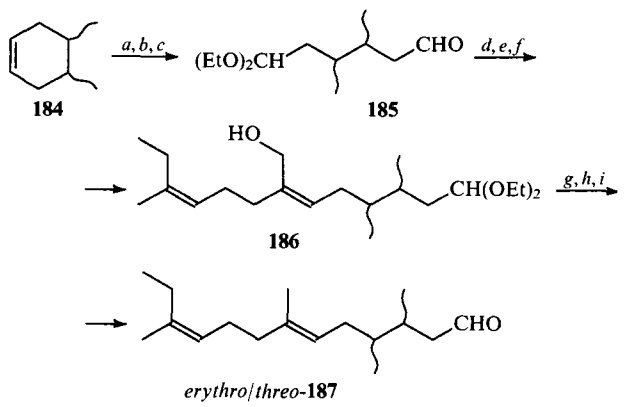
(*a*) O_3–MeOH; (*b*) H_2–Pd–$CaCO_3$–PbO; (*c*) MeOH–NH_4Cl; (*d*) $Me_3SiCH_2CO_2Et$–LDA; (*e*) PPTS–H_2O; (*f*) MeMgI; (*g*) PCC; (*h*) CH_2Br_2–$TiCl_4$–Zn; (*i*) $LiAl(OBu^t)H_3$; (*j*) EtCOCl–Et_3N.

Application of the copper-salt-catalysed 2π + 2π photocycloaddition reaction to terminal 1,6-dienes leads to photobicyclisation products, which has been used in the synthesis of grandisol **183** — the sex pheromone of the cotton-boll weevil (*Anthonomus grandis*).[120] It has been suggested[121] that, in the presence of copper trifluoromethanesulfonate, the dienol **179** gives rise to the tridentate complex **180**, which ensures the stereoselective formation of the bicyclic compound **181**. The latter is readily converted subsequently into the target pheromone **183** by ozonolysis of the product of its regioselective dehydration — the bicyclene **182**.

erythro-(3*S*,4*R*,6*E*,10*Z*)-3,4,7,11-Tetramethyltrideca-6,10-dienal (pharanal) **187** has been identified as the pheromone of the pharaoh ant (*Monomorium pharaonis L.*), which is a carrier of pathogenic bacteria. Several methods have been developed for the synthesis of racemic analogues of pharanal on the basis of the Wittig reaction. Thus 6,6-diethoxy-3,4-dimethylhexanol **185**, obtained by the ozonolysis of a mixture of the *cis*- and *trans*-isomers of dimethylcyclohexene **184**, was converted into an alkene by treatment with the phosphorane **188** and subsequent Cory hydroxymethylation of the intermediate; this led to the hydroxyacetal **186**, which was subsequently converted into the pheromone **187** as a mixture of the *erythro*- and *threo*-isomers.[122]



(*a*) EtONa; (*b*) $H_2C=C(Me)CH_2Cl$; (*c*) NaOH, Δ; (*d*) $H_2C=CHMgBr$; (*e*) *hν*, CuOTf; (*f*) HMPA (hexamethylphosphoramide); (*g*) O_3–AcOH; (*h*) Zn; (*i*) H_2CrO_4; (*j*) Me_3SiCH_2MgCl; (*k*) $SOCl_2$; (*l*) $LiAlH_4$.



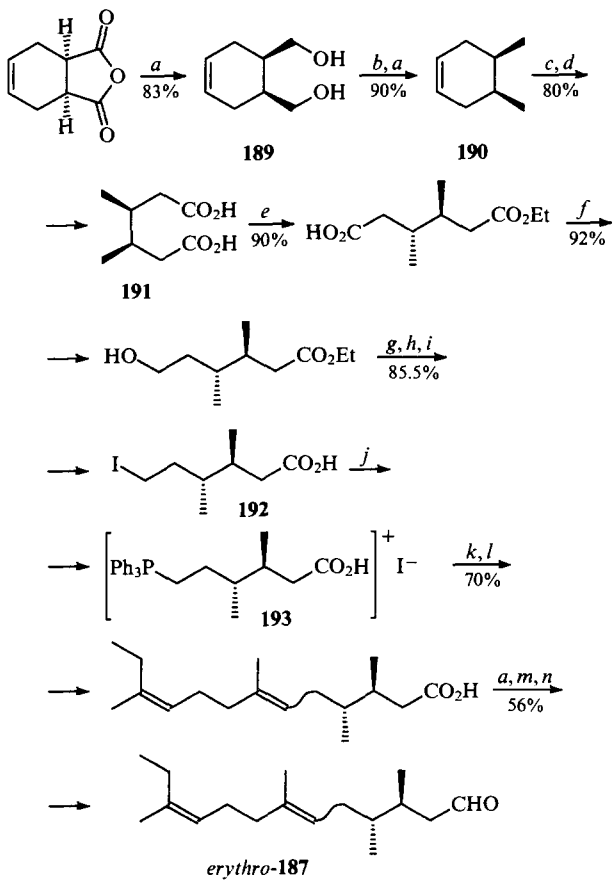
erythro/*threo*-**187**

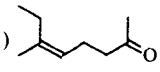
(*a*) O_3; (*b*) Me_2S; (*c*) $HC(OEt)_3$–HCl; (*d*) (**188**);

(*e*) *s*-BuLi; (*f*) $(CH_2O)_n$; (*g*) Py·SO_3; (*h*) $LiAlH_4$; (*i*) H_2SO_4.

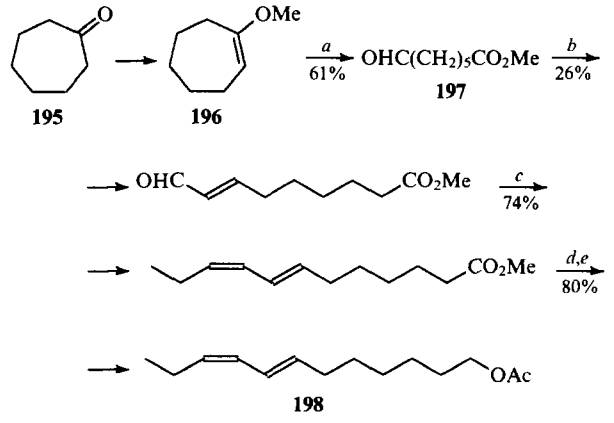
The racemic *erythro*-(3*SR*,4*RS*)-pharanal was synthesised from *cis*-1,2,3,6-tetrahydrophthalic anhydride, which was converted into *cis*-4,5-dimethylcyclohexene **190** via the diol **189**. This cycloalkene was converted by ozonolysis into *erythro*-3,4-dimethyladipic acid **191** and further, via the iodo-derivative **192**, into the phosphonium salt **193**. Coupling of the phosphorane generated from the salt **193** with the ketone **194** yielded an aldehyde with the *erythro*-configuration in the form of a mixture of Δ^6-Z/E-isomers (46 : 54); *erythro*-pharanal **187** was isolated from the latter by preparative gas–liquid chromatography (GLC).[123]

Methods of synthesis of a series of insect pheromones having the structure of unsaturated alcohol acetates have been developed on the basis of the products of reductive ring opening of the ozonides of the alkyl ethers of the enolic form of cycloheptanone.[124,125] Thus the aldehydoester **197**, obtained from 1-methoxycycloheptene **196**, was made to undergo an (*E*)-stereoselective alkene formation reaction (by treatment with formylmethylidenetriphenylphosphorane) and the product was then



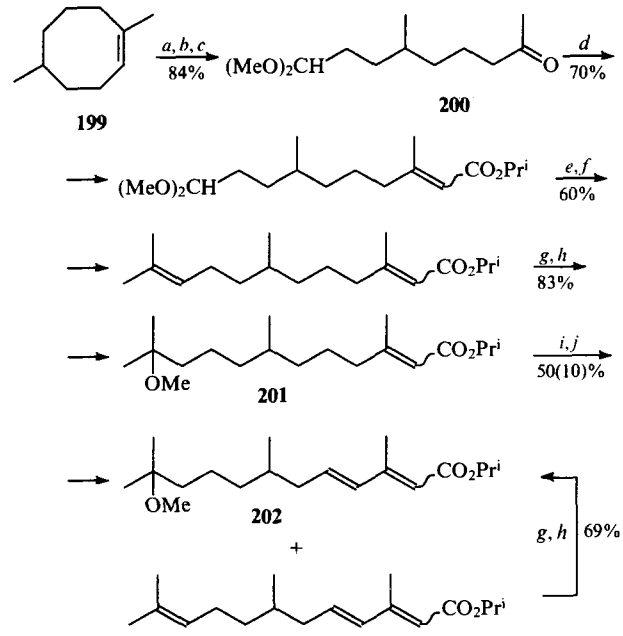
(*a*) $LiAlH_4$; (*b*) MsCl–Py; (*c*) O_3; (*d*) H_2CrO_4; (*e*) EtOH–H_2SO_4; (*f*) B_2H_6; (*g*) TsCl–Py; (*h*) NaI; (*i*) KOH; (*j*) PPh_3; (*k*) NaH; (*l*)  (**194**); (*m*) PCC; (*n*) preparative GLC.

converted by means of a (*Z*)-stereoselective alkene formation reaction (by treatment with propylidenetriphenylphosphorane) into the pheromone **198** of the grape leafcurler (*Lobesia botrana*) containing 92% of the principal stereoisomer.[125]



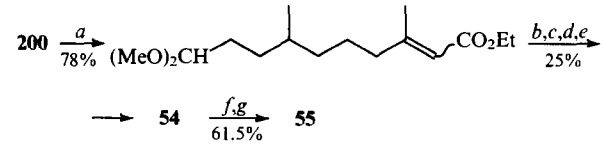
(*a*) O_3–PPh_3–CH_2Cl_2; (*b*) OHC–CH=PPh_3; (*c*) EtCH=PPh_3; (*d*) $LiAlH_4$; (*e*) Ac_2O–Py.

The isopropyl ester of (2*E*)-11-methoxy-3,7,11-trimethyldodec-2-enoic acid **201** has been obtained by the ozonolysis of 1,5-dimethylcyclooct-1-ene **199** and the subsequent transformations of the ketoacetal **200**, including isopropoxycarbonylmethyleneation at the keto-group and then conversion of the aldehyde group into an alkene component by treatment with isopropylidenetriphenylphosphorane and methoxylation of the isopropylidene group.[126] The allylic bromination of compound **201** and subsequent dehydrobromination led to the familiar juvenoid methoprene **202** in the form of an 82:18 mixture of the (2*E*,4*E*)- and (2*Z*,4*Z*)-isomers.



(*a*) O_3–MeOH; (*b*) H_2–Pd/$CaCO_3$–PbO; (*c*) MeOH–NH_4Cl; (*d*) $Me_3SiCH_2CO_2Pr^i$–LDA; (*e*) PPTS–H_2O; (*f*) Me_2C=PPh_3; (*g*) $Hg(OAc)_2$–MeOH; (*h*) $NaBH_4$–NaOH; (*i*) NBS–$(PhCO_2)_2$; (*j*) LiBr–Li_2CO_3.

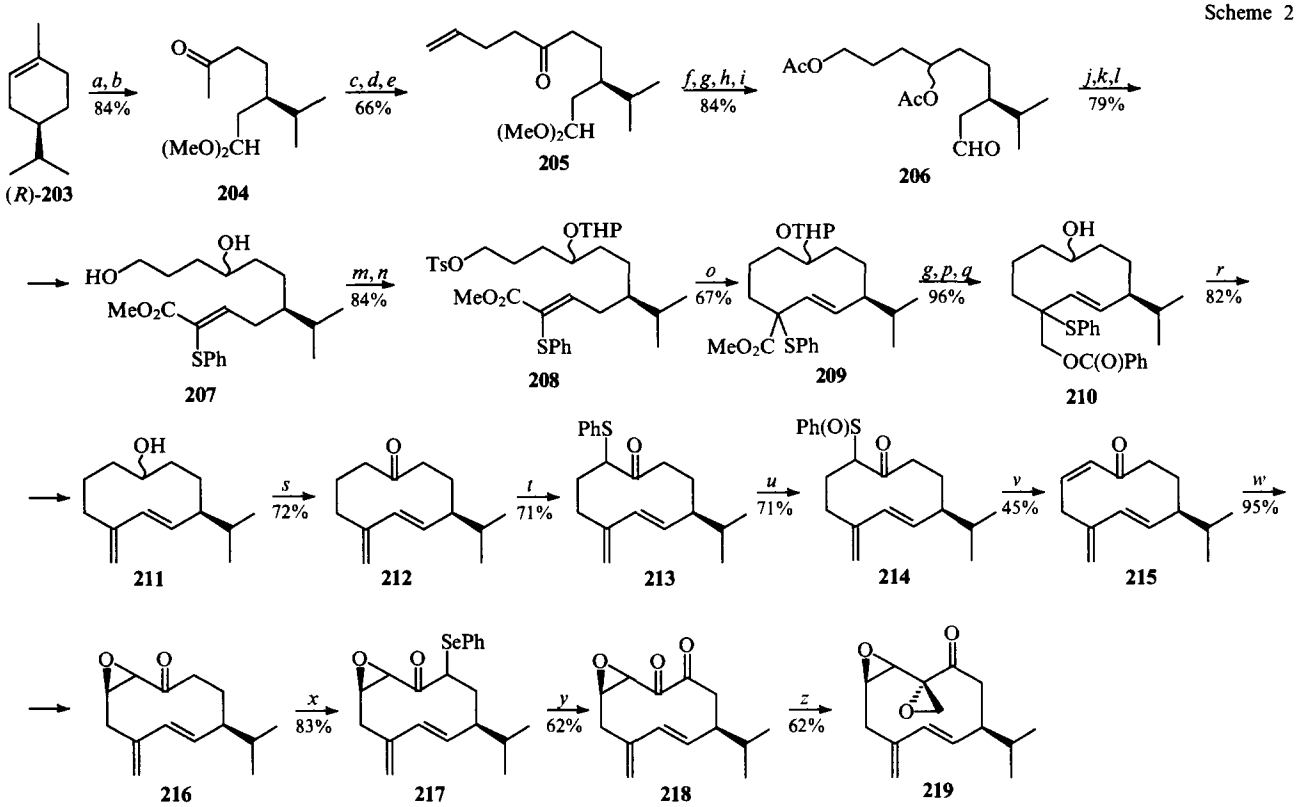
Hydroprene **55** has been obtained in the form of a 77:23 mixture of the (2*E*,4*E*)- and (2*Z*,4*E*)-isomers by the selective transformations of the ketoacetal **200**, including the ethoxycarbonylmethylenation of the keto-group, alkylation of the formyl group by isopropylmagnesium bromide with subsequent deoxygenation, and allylic bromination-dehydrobromination.[98]



(*a*) $Me_3SiCH_2CO_2Et$–LDA; (*b*) PPTS–H_2O; (*c*) Pr^iMgBr; (*d*) TsCl–Py; (*e*) Zn–NaI; (*f*) NBS–$(PhCO_2)_2$; (*g*) LiBr–Li_2CO_3

(+)-Dihydrolimonene (*R*)-**203** has served as the source of one of the chiral centres in the synthesis of (–)-periplanone B **219**—the sex pheromone of the American cockroach (*Periplaneta americana*).[127–129] The synthesis (Scheme 2) begins with the ozonolysis of the terpene (*R*)-**203** and the subsequent selective protection of the aldehyde group. The interaction of the carbanion generated from the dimethyl acetal of the ketoaldehyde **204** with allyl bromide led to the product **205**. Oxidative cleavage of the double bond in the latter, the subsequent reduction of the intermediate ketoaldehyde, and the acetylation and deblocking of the carbonyl group led to the aldehyde **206**. The latter was converted into the diol **207** by condensation with the carbanion generated from methyl benzenesulfonylacetate and subsequent dehydration and hydrolysis. The tosylation of the primary alcoholic group of the latter, accompanied by the blocking of the secondary hydroxy-group, afforded compound **208**, the deprotonation of which led to cyclisation. The product **209** was converted in several stages into the dienol **211** with endocyclic and exocyclic conjugated double bonds. The oxidation of the dienol **211** to the corresponding ketone **212** and its

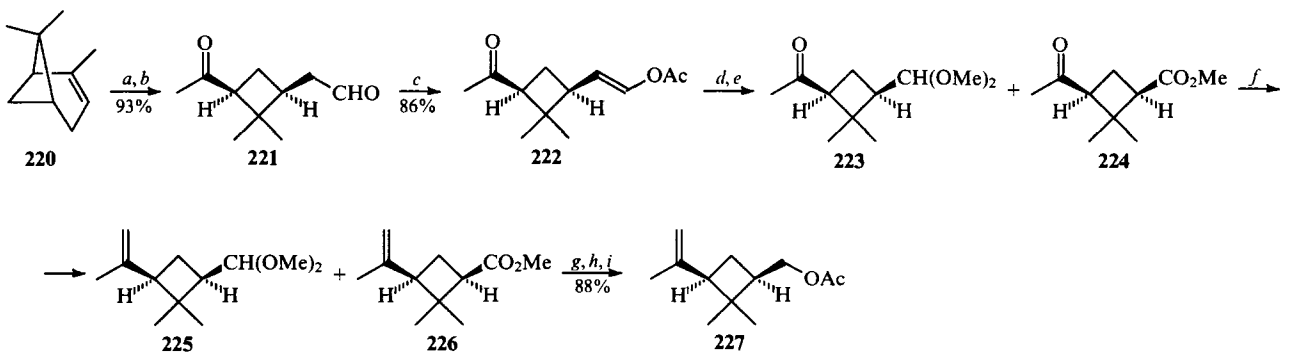
Scheme 2



(*a*) O_3–MeOH; (*b*) Me_2S, TsOH; (*c*) $(MeO)_2CO$, NaH; (*d*) $H_2C{=}CHCH_2Br$; (*e*) KOH–MeOH; (*f*) OsO_4–$NaIO_4$; (*g*) $LiAlH_4$; (*h*) Ac_2O–Py; (*i*) HCl; (*j*) $PhSCH_2CO_2Me$–LDA; (*k*) Ac_2O–AcONa; (*l*) MeONa–MeOH; (*m*) TsCl–DMAP (4-4-dimethylaminopyridine)–Et_3N; (*n*) DHP (dihydropyran)–PPTS; (*o*) $NaN(SiMe_3)_2$; (*p*) PhCOCl–DMAP–Py; (*q*) Dowex 50W (H^+); (*r*) Na–$C_{10}H_8$ (naphthalenesodium); (*s*) PCC–NaOAc; (*t*) $PhSSO_2Ph$–$LiN(SiMe_3)_2$; (*u*) $NaIO_4$; (*v*) $CaCO_3$, 110 °C; (*w*) Bu^tOOH–KH; (*x*) PhSeBr–$LiN(SiMe_3)_2$; (*y*) H_2O_2–Ac_2O–AcONa, K_2CO_3; (*z*) $Me_2S{=}CH_2$.

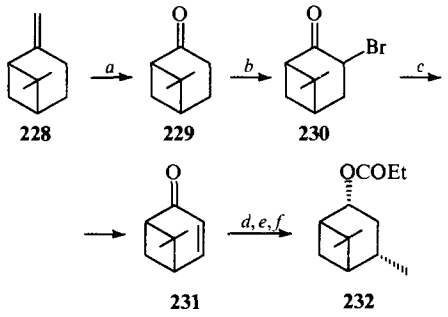
α-phenylsulfanylation afforded the sulfide **213**, which was oxidised to the sulfoxide **214**; the thermal elimination of PhSOH led to the cyclic ketotriene **215**. Its epoxidation by the *tert*-butyl hydroperoxide–base system[130] took place regioselectively with the preferential formation of the epoxide **216**. The latter was oxidised via the phenyl selenide **217** to the diketone **218**, the interaction of which with methylidenedimethyl-λ^4-sulfane took place selectively at one of the keto-groups and led to the target diepoxide **219**.

The readily available (+)-α-pinene **220** served as the initial compound for the synthesis of (+)-*cis*-(1*R*, 3*R*)-1-acetoxymethyl-3-isopropenyl-2,2-dimethylcyclobutane **227** — the sex pheromone of the grape mealybug (*Planococcus citri*).[131] The ozonolysis of compound **220** gives rise to the ketoaldehyde **221** in which the configurations of the asymmetric centres correspond to those of the natural pheromone. The necessary shortening of the side chain was achieved via the enol acetate **222** with its subsequent ozonolysis, which led to a mixture of the acetal **223** and the ester **224**. A mixture of compounds **225** and **226** was obtained by Wittig methylenation and was then converted in three stages into the acetate **227**. The optical isomer of the pheromone was synthesised in accordance with the same scheme from (–)-α-pinene.[132]



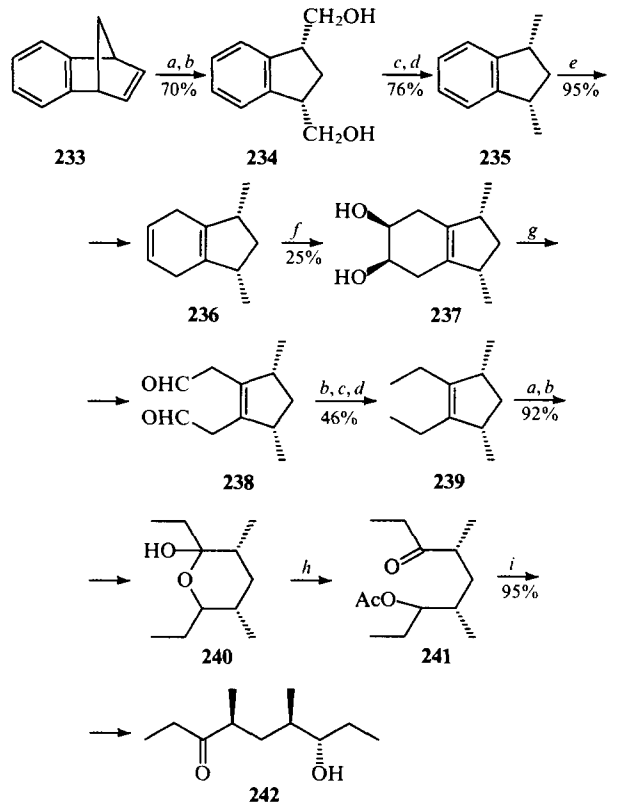
(*a*) O_3–MeOH; (*b*) H_2–Pd–$CaCO_3$–PbO; (*c*) Ac_2O–Et_3N; (*d*) O_3–SiO_2; (*e*) MeOH–TsOH; (*f*) $H_2C{=}PPh_3$; (*g*) PPTS–H_2O; (*h*) DIBALH; (*i*) Ac_2O–Py.

The product of the ozonolysis of β-pinene **228** — nopinone **229** — has found extensive application in the synthesis of insect pheromones.[133–135] For example, it is known that the bicyclic propionate **232** possesses sex pheromone activity for cockroaches. Transformation of ketone **229** gives apoverbenone **231**, converted into the sex pheromone **232** by stereoselective coupled addition of the lithium cuprate reagent and subsequent Meerwein – Ponndorf – Verley reduction of the carbonyl group.[133]



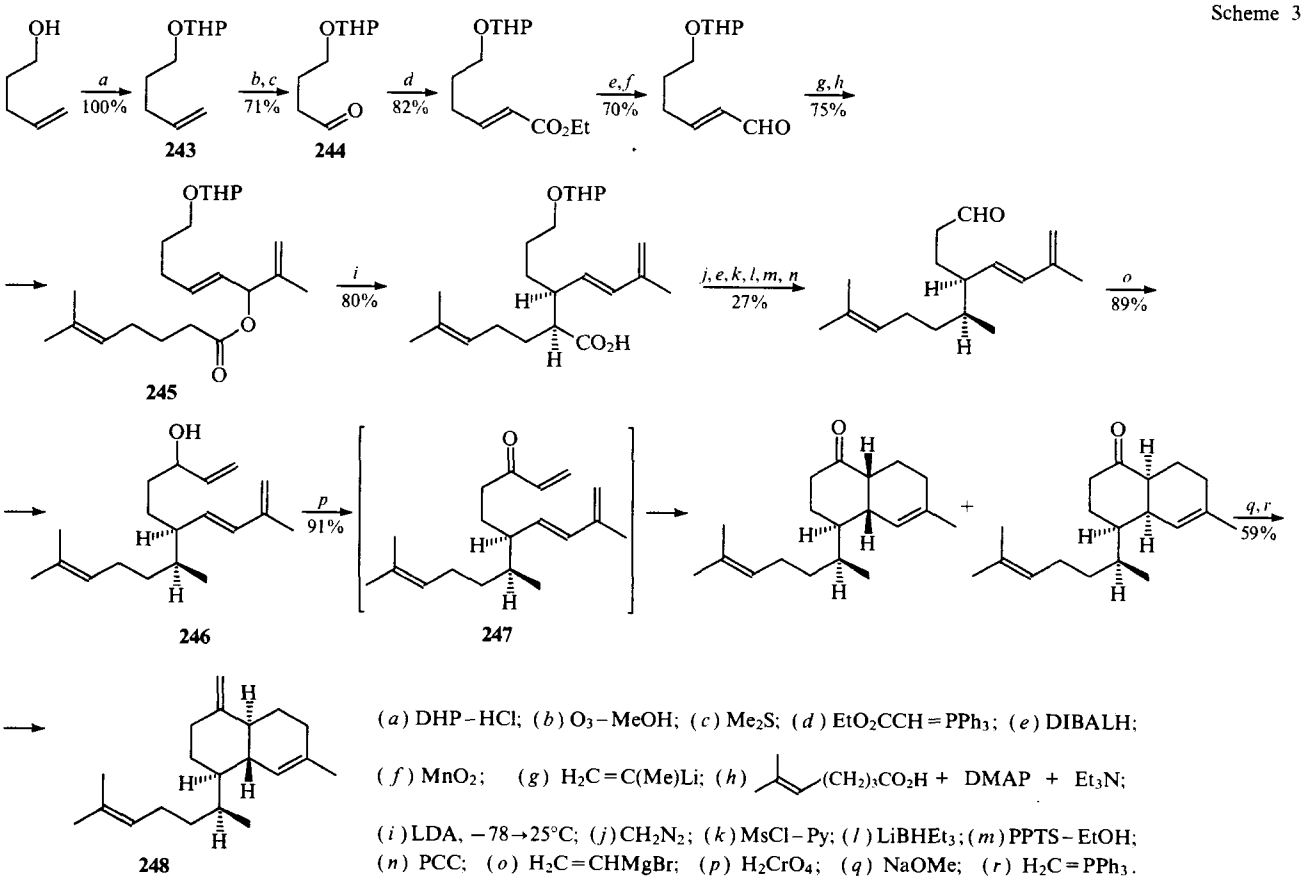
(*a*) O_3–MeOH; (*b*) Br_2; (*c*) DBU {1,8-diazabicyclo[5.4.0]undec-7-ene}; (*d*) Me_2CuLi; (*e*) $(Pr^iO)_3Al$–Pr^iOH; (*f*) $(EtCO)_2O$.

A recently developed approach[136] to the synthesis of (±)-serricornine **242** — the sex pheromone of the tobacco beetle (*Lasioderma serricorne*) — is based on the ozonolysis of benzonorbornadiene **233** to the diol **234**, which is converted via the corresponding methanesulfonate into *cis*-1,3-dimethylindane **235**. Its reduction (via the Birch reaction) gives rise to the diene **236**, the *cis*-hydroxylation of which and subsequent oxidative degradation of the resulting 1,2-diol **237** lead to the dialdehyde **238**. The latter is converted by the reduction–methanesulfonation–reduction procedure into the tetrasubstituted cyclopentene **239**. Repeated ozonolysis of compound **239** leads to the lactol **240**, which is converted into the target ketoalcohol **242** via the ketoacetate **241**.



(*a*) O_3–CH_2Cl_2; (*b*) $NaBH_4$; (*c*) MsCl–Et_3N; (*d*) $LiAlH_4$; (*e*) Li–NH_3– EtOH; (*f*) OsO_4–*N*-methylmorpholine *N*-oxide; (*g*) $Pb(OAc)_4$; (*h*) Ac_2O–DMAP; (*i*) DBU.

Scheme 3

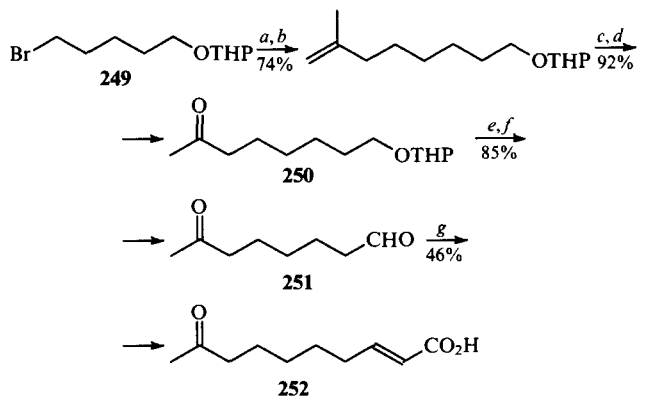


(*a*) DHP–HCl; (*b*) O_3–MeOH; (*c*) Me_2S; (*d*) $EtO_2CCH{=}PPh_3$; (*e*) DIBALH; (*f*) MnO_2; (*g*) $H_2C{=}C(Me)Li$; (*h*)

+ DMAP + Et_3N; (*i*) LDA, −78→25°C; (*j*) CH_2N_2; (*k*) MsCl–Py; (*l*) $LiBHEt_3$; (*m*) PPTS–EtOH; (*n*) PCC; (*o*) $H_2C{=}CHMgBr$; (*p*) H_2CrO_4; (*q*) NaOMe; (*r*) $H_2C{=}PPh_3$.

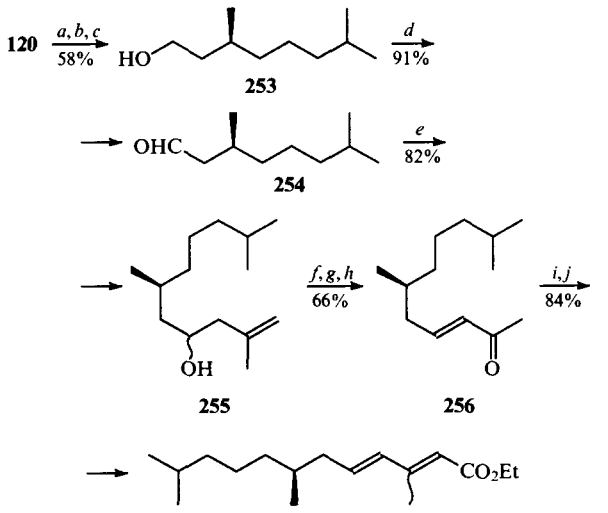
The bicyclic diterpene component of the protective secretion of termites (*Cubitermes umbratus*) (compound **248**) has been synthesised stereoselectively[137] (Scheme 3) from the product of the ozonolysis of the tetrahydropyranyl ether of pent-4-enol **243**. The key stages are the stereoselective Claisen rearrangement of the (*Z*)-enolate of the ether of the 2,8-disubstituted 1,4-dien-3-ol **245** and the spontaneous intramolecular Diels–Alder reaction of the oxidation product of the alcohol **246**.

In the majority of the syntheses of (2*E*)-9-oxodec-2-enoic acid **252** — the 'royal jelly' of honey bees (*Apis mellifera*) — the concluding stage is the condensation of 7-oxooctanal **251** with malonic acid via the Doebner reaction. An effective method has been proposed for the synthesis of the ketoaldehyde **251** on the basis of the coupling of the THP ether of 5-bromopentanol **249** with methylallyl chloride and subsequent ozonolysis of the resulting terminal alkene.[138]



(*a*) Mg; (*b*) $H_2C=C(Me)CH_2Cl$–CuI–2,2′-bipy; (*c*) O_3–MeOH; (*d*) H_2–Pd–$CaCO_3$–PbO; (*e*) TsOH–MeOH–H_2O; (*f*) PCC; (*g*) $H_2C(CO_2H)_2$–Py–piperidine.

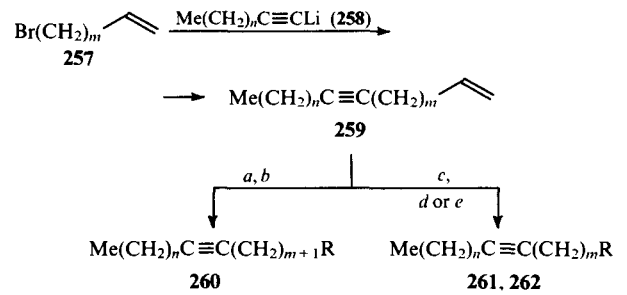
The synthesis of the enantiomerically enriched juvenoid hydroprene.[139] (*S*)-**55** in the form of a 7:3 mixture of the (2*E*,4*E*)- and (2*Z*,4*E*)-stereoisomers has been achieved by the selective transformations of the readily available tetrahydrogeraniol **253** [obtained from (*S*)-dihydromyrcene **120**], involving the ozonolysis of the homoallyl alcohol **255**, in the preparation of the key conjugated enone **256**.



(*a*) Bu^i_3Al; (*b*) O_2; (*c*) H_2–Pd/C; (*d*) PCC; (*e*) $H_2C=C(Me)CH_2MgCl$; (*f*) O_3–CH_2Cl_2–MeOH; (*g*) Me_2S; (*h*) TsOH–Na_2SO_4; (*i*) EtMgBr–$HC\equiv COEt$; (*j*) H_2SO_4.

In the synthesis of Lepidoptera pheromones, which consist as a rule of unsaturated alcohols, acetates, and aldehydes,[35] the so called 'acetylenic' path is usually employed. It consists in the coupling of alkali metal alkynylides with alkyl halides having an oxygen-containing functional group in the ω-position; the subsequent stereoselective reduction of the triple bond affords alkenes with either (*Z*)- or (*E*)-configurations.[34,35]

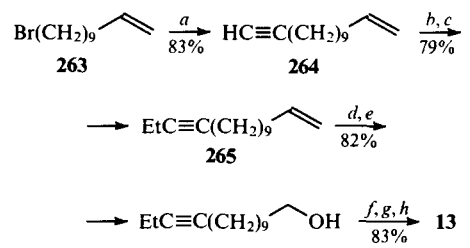
An alternative approach, based on the condensation of lithium alkynylides **258** with ω-bromoalkenes **257** and expanding significantly the synthetic possibilities of the 'acetylenic' path, has been developed recently.[140,141] The terminal double bond in the coupling product **259**, introduced with the aid of the ω-bromoalkene **257**, is smoothly transformed into the required oxygen-containing functional group. This is achieved, for example, by hydration via an organoboron intermediate to the corresponding ethyne alcohol **260** or by ozonolysis with formation (depending on the method of treatment of the peroxide product) of the alkyn-1-ol **261** or the alkynal **262** with a carbon chain shorter by one atom than in the alkenyne precursor **259**.



R = CH_2OH (**260**, **261**), CHO (**262**).

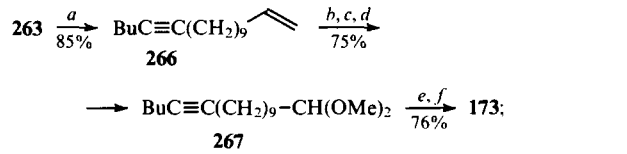
(*a*) BBN; (*b*) H_2O_2–NaOH; (*c*) O_3; (*d*) $NaBH_4$; (*e*) Me_2S.

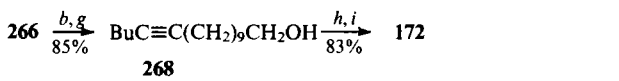
This approach has been used in the synthesis[141] of the sex pheromone **13** of the green oak moth based on the ozonolytic cleavage of the double bond in pentadec-1-en-12-yne **265**, obtained by the ethynylation of undecenyl bromide **263** with subsequent ethylation of the terminal alkenyne **264**.



(*a*) $HC\equiv CLi$; (*b*) $LiNH_2$; (*c*) EtBr; (*d*) O_3–cyclo-C_6H_{12}–MeOH; (*e*) $NaBH_4$; (*f*) BBN; (*g*) AcOH; (*h*) Ac_2O–Py.

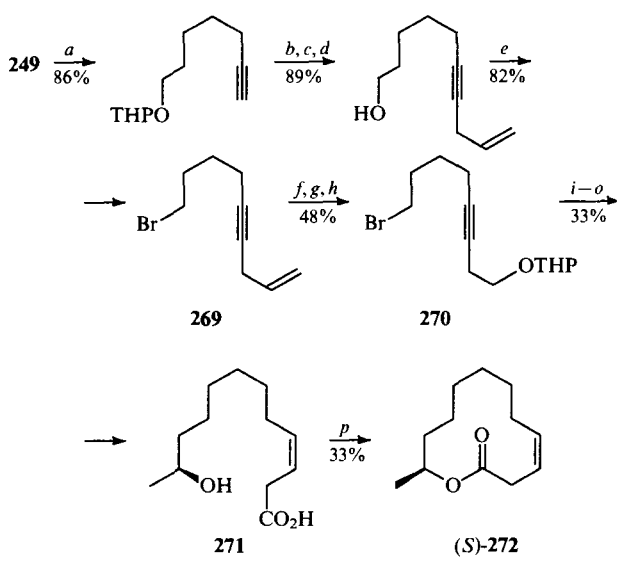
The components of the pheromones of the cabbage moth (*Mamestra brassicae*) and the cotton bollworm (*Heliothis armigera*) (compounds **172** and **173**) have been synthesised[140,141] via heptadec-1-en-12-yne **266**, obtained by the reaction of the bromo-derivative **263** with lithium hex-1-ynylide. The ozonolysis of the enyne **266** led (depending on the reductant employed) either to the alkyne acetal **267** or to the alcohol **268**, which are readily transformable into the target aldehyde **173** or the acetate **172** respectively.





(*a*) $C_4H_9C{\equiv}CLi$; (*b*) O_3–cyclo-C_6H_{12}–MeOH; (*c*) Me_2S; (*d*) MeOH–TsOH; (*e*) H_2–Pd–$CaCO_3$–PbO; (*f*) PPTS–H_2O; (*g*) $NaBH_4$; (*h*) Bu^iMgBr–Cp_2TiCl_2 (Cp = η^5-cyclopentadienyl); (*i*) Ac_2O–Py.

An effective synthesis of the optically pure (*S*)-(3*Z*)-dodec-3-en-11-olide (*S*)-**272** [ferrulactone II—a component of the aggregation pheromone of the rusty grain beetle (*Cryptolestes ferrugineus*)] is based on the macrolactonisation of the acid (*S*)-**271**, obtained by the cross-coupling of the protected bromohydroxy-derivative **270** with the optically active epoxide **273**. The ethyne C_8 block **270** was synthesised by the partial ozonolysis of the 1,4-enynyl bromide **269**—the product of the successive increase in the length of the linear chain of the precursor **249** by reaction with lithium ethynylide and allyl bromide.[142]

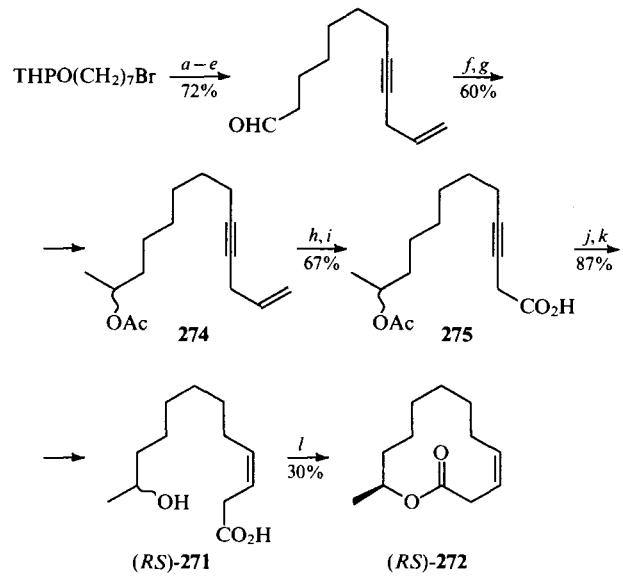


(*a*) HC≡CLi; (*b*) EtMgBr–CuI; (*c*) $H_2C{=}CHCH_2Br$; (*d*) TsOH–MeOH–H_2O; (*e*) $Br_2{\cdot}PPh_3$; (*f*) O_3–cyclo-C_6H_{12}–MeOH; (*g*) $NaBH_4$; (*h*) DHP–TsOH; (*i*) Mg, CuBr–Me_2S; (*j*)  (**273**); (*k*) Ac_2O–Py–DMAP; (*l*) PPTS–EtOH; (*m*) H_2CrO_4; (*n*) K_2CO_3–MeOH; (*o*) H_2–P2-Ni ($NaBH_4$-reduced nickel with ethylenediamine); (*p*) BPDS (2,2′-bipyridyl disulfide)–PPh_3–$AgClO_4$.

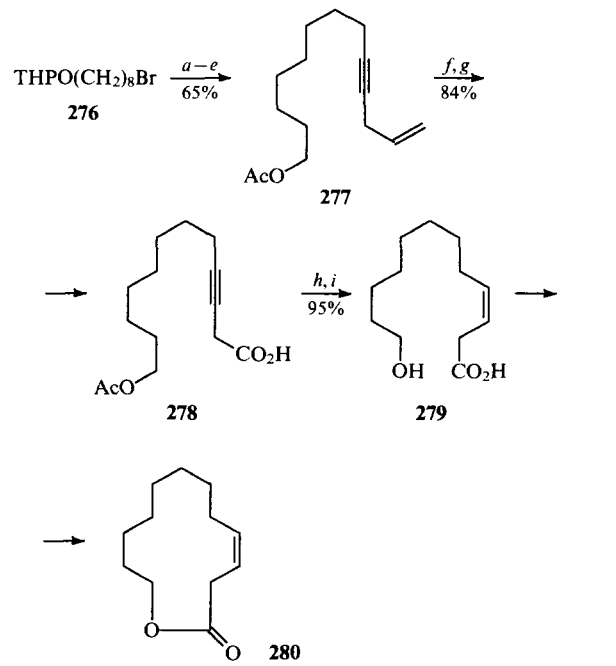
Since the racemic ferrulactone II (*RS*)-**272** is also biologically active, its synthesis is likewise of practical value. A new synthesis has been proposed[143,144] for the acyclic precursor (*RS*)-**271** of the pheromone, in which the acetoxyenyne **274** is used in one of the key stages of the selective ozonolysis. The ozonolysis involves exclusively the double bond and leads (after the oxidation of the peroxide product by the Jones reagent) to the ethyne acetoxyacid **275**, which is converted into the target macrolide (*RS*)-**272** by a standard method.

(3*Z*)-12-Hydroxydodec-3-enoic acid **279**—the acyclic precursor of (3*Z*)-dodec-3-en-12-olide **280** [a component of the aggregation pheromone of the flat grain beetle (*Cryprolestes pusillis)*] has been synthesised, by means of analogous transformations but in a smaller number of stages, from the THP ether of 8-bromooctan-1-ol **276**.

A method proposed for the synthesis of the stereoisomeric components of the sex pheromone of the southern green stink bug (*Nezara viridula*) (compounds **288** and **289**) is based on the

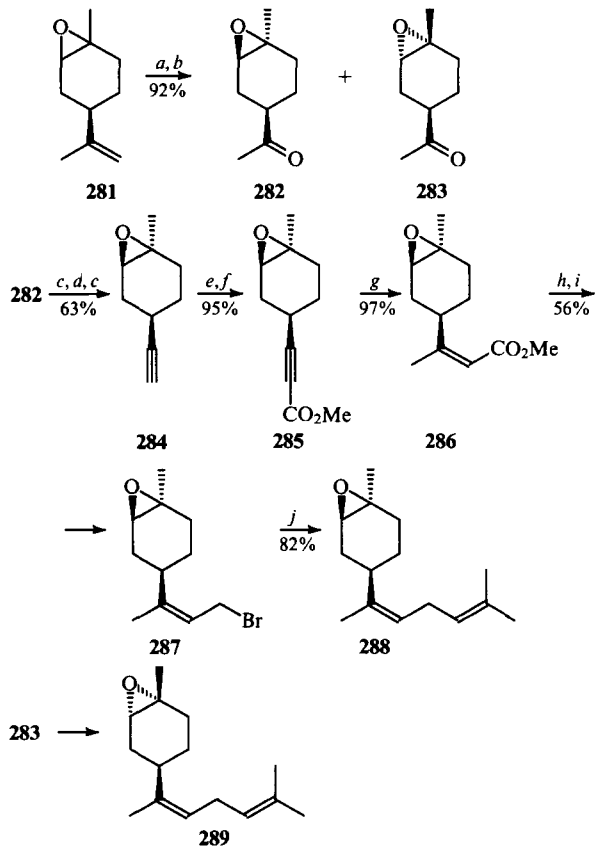


(*a*) HC≡CLi; (*b*) EtMgBr–CuI; (*c*) $H_2C{=}CHCH_2Br$; (*d*) TsOH–MeOH–H_2O; (*e*) PCC; (*f*) MeMgI; (*g*) Ac_2O; (*h*) O_3–cyclo-C_6H_{12}–MeOH; (*i*) H_2CrO_4; (*j*) K_2CO_3–MeOH; (*k*) H_2–P2-Ni; (*l*) DDS–PPh_3–$AgClO_4$.



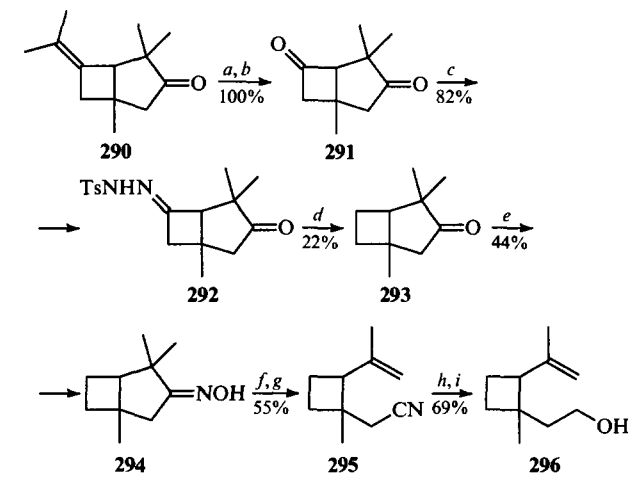
(*a*) HC≡CLi; (*b*) EtMgBr–CuI; (*c*) $H_2C{=}CHCH_2Br$; (*d*) TsOH–MeOH–H_2O; (*e*) Ac_2O–Py; (*f*) O_3–cyclo-C_6H_{12}–AcOH; (*g*) H_2CrO_4; (*h*) K_2CO_3–MeOH; (*i*) H_2–P2-Ni.

ozonolysis of (*R*)-(+)-limonene oxide **281**, which is available as an equimolar mixture of the α- and β-epoxides. The product of the reduction of the ozonide is the corresponding mixture of the ketones **282** and **283**, which was separated chromatographically. In order to obtain the component **288**, the diastereoisomer **282** was converted via the corresponding vinyl phosphate into the terminal ethyne **284** and further into the ester **285**. The regio- and stereo-specific coupled addition of dimethyllithium cuprate led to the (*Z*)-alkene **286**, which was converted into the bromide **287** via the corresponding alcohol. The target *endo*-epoxide **288** was obtained in the concluding stage—the condensation of the bromide **287** with 1-lithio-2-methylpropene. The component **289** has been synthesised similarly from the diastereoisomer **283**.[145]



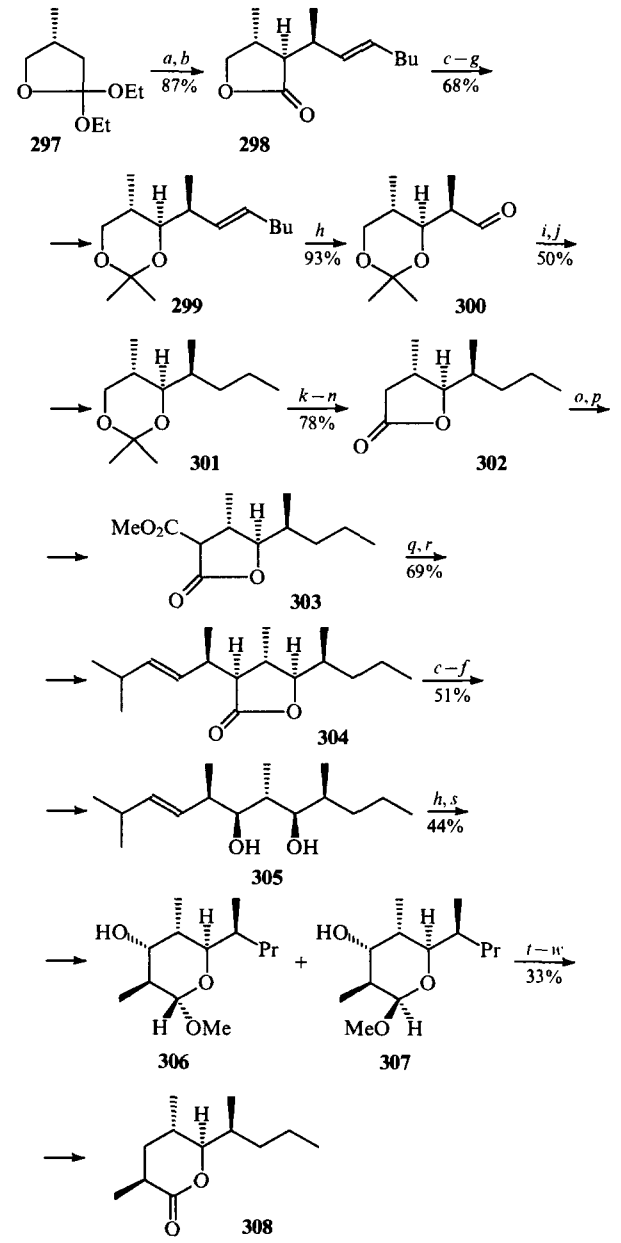
(*a*) O_3; (*b*) PPh_3; (*c*) LDA; (*d*) $(EtO)_2P(O)Cl$; (*e*) BuLi; (*f*) $ClCO_2Me$; (*g*) Me_2CuLi; (*h*) DIBALH; (*i*) CBr_4-PPh_3; (*j*) $Me_2C=CHBr-Bu^tLi$.

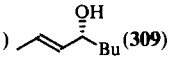
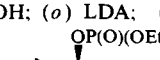
The synthesis of 1,4,4-trimethylbicyclo[3.2.0]heptan-3-one **293** — a key intermediate[146] in the synthesis of grandisol **296** [a component of the sex pheromone of the cotton-boll weevil (*Anthonomus grandis*)] — was based on the ozonolysis of the bicyclic compound **290**, which was converted quantitatively into the diketone **291** with subsequent selective reduction of one of the carbonyl groups via the corresponding tosylhydrazone **292**. The bicyclic ketone **293** was subsequently converted into the oxime **294**, in the tosylate of which regioselective fragmentation occurred on deprotonation of one of the methyl groups with the opening of the five-membered ring and the formation of the unsaturated nitrile **295**.[147] Two-stage reduction (via an intermediate aldehyde) completed the synthesis of grandisol **296**.



(*a*) $O_3-MeOH-CH_2Cl_2$; (*b*) Me_2S; (*c*) $TsNHNH_2$; (*d*) $NaBH_4$; (*e*) $H_2NOH\cdot HCl$, KOH; (*f*) TsCl–2,6-lutidine; (*g*) Py–5% NaOH; (*h*) DIBALH; (*i*) $LiAlH_4$.

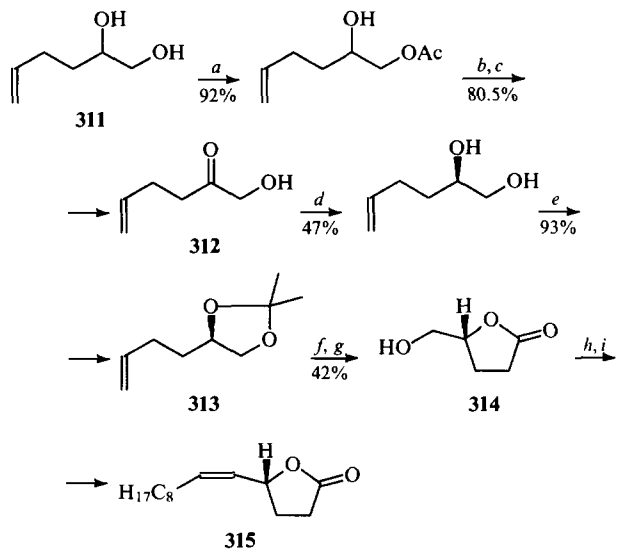
In the synthesis of (+)-invictolide **308** — the optical isomer of the pheromone of the fire ant (*Solenopsis invicta*) [developed on the basis of (*R*)-3-methyl-γ-butyrolactone], the ozonisation was effectively used in three stages.[148] In the first of these, the unsaturated ketal **299** was ozonolysed. Compound **299** was obtained from the diethylortholactone **297** by transesterification with the alcohol **309**, the Claisen rearrangement, epimerisation, the Baeyer–Villiger oxidation of the lactone **298**, and protection of the diol. The ozonolysis product — the aldehyde **300** — was converted into the unsaturated ketal **301** via alkene formation and hydrogenation stages and then into the lactone **302**. The latter was converted into the methoxycarbonyl derivative **303** and was



(*a*)  (**309**)–Me_3CCO_2H; (*b*) Bu^tOK-Bu^tOH; (*c*) MeLi; (*d*) H_2O_2-AcOH; (*e*) $Ac_2O-DMAP-Et_3N$; (*f*) KOH–MeOH; (*g*) $Me_2C(OMe)_2-TsOH$; (*h*) O_3-MeOH, Me_2S; (*i*) $MeCH=PPh_3$; (*j*) H_2–Ra-Ni; (*k*) HCl; (*l*) TsCl–Py; (*m*) NaCN; (*n*) HCl–MeOH; (*o*) LDA; (*p*) $NCCO_2Me$; (*q*) $NaH-Pd(PPh_3)_4-PPh_3$,  (**310**); (*r*) LiCl–DMSO–H_2O; (*s*) $HC(OMe)_3-TsOH$; (*t*) BuLi–PhOSCl; (*u*) Bu_3SnH–AIBN (azobisisobutyronitrile); (*v*) O_3–EtOAc; (*w*) $TsOH-CH_2Cl_2$.

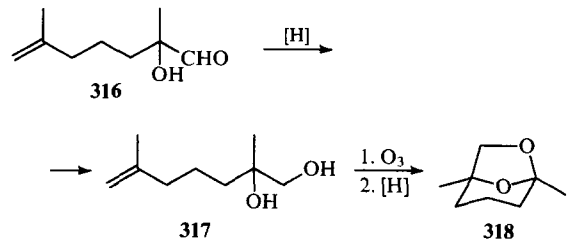
alkylated by the allyl phosphate **310** with subsequent demethoxycarbonylation; this led to the unsaturated lactone **304**, which was oxidised, by a procedure similar to that used for the oxidation of compound **298**, to the diol **305**. Its ozonisation, followed by treatment of the peroxide product with dimethyl sulfate and methyl orthoformate, led to a mixture of the axial (compound **306**) and equatorial (compound **307**) cyclic methoxyacetals, the last of which was oxidised by ozone to the target invictolide **308** after deoxygenation.

An effective procedure has been proposed for the preparation of the key hydroxylactone **314** in the synthesis of the sex pheromone **315** of the Japanese beetle (*Popilia japonica*).[149] It is based on the ozonolysis of the monoene acetal **313**, obtained by enzymic reaction involving the regio-specific acylation of the vicinal diol **311** and the enantioselective reduction of the intermediate ketoalcohol **312**.

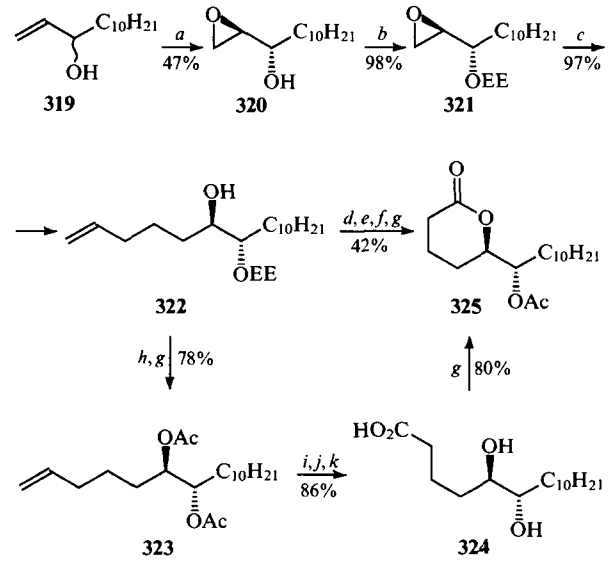


(*a*) Ac_2O–PPL (pig pancreas lipase); (*b*) H_2CrO_4; (*c*) NaOH; (*d*) Baker's yeast; (*e*) $H_2C{=}C(Me)OMe{-}H^+$; (*f*) O_3, Me_2S; (*g*) $Ag_2O{-}OH^-$; (*h*) PCC; (*i*) $C_8H_{17}CH{=}PPh_3$.

Frontaline **318** — the aggregation pheromone of insects of the genus *Dendroctonus* — has been synthesised by ozonising the unsaturated vicinal diol **317** (readily obtainable from the aldehydoalcohol **316**) with subsequent reduction of the peroxide ozonolysis product accompanied by cyclisation.[150]

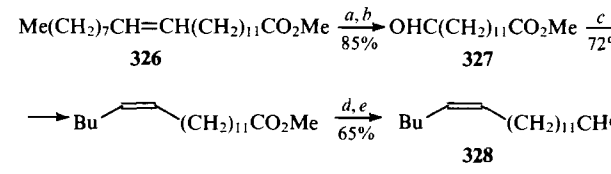


(2*R*,3*S*)-(+)-1,2-Epoxytridecan-3-ol **320** has been obtained by a modified reaction involving the enantioselective epoxidation of tridec-1-en-3-ol **319**. A short path to the conversion of compound **320** into the main component of the egg-laying pheromone **325** of the mosquito *Culex pipiens* has been found. The key stage of this transformation is the ozonolysis of compound **322** — the product of the coupling of the epoxyether **321** with but-3-en-1-ylmagnesium bromide, which proceeds with complete retention of the configuration of the asymmetric centres. The pheromone **325** and its optical isomer have also been synthesised by the ozonolysis of the diacetate **323**.[151–153]



(*a*) $Ti(OPr^i)_4$–(+)-DET (diethyl tartrate)–Bu^tOOH; (*b*) $H_2C{=}CHOEt$–TsOH; (*c*) $H_2C{=}CH(CH_2)_2MgBr$–CuBr; (*d*) O_3–AcOH; (*e*) H_2O_2–SeO_2–Ac_2O; (*f*) TsOH–PhH; (*g*) Ac_2O–Py; (*h*) HCl; (*i*) O_3–MeOH; (*j*) H_2O_2–HCO_2H; (*k*) K_2CO_3.

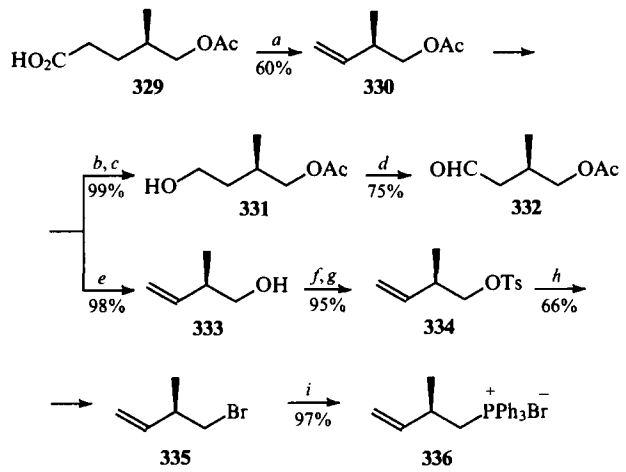
A convenient procedure for the preparation of α,ω-bifunctional reagents used in the synthesis of insect pheromones involves the ozonolysis of derivatives of higher monounsaturated carboxylic acids, for example, oleic and undecenoic.[154–158] Thus, methyl 12-formyldodecanoate **327**, which is necessary for the construction of the carbon skeleton of (*Z*)-octadec-13-enal **328** [a component of the pheromone of the Asiatic rice borer (*Chilo suppressalis*)], has been synthesised by the ozonolysis of the methyl ester of brassidic (or erucic) acid **326**.[154]



(*a*) O_3–CH_2Cl_2; (*b*) PPh_3; (*c*) $BuCH{=}PPh_3$; (*d*) $LiAlH_4$; (*e*) PCC.

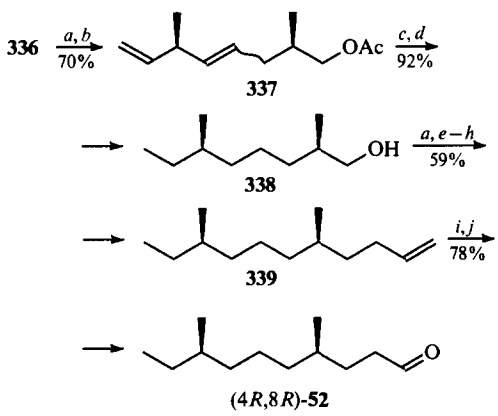
(*R*)-(+)-5-Acetoxy-4-methylpentanoic acid, isolated from the products of the oxidative degradation of the side chain of the (25*R*)-series sapogenins in the manufacture of steroid medicinal preparations, provides extensive possibilities for the synthesis of optically pure chiral pheromones.[159] This bifunctional chiral block has been used to synthesise pheromones with one or several asymmetric carbon atoms. Thus, (*R*)-2-methylbut-3-en-1-yl acetate **330** (the product of the oxidative decarboxylation of the acid **329**) and (*S*)-2-methylbutan-1-ol **340** (a readily available product of the fermentation of sugar) served as a basis[160] for the synthesis of two optically pure stereoisomers of 4,8-dimethyldecanal **52**.

The synthesis of the (4*R*,8*R*)-stereoisomer **52** includes[160] the independent syntheses of the acetoxyaldehyde **332** and the phosphonium salt **336**. The aldehyde **332** was obtained from the alkene **330** via the acetoxyalcohol **331**. The alkene has also been used in the synthesis of the bromo-derivative **335** via the intermediate alcohol **333** and the tosylate **334**. The bromo-derivative **335** was converted into compound **336** by a high-pressure method.



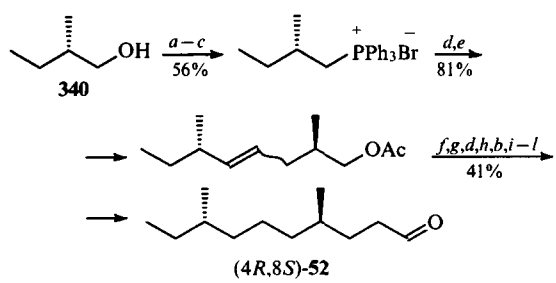
(*a*) $Pb(OAc)_4$, $Cu(OAc)_2 \cdot H_2O$; (*b*) BBN; (*c*) H_2O_2–AcONa; (*d*) PCC; (*e*) KOH; (*f*) BuLi; (*g*) TsCl; (*h*) NaBr; (*i*) PPh_3, 14 kbar.

The Wittig coupling of the aldehyde **332** to the ylide generated from the salt **336** led to the dienyl acetate **337**, which was converted in two stages into the alcohol **338** and further, via the corresponding bromo-derivative, into the alkene **339**. The latter was transformed into the pheromone (4*R*,8*R*)-**52** by ozonisation.



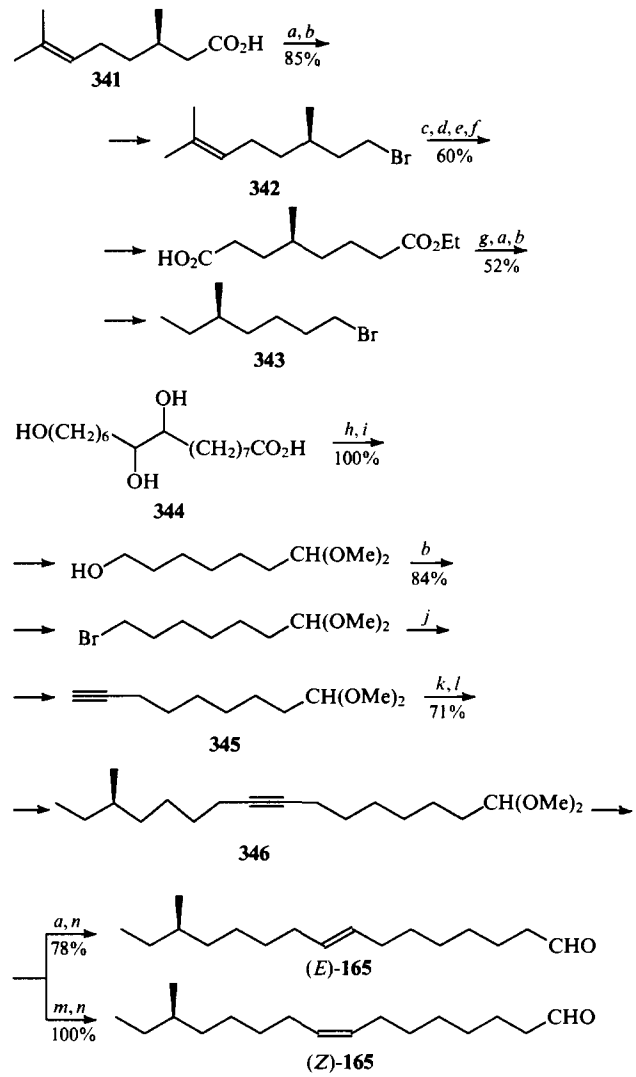
(*a*) BuLi; (*b*) **332**; (*c*) H_2–Pd/C; (*d*) KOH; (*e*) TsCl; (*f*) NaBr; (*g*) Mg; (*h*) $H_2C{=}CHCH_2Br$; (*i*) O_3–CH_2Cl_2; (*j*) Me_2S.

The (4*R*,8*S*)-stereoisomer of compound **52** was synthesised by a procedure in which the chiral alcohol **340** was used in the construction of the (8*S*)-asymmetric centre and this synthesis does not differ fundamentally from that described above.[160]



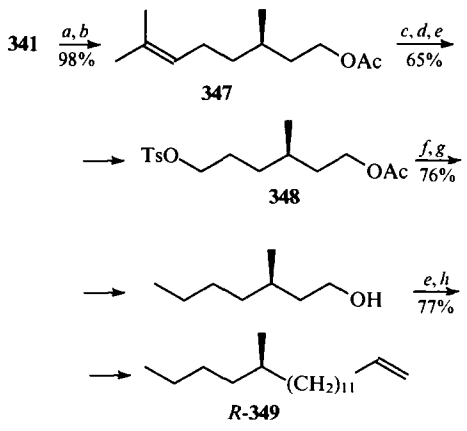
(*a*) Ts–Py; (*b*) NaBr; (*c*) PPh_3; (*d*) BuLi; (*e*) **332**; (*f*) H_2–Pd/C; (*g*) KOH; (*h*) TsCl; (*i*) Mg; (*j*) $H_2C{=}CHCH_2Br$; Me_2S.

(*R*)-(+)-Citronellic acid **341**, obtained by the acid cleavage of the readily available (*R*)-(+)-pulegone, has found extensive application as an optically active unit.[161] (*R*)-5-Methylhept-1-yl bromide **343** has been used as the chiral block in the syntheses of the (*R*)-trogodermals with the (*Z*)- or (*E*)-configuration of the double bond [compound (*Z*)-**165** or (*E*)-**165**]. Compound **343** was obtained by converting the acid **341** in two stages into (*R*)-citronellyl bromide **342**, the subsequent transformations of which included stages involving malonic ester synthesis and ozonolysis with oxidative cleavage of the ozonide. The achiral unit **345** was obtained by the oxidative cleavage of aleuritic acid **344**. Its subsequent alkylation by the bromo-derivative **343** with the (*R*)-configuration afforded the ethyne precursor of the target pheromone **346**.[162,163]



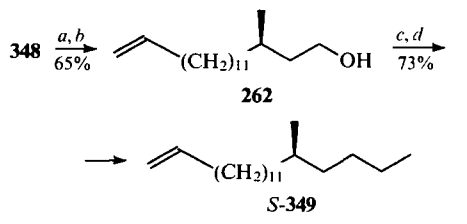
(*a*) $LiAlH_4$; (*b*) Br_2–PPh_3; (*c*) $NaCH(CO_2Et)_2$; (*d*) LiCl–H_2O; (*e*) O_3–MeOH; (*f*) H_2CrO_4; (*g*) $AgNO_3$–$K_2S_2O_8$; (*i*) MeOH–HCl; (*j*) $HC{\equiv}CNa$; (*k*) BuLi; (*l*) **343**; (*m*) H_2–P2-Ni; (*n*) PPTS–H_2O.

The bifunctional nature of (*R*)-citronellic acid **341** made it possible to synthesise from the latter both optical isomers of 14-methyloctadec-1-ene **349** — the sex pheromone of the peach mining moth (*Lyonetia clerckella*).[164] In the synthesis of the (*R*)-enantiomer of compound **349**, citronellyl acetate **347** was converted, after ozonolysis, into the α,ω-acetoxytosylate **348**, the subsequent alkylation of which with dimethyl- and di(undec-10-enyl)-lithium cuprates completed the synthesis of the target pheromone.



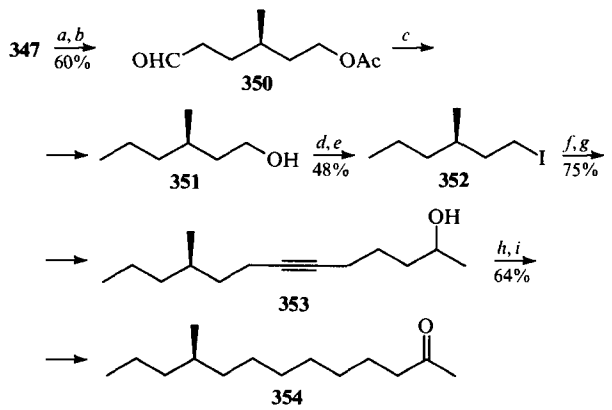
(*a*) $LiAlH_4$; (*b*) Ac_2O–Py; (*c*) O_3–MeOH–CH_2Cl_2; (*d*) $NaBH_4$; (*e*) TsCl–Py; (*f*) Me_2CuLi; (*g*) NaOH; (*h*) $[H_2C{=}CH(CH_2)_9]_2CuLi$.

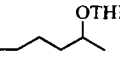
In order to obtain the (*S*)-optical isomer (*S*)-**349**, the intermediate acetoxytosylate **348** was alkylated in the reverse order. i.e. the alkene component of the target molecule was constructed initially.



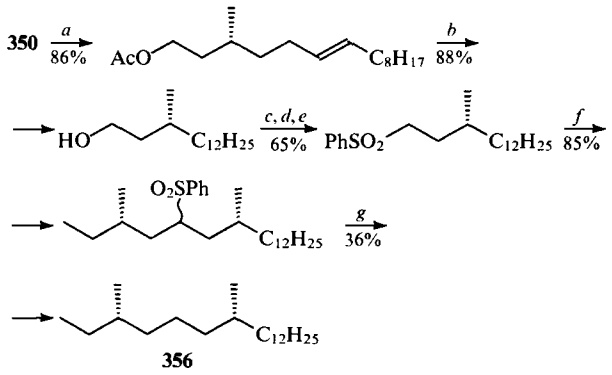
(*a*) $[H_2C{=}CH(CH_2)_8]_2CuLi$; (*b*) NaOH; (*c*) TsCl–Py; (*d*) Et_2CuLi.

10-Methyltridecan-2-one **354**—the optically active pheromone of the spotted cucumber beetle (*Diabrotica undecimpunctata*) with the (*R*)-configuration—has been synthesised from citronellyl acetate **347**, the ozonolytic cleavage of which afforded the acetoxyaldehyde **350**. The Kishner reduction of the latter led to (*R*)-3-methylhexan-1-ol **351**, which was converted into the iodide **352** and the alkynol **353** was obtained by coupling with the ethynylide **355**. Hydrogenation and oxidation of compound **353** led to the target pheromone.[165]



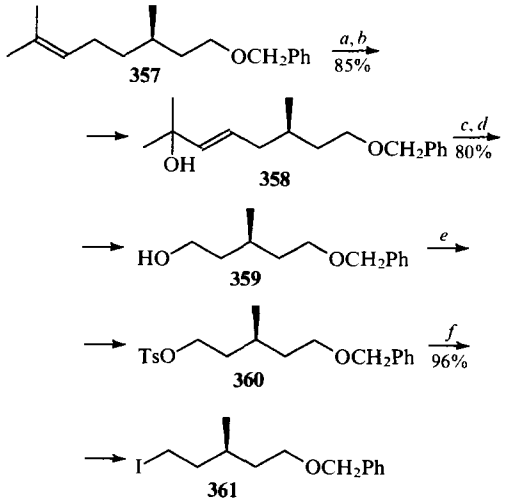
(*a*) O_3–MeOH–CH_2Cl_2; (*b*) Me_2S; (*c*) $N_2H_4 \cdot H_2O$–KOH; (*d*) TsCl–Py; (*e*) NaI; (*f*)  (**355**); (*g*) TsOH–MeOH; (*h*) H_2–Pd/C; (*i*) H_2CrO_4.

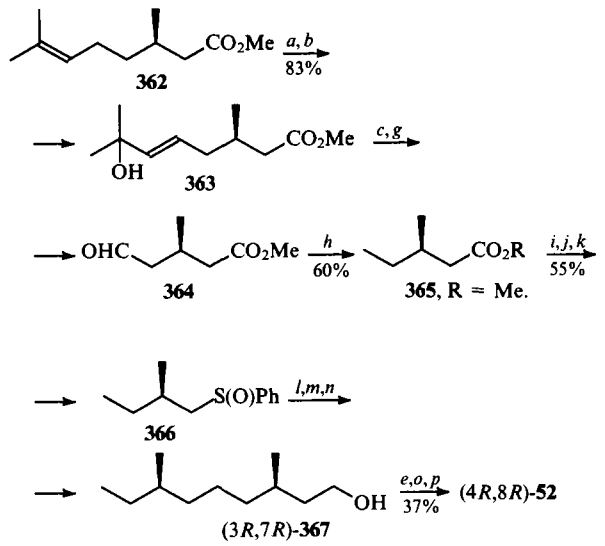
The chiral acetoxyaldehyde **350** has found an application in the synthesis of the sex pheromone **356** of the alfalfa blotch leafminer (*Agromyza frontella Rondarni*) in the construction of the (7*R*)-asymmetric centre.[166]



(*a*) $H_{17}C_8CH{=}PPh_3$; (*b*) $LiAlH_4$–$CoCl_2$; (*c*) TsCl–Py; (*d*) PhSNa; (*e*) MCPBA; (*f*) BuLi,  ; (*g*) Na–Hg–EtOH.

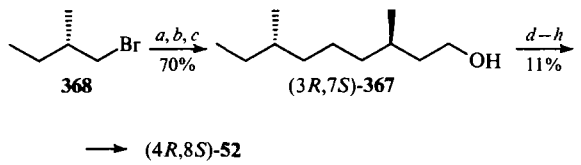
All four stereoisomers of 4,8-dimethyldecanal **52** have been synthesised from the acid **341**.[167] In the synthesis of (4*R*,8*R*)-**52** and (4*R*,8*S*)-**52**, the initial benzyl ether of citronellol **357** was oxidised to the allyl alcohol **358**, the ozonolysis of which (after reductive treatment) afforded the alcohol **359**. Its tosylate **360** and iodide **361** were used to construct the (4*R*)-asymmetric centre in the molecule of compound **52**. The sulfoxide **366**, obtained from the allyl alcohol **363** [the product of the oxidation of (*R*)-methyl citronellate **362**], was used to form the (8*R*)-centre. The ozonolysis of compound **363** yielded the aldehydoester **364**, which was subjected to the Huang-Minlon reduction to the acid **365**. The latter was converted in three stages into the sulfoxide **366**. Its coupling with the iodide **361** and subsequent hydrogenolysis led to the alcohol (3*R*,7*R*)-**367**, the increase in the chain length of which to give the target aldehyde (*R*, *R*)-**52** was carried out via the intermediate nitrile.





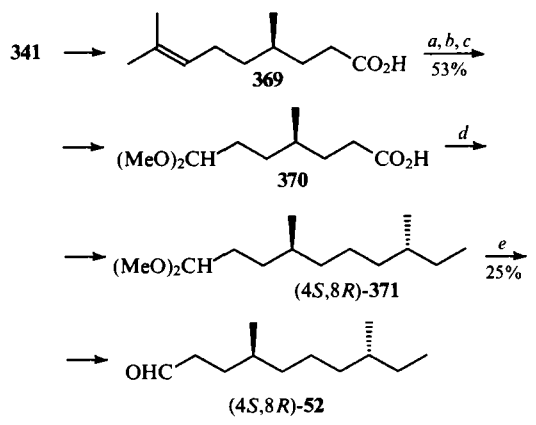
(*a*) $Ph_2Se_2-H_2O_2$; (*b*) Bu^tOOH; (*c*) $O_3-CH_2Cl_2-MeOH-NaHCO_3$; (*d*) $NaBH_4$; (*e*) TsCl–Py; (*f*) NaI; (*g*) Me_2S; (*h*) $N_2H_4 \cdot H_2O-KOH$; (*i*) $Pb(OAc)_4-I_2$; (*j*) PhSNa; (*k*) MCPBA; (*l*) BuLi; (*m*) **361**; (*n*) $Li-EtNH_2$; (*o*) NaCN; (*p*) DIBALH.

The (8*S*)-centre in the (4*R*,8*S*)-stereoisomer of compound **52** was constructed with the aid of the readily available (*S*)-2-methylbutyl bromide **368**, the coupling of which with the tosylate **360** led to the alcohol (3*R*,7*S*)-**367**. It was converted into the pheromone with the (4*R*,8*S*)-configuration via the corresponding nitrile.[167]



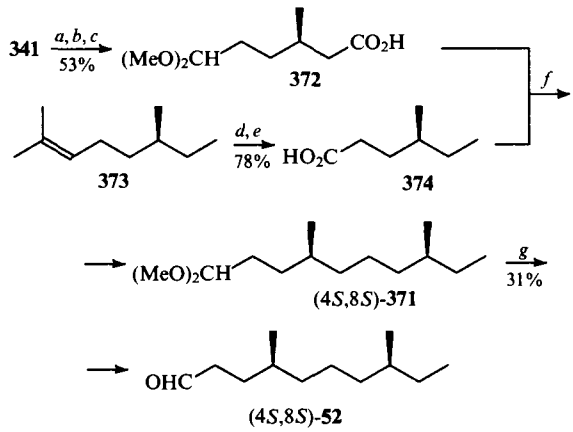
(*a*) Mg; (*b*) **360**–Li_2CuCl_4; (*c*) H_2–Pd/C; (*d*) TsCl–Py; (*e*) NaCN; (*f*) NaOH; (*g*) $LiAlH_4$; (*h*) PCC.

In the synthesis of the (4*S*,8*R*)-isomer, the chiral units for the construction of the skeleton of the sex pheromone were the acids **365** (R = H) and **370**. The latter was obtained by the ozonolysis of homocitronellic acid **369**. The Kolbe condensation of the acid correspondimg to **365** and **370** led to the acetal (4*S*,8*R*)-**371**, the hydrolysis of which afforded the aldehyde **52** with the (4*S*,8*R*)-configuration.[168]



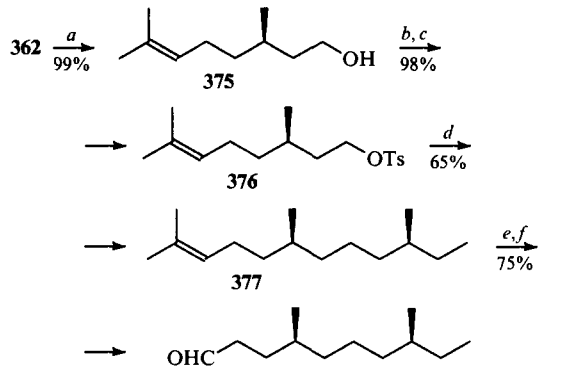
(*a*) O_3–MeOH; (*b*) Me_2S; (*c*) TsOH–MeOH; (*d*) NaOMe–MeOH, **365** (R = H) + e^- (Pt, 24 V, 0.8–1.2 A); (*e*) $HClO_4$.

The (*S*,*S*)-isomer of the pheromone **52** was synthesised in accordance with the same principle. The chiral units were the acids **372** and **374**, obtained by the ozonolysis of citronellic acid **341** and tetrahydromyrcene **373** respectively. The acetal (4*S*,8*S*)-**371**, obtained in the electrolysis of an equimolar mixture of the acids **372** and **374**, was readily converted into the target aldehyde (4*S*,8*S*)-**52**.



(*a*) O_3–MeOH; (*b*) Me_2S; (*c*) TsOH–MeOH; (*d*) O_3-Me_2CO; (*e*) H_2CrO_4; (*f*) NaOMe–MeOH, e^- (Pt, 24 V, 1.5 A); (*g*) 35% $HClO_4$–THF.

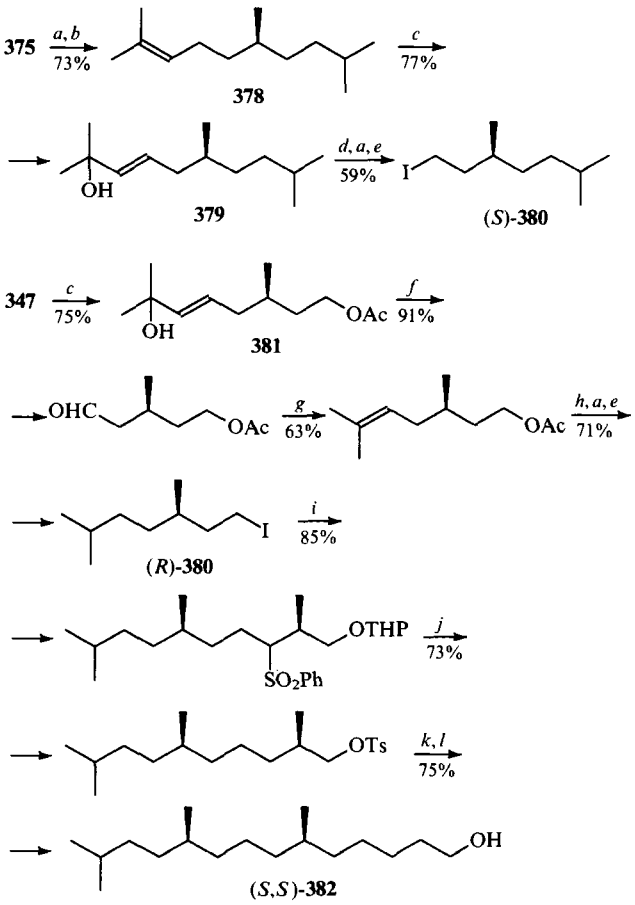
Yet another short path to the synthesis[169] of the enantiomerically pure (4*S*,8*S*)-dimethyldecanal involves the use of readily available chiral units—(*R*)-methyl citronellate **362** and (*S*)-2-methylbutan-1-ol **340**. The former reagent was converted in two stages, via the intermediate (*R*)-citronellol **375**, into the tosylate **376**, while the latter was converted into the bromide **368**, the Wurtz cross-coupling of these precursors afforded 2,6,10-trimethyldodec-2-ene **377**, which was converted by ozonolysis into the aldehyde **52** with the (4*S*,8*S*)-configuration.



(*a*) DIBALH; (*b*) BuLi; (*c*) TsCl; (*d*) **368** + Mg–Li_2CuCl_4; (*e*) O_3–MeOH–CH_2Cl_2; (*f*) Me_2S.

The phenyl sulfone (*S*)-**383** and the iodide **380** with the (*R*)- and (*S*)-configurations were used as the chiral building blocks in the syntheses of all four stereoisomers of 6,10,13-trimethyltetradecan-1-ol **382**—the aggregation pheromone of the predatory stink bug (*Stiretrus anchorago*).[170] [The reactions leading to (6*S*,10*S*)-**382** are shown in the scheme below.]

The carbon skeleton of (*S*)-**380** was constructed by converting (*R*)-citronellol **375** into 2,6,9-trimethyldec-2-ene **378**, its allylic oxidation (with rearrangement), and the subsequent ozonolysis of the product **379**. The iodide **380** with the (*R*)-configuration was synthesised by the ozonolytic cleavage of the allyl alcohol **381**, which can be readily obtained from citronellyl acetate **347** by the method described by Hori and Sharpless.[168]

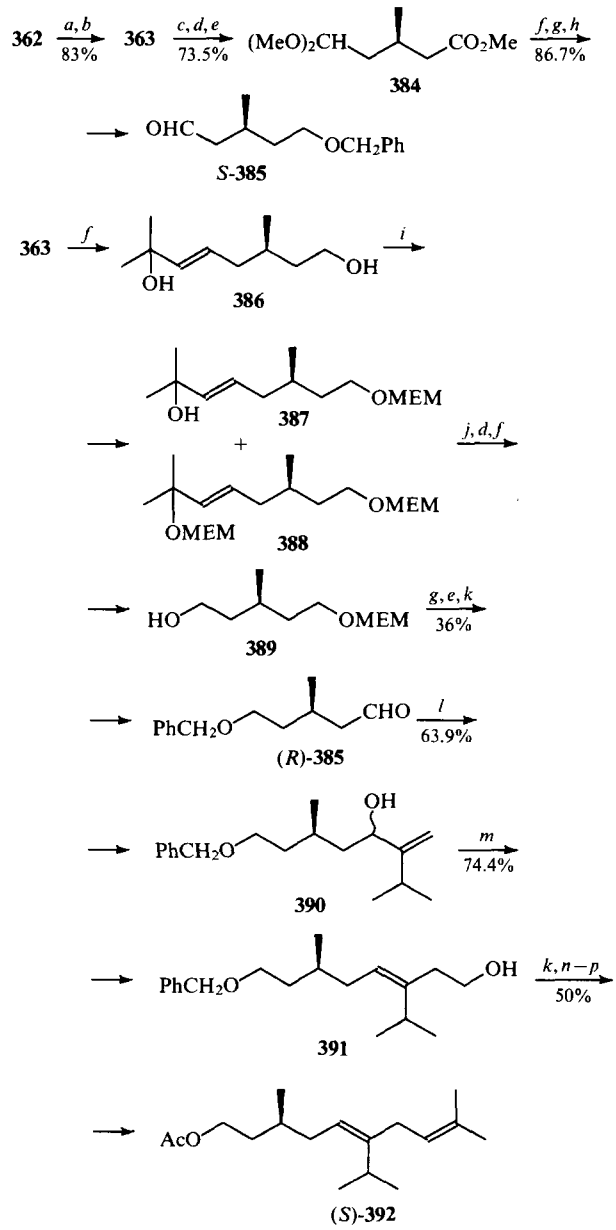


(*a*) TsCl–Py; (*b*) $Me_2CHMgBr–Li_2CuCl_4$; (*c*) $Ph_2Se_2–H_2O_2$, Bu^tOOH; (*d*) O_3, $NaBH_4$; (*e*) NaI; (*f*) O_3, Me_2S; (*g*) $Me_2C=PPh_3$; (*h*) $LiAlH_4–CoCl_2$;

(*i*) THPO–≡–SO_2Ph [(*S*)-**383**]–BuLi; (*j*) Na–Hg–EtOH; (*k*) $Cl(CH_2)_4OTHP–Mg–Li_2CuCl_4$; (*l*) TsOH–MeOH.

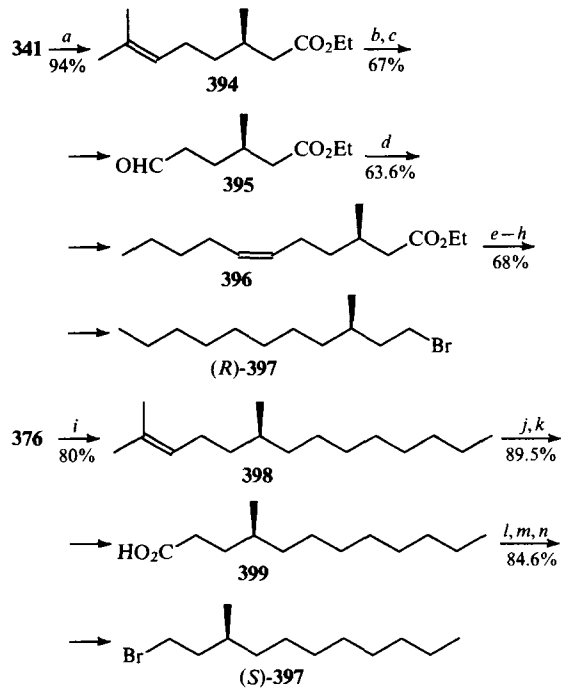
The allyl alcohol **363** — the product of the allylic oxidation of (*R*)-methyl citronellate **362** by a diselenide — has been used to synthesise the (*R*)- and (*S*)-enantiomers of (5*E*)-6-isopropyl-3,9-dimethyldeca-5,8-dienyl acetate **392** — the sex pheromone of the yellow scale (*Aonidiella citrina*).[171] The (3*R*)-centre in the molecule of compound **392** was formed by the conversion of the allyl alcohol **363**, by ozonolysis with reductive cleavage of the ozonide, into the dimethyl acetal **384**, which was converted by means of standard procedures into the key aldehydoester (*S*)-**385**. The optical isomer of the latter — the aldehyde (*R*)-**385** — was obtained from the same allyl alcohol **363** by its transformation via the diol **386** into a mixture of the mono- and di-esters **387** and **388**, the ozonolysis of which and two-stage reduction afforded the monosubstituted diol **389**. The latter was converted via its benzyl ether into the other key aldehydoester (*R*)-**385**. The further transformations of the aldehydes† (*S*)-**385** and (*R*)-**385** included stages involving interaction with the Grignard reagent derived from 2-bromo-3-methylbut-1-ene **393** and the 2,3-sigmatropic rearrangement of the resulting allyl alcohols **390** via their stannyl derivatives to the (*E*)-homoallyl alcohols **391**. The latter were oxidised to the corresponding aldehyde and were converted into the target (*S*)- or (*R*)-**392** by means of the Wittig alkene formation reaction.

† The scheme below indicates the reaction leading to the biologically active (*S*)-enantiomer of compound **392**.



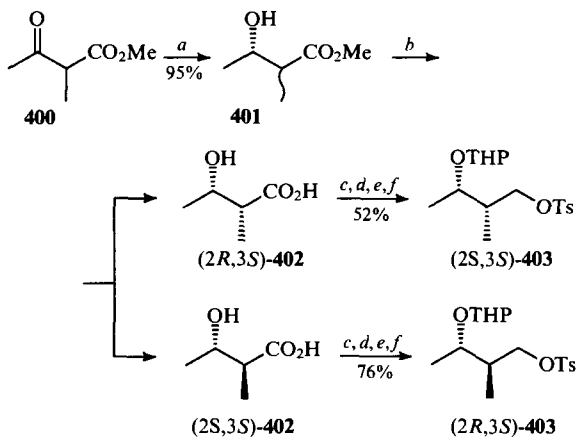
(*a*) $Ph_2Se_2–H_2O_2$; (*b*) Bu^tOOH; (*c*) O_3–MeOH; (*d*) Me_2S; (*e*) TsOH–MeOH; (*f*) $LiAlH_4$; (*g*) $PhCH_2Br–NaH$; (*h*) $HClO_4$; (*i*) NaH–MEMCl ($MeOCH_2CH_2OCH_2Cl$); (*j*) $O_3–CH_2Cl_2–MeOH–NaHCO_3$; (*k*) $CrO_3 \cdot 2Py$; (*l*) $H_2C=C(Pr^i)MgBr$ (**393**); (*m*) $Bu_3SnCH_2I–KH$, BuLi; (*n*) $Me_2C=PPh_3$; (*o*) $Li–NH_3$; (*p*) Ac_2O–Py.

Citronellic acid **341** has also been used in the synthesis of the isomers of 3,7-dimethylpentadec-2-yl acetate **53**, which forms part of the composition of the sex pheromone of the pine sawflies belonging to the genera *Diprion* and *Neodiprion*.[172] The synthesis consists of two stages. In the first of these, the C_{12} and C_5 blocks (**397** and **403** respectively) are formed simultaneously, while in the second they are coupled and the product is subjected to further transformation to give the target compounds. The acid **341** serves as the starting material for the synthesis of the C_{12} block **397** having both the (*R*)- and (*S*)-configurations. Compound (*R*)-**397** was synthesised by the ozonolysis of its ethyl ester **394** to give the aldehydoester **395** and its subsequent conversion into the unsaturated ester **396**. The optical isomer (*S*)-**398** was synthesised by alkylating (*R*)-citronellyl tosylate **376** and by the ozonolysis of the resulting alkene **398** to the acid **399**, which was then subjected to the Hunsdiecker reaction.



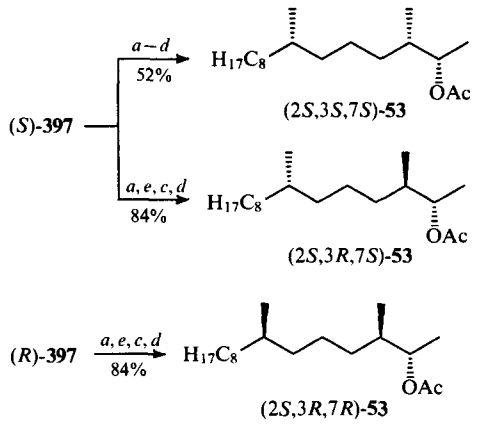
(*a*) EtBr; (*b*) O_3–MeOH; (*c*) H_2–Pd/C; (*d*) $BuCH{=}PPh_3$; (*e*) H_2–PtO_2; (*f*) $LiAlH_4$; (*g*) TsCl–Py; (*h*) LiBr; (*i*) n-$C_6H_{13}MgCl$–CuI; (*j*) O_3–CH_2Cl_2; (*k*) H_2O_2–HCO_2H; (*l*) NaOH; (*m*) $AgNO_3$; (*n*) Br_2.

The synthesis of the C_5 block with two chiral centres requires greater effort. The diastereoselective asymmetric reduction of methyl 2-methyl-3-oxobutyrate **400** led to a 3:1 mixture of the optically active *erythro*- and *threo*-alcohols **401**, which was separated by fractional crystallisation initially of their sodium salts and then of their ammonium salts. The products of such fairly laborious operations — the hydroxyacids (2*R*,3*S*)-**402** and (2*S*,3*S*)-**402** — were converted in four stages into the corresponding differentially protected diols (2*S*,3*S*)-**403** and (2*R*,3*S*)-**403**, which are necessary for the synthesis of the target products.



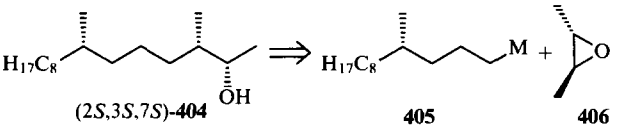
(*a*) H_2–Ni–(*S*,*S*)-$(HO_2CCHOH)_2$; (*b*) crystallisation; (*c*) CH_2N_2; (*d*) DHP–TsOH; (*e*) $LiAlH_4$; (*f*) TsCl–Py.

By combining the stereoisomers of the C_5 and C_{12} blocks in coupling reactions of the organomagnesium derivatives with the tosylates, three optically pure stereoisomers of diprionyl acetate **53** were obtained.

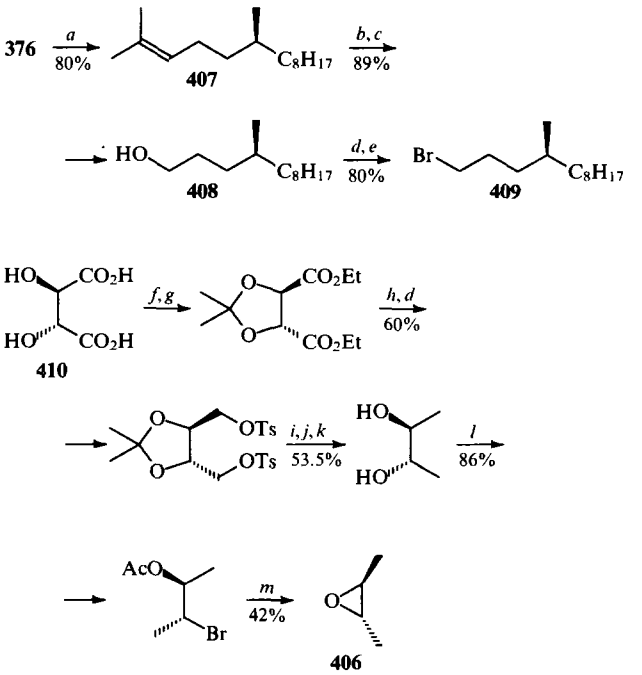


(*a*) Mg; (*b*) (2*S*,3*S*)-**403**–CuI; (*c*) TsOH–MeOH; (*d*) Ac_2O–Py; (*e*) (2*R*,3*S*)-**403**–CuI.

The retrosynthetic analysis of the structure of diprionol (2*S*,3*S*,7*S*)-**404** showed that it can be obtained by the reaction of the organometallic nucleophile **405** with (*S*,*S*)-2,3-epoxybutane **406**.

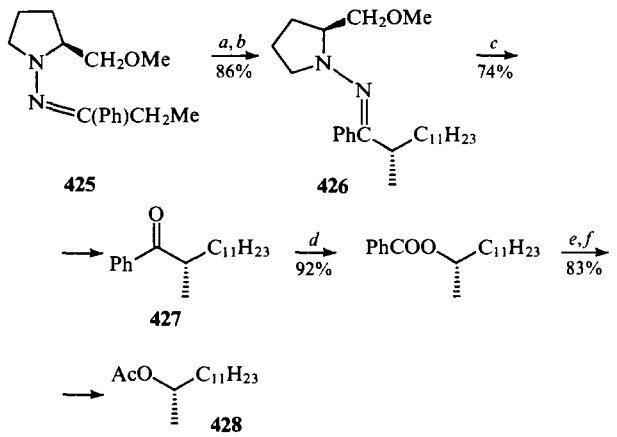


The real chiral building block corresponding to the fragment **405** — (*S*)-(+)-1-bromo-4-methyldodecane **409** — has been synthesised[173] from (*R*)-(+)-citronellyl tosylate **376** by coupling the latter with dihexyllithium cuprate and subsequent ozonolysis of the alkene **407** to the alcohol **408**. The complementary epoxide **406** was obtained from L-(+)-tartaric acid **410** in nine stages. On reaction with the epoxide **406**, the dialkyllithium cuprate prepared from compound **409** afforded the target diprionol **404** with a high configurational homogeneity of all three chiral centres.



The proposed method of synthesis[177] of the pheromone component **423** of the small wood ant (*Formica polyctena*) and the red wood ant (*Formica rufa*) was based on the Michael addition of the azaenolate generated from the hydrazone (*S*)-**419** to the (2*E*)-methyl pent-2-enoate **424** with the asymmetric induction of two chiral centres. The subsequent ozonolysis of the hydrazone **420** led to the aldehyde **421**, which was converted into the target pheromone **423** via the dithioacetal **422**.

A similar approach has been used in the enantioselective synthesis[178] of a component of the aggregation pheromone **428** of the fruit fly *Drosophila mulleri*, the key stages of which are the asymmetric α-alkylation of the azaenolate derived from the hydrazone **425**, the ozonolysis of the hydrazone **426**, and the Baeyer – Villiger oxidation of the ketone **427** accompanied by the inversion of the configuration.



(*a*) LDA; (*b*) $C_{11}H_{23}Br$; (*c*) $O_3-CH_2Cl_2$; (*d*) MCPBA; (*e*) $LiAlH_4$; (*f*) Ac_2O-Py.

Thus the present review of literature gives grounds for the conclusion that there is a growing interest in the use of the ozonolysis of unsaturated compounds at various stages of the total synthesis of insect pheromones and juvenoids, which frequently determine the success in the application of the chosen procedure.

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Current state of radiation processing

A K Pikaev

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Abstract. A review of common trends in the development of modern radiation processing is presented. The sources of ionising radiation and the most important processes practically induced under the influence of this radiation are discussed. It is shown that radiation methods can be used successfully for the modification of materials, for the sterilisation of medical articles, for the solution of ecological problems, for the treatment of food products, in radiation engineering, etc. Special attention is paid to processes at the pilot plant and industrial scales. The bibliography includes 548 references.

I. Introduction

The aim of radiation technology is to study, develop, and improve the methods, apparatus, and assemblies used to apply ionising radiations. Radiation methods are used to generate or to improve new properties in materials, new methods of exploiting them, new means of production, etc., and also to solve ecological problems, some problems in nuclear technology, and various other problems. Radiation processing is a relatively new field of study. The first radiation processes (radiation sterilisation of medical items and radiation cross-linking of the polyethylene insulation of wires) were introduced into industrial practice in the mid-1950s,[1] so that the introduction and development of radiation technology as a separate science has now been going on for 35–40 years.

In spite of the shortness of its past history this field of study has already achieved some definite successes. This is shown by the very abundant scientific and technical literature, which includes thousands of original papers and reviews, many patent disclosures and claims, specialised monographs,[1–64] and pamphlets in the 'Radiation-chemical technology' series,[65–87] and representative meetings of specialists held in various countries (in particular, international conferences on radiation technology organised every 2–3 years).[88–96]

Radiation technology still occupies a relatively modest place in the overall volume of industrial and agricultural production. The rate of growth of production by radiation methods is increasing continuously: ~15%–20% per annum. Thus, in foreign countries industrial products worth about 10^{10} US dollars are produced every year by radiation methods. In the not too distant future this could make the industrial production by radiation processes comparable in importance with conventional processes.

Radiation technology can be divided into radiation-chemical, radiation-physical, and radiation-biological processing. Modern radiation-chemical technology is being developed mainly along the following directions: (1) the radiation modification of materials (mainly polymeric); (2) radiation polymerisation, including radiation hardening and radiation graft polymerisation; (3) radiation degradation (mainly of polymeric materials); (4) ecology. The main aims of radiation-biological technology are the radiation sterilisation of medical articles and the radiation treatment of food products. The radiation-physical technology includes the radiation doping of semiconductors, ion implantation, the radiation treatment of articles used in electronic technology, etc. However, the boundary between these divisions of radiation technology is not sharp. A topic common to all these divisions is the construction of radiation apparatus (the production and assembly of sources of ionising radiation and of radiation equipment and the technological dosimetry of ionising radiations).

Regions of radiation-biological technology such as the radiation sterilisation of medical articles and preparations and the radiation treatment of food products are usually classified with the radiation-chemical technology. An important part of these problems is the radiation stability of the polymeric materials from which the medical articles and the medicinal preparations are manufactured, the qualitative and quantitative determination of the composition of the substances formed in the food products during their irradiation, and the identification of the irradiated products. Problems common to radiation-chemical and radiation-physical technology include the increase in the

A K Pikaev Institute of Physical Chemistry of the Russian Academy of Sciences, Leninskii prosp. 31, 117915 Moscow. Fax (7-095) 335 17 78

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corrosion resistance of metals and alloys during ion implantation, the radiation doping of semiconductors, etc.

This paper is a review of the current state of radiation processing, with special emphasis on processes realised under pilot plant and under industrial scales. It was written mainly from data published in the last 10–15 years.

II. Sources of ionising radiation

The following sources of ionising radiation are commonly used in radiation processing: ^{60}Co (and more rarely ^{137}Cs) sources of γ radiation, electron accelerators, $^{90}Sr + ^{90}Y$ sources of β radiation, ion implanters, and (very rarely) nuclear reactors.

1. ^{60}Co sources of γ radiation

γ Irradiators are used mainly in the radiation sterilisation of medical equipment and (to a smaller extent) in the radiation treatment of food products. More than 180 industrial γ irradiators based on ^{60}Co are currently operating over the world. The activity of ^{60}Co in one γ irradiator can be as high as 10 MCi. The largest foreign producer and supplier of industrial γ irradiators based on ^{60}Co is the Canadian 'Nordion International Inc.' company. Modern industrial irradiators are housed in specially equipped structures and are usually automated.

2. Electron accelerators

The total number of electron accelerators currently used in radiation processing (including research assemblies) is greater than 1000. The energy of the electron beams generated by electron accelerators is 0.15–10 MeV. Beams with an energy lower than 0.15 MeV are very seldom used because of their unacceptably low penetrating power. At energies greater than 10 MeV the irradiated objects begin to show a significant amount of induced radioactivity.

Industrial electron accelerators can be divided into three groups.[97]

(1) Low-energy accelerators, with an electron energy of 0.15–0.5 MeV and beam powers up to 300–350 kW. The characteristics of accelerators produced in various countries are summarised in Table 1.[1,98] More than 400 of these machines are currently operating over the world: more than 250 of them are used in industry. They are used mainly for hardening coatings, and for treating surfaces and thin-film items.

Low-energy accelerators can themselves be divided into three subgroups:[100] with a scanning beam, with an extended cathode, and with a multiple cathode. The first subgroup includes, for example, accelerators of the 'Aurora' type, the second includes accelerators of the 'Electrocurtain' type, and the third accelerators of the 'Broad Beam' type. We note that in recent years

Table 1. Characteristics of low-energy electron accelerators.

Type of accelerator	Producer	Energy/MeV	Power/kW	Beam width/m
ESH	Polymer-Physik (Germany)	0.15–0.28	Up to 56	0.22–2.5
EPS	Nissin High Voltage Co., Ltd. (Japan)	0.3 0.3 0.3	7.5 19.5 30	0.45 1.2 1.8
Aurora-2	NIIEFA (Russia)[a]	0.3–0.5	25	0.5–2.0
EOL-400	Radiotechnical Institute (Russia)	0.4	14	Up to 2.0
Electrocurtain	Energy Sciences Inc. (USA)	0.15–0.3	Up to ~100	0.5–2.0
BroadBeam	RPC Industries (USA)	0.15–0.3	Up to 360	0.3–2.5
LEA[b]	Institute of Surface Modification (Germany)	0.15–0.2	Up to 60	Up to 1.5
Elektron-16	NIIEFA (Russia)[a]	0.25–0.3	30	Up to 2.0
TUR-M	NTTs 'Energiya' (Russia)	0.15–0.28	10	Up to 1.8
Astra-11	NPO 'Astrofizika' (Russia)	0.2–0.3	25	0.6[c]
Tapir	'Tekra' Company (Russia)	0.3	30	1.2–2.1
Kangaroo	"	0.25	5	0.36
Finback whale[d]	"	0.3	150	6.0[e]

[a] Efremov Research Institute for Electrophysical Instrumentation, S. Petersburg.
[b] From Ref. 99.
[c] An appropriate distribution of moduli having these parameters can be used to establish a production line of any width.
[d] Project aimed at producing an accelerator with several exit windows. The quoted parameters are for a machine with 12 windows.
[e] Cross-sectional area of the beam, m^2.

Table 2. Parameters of moderately powerful electron accelerators.

Type of accelerator	Producer	Energy/MeV	Maximum power/kW
ELT electron transformer[a]	Institute of nuclear physics of the Siberian section of the Russian Academy of Sciences	1.5 – 2.2	15
ELV electron transformer	Institute of nuclear physics of the Siberian section of the Russian Academy of Sciences and Vladimir Il'ich Moscow works (Russia)	0.2 – 2.5	~100
ILU resonator linear accelerator	"	0.5 – 2.5	30
ICT transformer with insulated core[a]	High Voltage Engineering Corp. (USA)	0.3 – 2.5	125
FDJ transformer with insulated core	Research Institute of Automation for Machine-Building Industry (PRC)	0.3 – 1.2	24
'Elektron' (Cockcroft and Walton type)	NIIEFA (Russia)	0.75 – 2.5	~100
EPS (Cockcroft – Walton type)	Nissin High Voltage Co., Ltd. (Japan)	0.8 – 5.0	~150 – 200
Dynamitron	Radiation Dynamics Inc. (USA)	0.55 – 5.0	~200

[a]Production discontinued.

Table 3. Parameters of the linear accelerators used in radiation technology.

Brand of accelerator	Producer	Energy/MeV	Power/kW
LUE-8-5V	NIIEFA (Russia)	8	5
LUE-8-15S	"	8	15
UELV-10-10 (Elektronika-10-10)	NPO 'Torii' (Russia)	10	10
CIRCE II	MeV Industrie (France)	10	20
CIRCE III	"	5 and 10	20 at 5 MeV; 10 at 10 MeV
EB10	Scanditronix AB (Sweden)	10	30
IMPELA	AECL Accelerators (Canada)	10	50
Rhodotron	Ion Beam Applications S.A. (Belgium)	5 and 10	30 at 5 MeV; 50 at 10 MeV[a]

[a]The stated beam powers are guaranteed: a power of 100 kW can probably be achieved.

multicathode accelerators with powers of up to 400 – 500 kW and beam widths up to 3.2 m have been developed.[100]

(2) Intermediate-energy accelerators, with an electron energy of 0.5 – 5.0 MeV and a beam power of up to 300 – 350 kW. More than 500 of these machines are operating over the world. The parameters of accelerators of this group are shown in Table 2.[1,49,50,101–104]

Accelerators of the 'Dynamitron' type are the most widely used accelerators of this type outside the Russian Federation: about 150 of these machines were functioning in 1990.[105] Among the accelerators produced in Russia the most widely used are those of the ELV type (approximately 70 of these machines having been produced so far)[106] and of the ILU type (23 machines produced so far).[107] The nuclear physics institute of the Siberian Section of the Russian Academy of Sciences has developed an ELV-6M accelerator (electron energy 0.5 – 1.0 MeV and maximum beam power 200 kW) and a 'Torch' accelerator (energy 0.5 – 1.0 MeV, maximum beam power 500 kW).[108] In the USA an electron accelerator of the induction type with a beam energy of up to several megawatts is being developed.[109]

Intermediate-energy accelerators are used in many areas of radiation processing: for cross-linking the polyolefin insulation of cables, for the production of thermally formed articles and of foamed polyethylene, for the vulcanisation of the components of tyres, for the purification of waste water and gas discharges, etc.

(3) High-energy accelerators, with an electron energy of 5 – 10 MeV and a beam power of up to 100 kW. These are mostly linear accelerators: about 30 of these machines are used in

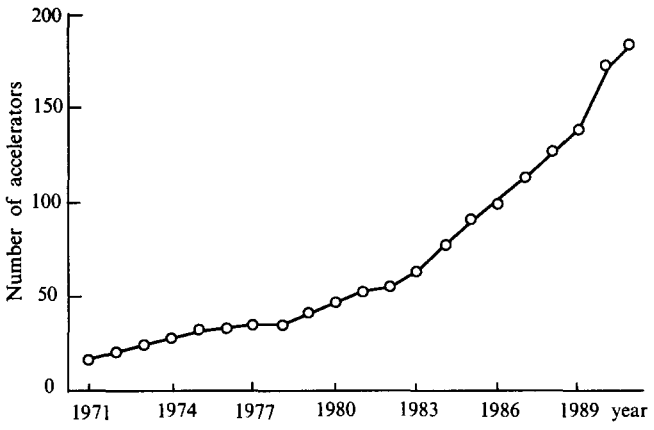


Figure 1. Increase in the production of electron accelerators by the Japanese firm 'Nissin High Voltage Co., Ltd.'

radiation technology. The parameters of some of them are given in Table 3.[1,50,98,110–115] They are used for the radiation sterilisation of medical articles and (to a smaller extent) for the radiation processing of food products.

At the present stage of development of radiation technology electron accelerators are much more generally used than sources of γ radiation. This is because of the greater operational safety and the greater power of the electron accelerators. The rates of development of electron-beam processes are illustrated in Fig. 1, which shows the increase in the number of electron accelerators produced by the Japanese firm 'Nissin High Voltage Co., Ltd.' for radiation technology during the period 1971 – 1991.[104]

3. Other sources

$^{90}Sr + {}^{90}Y$ β sources are used in radiation-physical technology, mainly in the surface treatment of semiconductor devices. Ion beams are also used for the same purpose, and ion implanters are very widespread. For example, about 800 implanters were operating in Japan in 1987.[116] Nuclear reactors were used as sources of ionising radiation only in the radiation doping of semiconductors.[35]

In recent years the possibility of exploiting the breaking (breamsstrahlung) X-radiation with a maximum energy of 5 MeV generated by electron accelerators with a beam power of 200 – 300 kW[113,117–122] is being studied. An electron beam with an energy of 5 MeV and a power of 200 kW can generate a bremsstrahlung X-radiation with a power of ~15 kW when decelerated in a high atomic number metal (for example, tantalum), counting only the radiation in the same direction as the stream of electrons: this is equivalent to the power of γ radiation from a ^{60}Co sample with an activity of ~1 MCi. However, an X-ray beam can be used more effectively (by a factor of approximately 1.5 – 2.5)[118] than γ radiation because ^{60}Co emits its γ quanta isotropically, i.e. in all directions.

Possible applications of the bremsstrahlung X-radiation include the radiation sterilisation of medical items and the radiation treatment of food products. Several equipments based on electron accelerators have already been assembled by using appropriate converters of electron beams into bremsstrahlung X-radiation,[113] and one assembly with an accelerator of the Cockcroft – Walton type (electron energy 5 MeV, beam energy 150 kW) produced by the 'Radia Industry Co., Ltd.' (Japan) has been used on commercial applications[121] since 1992.

III. Radiation modification of materials

The radiation modification of materials is the controlled (and therefore useful) change in their properties produced by using irradiation. The ionising radiation is most often used to modify polymers, because of the high molecular mass of polymers, which allows even relatively small doses to produce marked changes in its properties.

The radiolytic conversion most useful in practice in polyolefins is cross-linking. This is used in various industrial processes, such as the modification of polyolefins [mainly polyethylene and poly(vinyl chloride)], the insulation of cables and wires, the preparation of stronger and heat resistant films, tubes, and manufactured articles, the production of polyethylene foams and (in a much smaller volume) of polypropylene foams, the vulcanisation of elastomers and items made from them (components of tyres, polysiloxane rubbers aimed at the production of thermally stable self-adhesive electrically insulating tapes and rubber-glass cloth, latex from natural raw rubber, rubber gloves, etc.).

1. Production of cables and wires with a radiation-cross-linked insulation

The radiation cross-linking of polyolefins increases their mechanical strength and heat resistance, improves their electrical insulation properties (especially at high temperatures), etc. For these reasons the process discussed in this section is widely used in the production of cables and wires.[1,5,6,10,17,20,50,79,123]

The radiation cross-linking of polyolefin insulation was first achieved in the USA in the 1950s. At present the list of countries in which this process is applied includes Japan, Great Britain, France, Germany, the PRC (China), and several others. In the former Soviet Union 16 industrial lines with electron accelerators of the ELV or ILU type (maximum power ~0.5 MW) were operated.[97,123] Many of these lines were found in the 'Belarus'kabel' plant (Belorussia); their combined maximum annual production was $(160-180)\times10^3$ km of wires with cross-sections between 0.12 and 6.0 mm^2 (see Gofshtein[124]). In Japan ~12% of the insulation produced is radiation-cross-linked.[125]

The radiation method is used to modify mainly polyethylene and poly(vinyl chloride) insulation. Radiation treatment is applied on a smaller scale to insulations of poly(vinylidene fluoride), chlorosulfonated polyethylene, the ethylene – propylene terpolymer, the copolymer of ethylene and tetrafluoroethylene, etc. Radiation-cross-linked polyurethane has recently started to be used as insulation.[126]

The sources of ionising radiation used to irradiate wires and cables are mainly electron accelerators with an energy of 0.3 – 5 MeV and powers of up to 100 – 150 kW. The dose needed to cross-link grades of polyethylene made abroad is 0.2 – 0.4 MGy,[127] whereas the indigenous grade of cable polyethylene requires 0.5 MGy.[123] This dose can be greatly lowered by adding sensitisers to the polyethylene. Typical sensitisers include dipropargyl succinate (which when used as an additive lowers the radiation dose to 0.1 – 0.12 MGy),[128] trimethylolpropane triacrylate and trimethylolpropane trimethylacrylate,[129] alkylamides and some aminoalcohols,[130] etc.

The use of sensitisers is specially valuable with a poly(vinyl chloride) insulation, because when exposed to relatively high doses (60 kGy and above)[131] this polymer undergoes marked structural degradation. Triallyl cyanurate,[132] tetraethyleneglycol dimethacrylate,[133] and other compounds have been proposed as sensitisers for this material.

An important scientific and technical problem, met in conjunction with the use of wires and cables with radiation-cross-linked insulation at high temperatures, is the need to inhibit processes leading to the thermal oxidation of the insulating polymeric material. This thermal oxidation can be suppressed by introducing special substances (antioxidants) into the polymer. In the case of polyethylene effective antioxidants include some phenolic compounds [for example, 1,1,3-tris-(2-methyl-4-hydroxy-5-*tert*-butylphenyl)butane], aromatic amines [for example, *N*,*N*′-diphenyl-*p*-phenylenediamine], and organic substances containing sulfur [for example, 4,4,thio-bis-(6-*tert*-butyl-3-methylphenol)].[134–138]

However, by reacting with the free radicals formed during the irradiation of the polymer the antioxidants increase the dose needed to achieve cross-linking. In this respect organosulfur antioxidants are better than phenolic compounds, since their use induces a much smaller increase in the dose.[137] We note that additives acting simultaneously as sensitisers and as antioxidants have been developed in Russia.[123]

Another important problem is the elimination of fire hazards from cable items having a radiation-cross-linked polymeric insulation. Additives which lower the inflammability (called antipyrenes) include decabromodiphenyl oxide, tetrabromobisphenol, condensed bromacenaphthalene, and aluminium hydroxide.[137,139-141] Condensed bromacenaphthalene (whose molecule contains 1-10 bromacenaphthalene units and 2-4 bromine atoms) is specially effective in the protection of chlorinated polyethylene and of the ethylene-propylene terpolymer.[141,142] Furthermore it is an antioxidant, and ensures radiation stability of the polymer up to 10 MGy. These properties are due to its grafting to the polymer chain during the irradiation.

The radiation cross-linking of polymers has a number of advantages over the chemical reaction, which uses peroxides as initiators.[143] They include better exploitation characteristics of the product, a cheaper process, lower energy losses, and a gain in the working areas. This explains why wires and cables with a radiation-cross-linked polymer insulation are now industrially produced in many countries. They are used in telecommunication systems, in military and in cosmic technology, in electronics and computer instrumentation, in the electric systems of automobiles, in nuclear reactors, etc.[20,131,139-141,144,145]

2. Preparation of densified and thermosetting items

The second radiation-chemical process realised in industry, based on the cross-linking of polymers (mainly polyethylene), is the preparation of densified and thermosetting items. They include thermosetting films, tapes, small bags, small and large tubes, hoses, flaps, and items of a more complex configuration used in the electrical industry, in the automobile and food industries, in electronics, in ship building, and in construction.[79,146-150]

The 'memory' effect (also known as 'shape memorising') provides the basis of the preparation of thermosetting items.[151] Essentially in this effect a polymeric material is irradiated with a dose smaller than the dose corresponding to gel formation, deformed at a temperature higher than the melting point of the crystallites, and then cooled rapidly. After a second heating to the same temperature, it tends to regenerate its initial form (owing to the formation of a three-dimensional network). If this material is stretched over any item it forms a tightly fitting shell after the heating process.

In addition to polyethylene we can use poly(vinyl chloride), poly(vinylidene fluoride), some rubbers, ethylene-ethyl acrylate and ethylene-vinyl acetate copolymers, etc. to prepare thermosetting items. In most cases electron accelerators are used in the production of thermosetting articles. Electron beams with an energy of 1-3 MeV are used to irradiate tubes, and with films and tapes the beams have an energy of 0.5-1.0 MeV.[147] Assemblies based on transformers with an insulated core and dynamitrons have been developed in the USA; in Russia accelerators of the 'Aurora', 'Elektron', ELV, and ILU type are used. In particular, in Russia a special workshop producing thermosetting polyethylene films and tubes[152] has operated 5 electron accelerators since 1978. The operating speed of this assembly is 1600 t a^{-1}. Two industrial lines have recently been mounted in Syzran' for the production of thermosetting polyethylene tapes: both are fitted with an accelerator of the ELV type (beam power 40 kW).[152] The operating speed of each line is 800 t a^{-1}. In foreign countries thermosetting items are produced by 'Raychem' (USA), 'Nitto' (Japan), and other firms.

The technology of the preparation of thermosetting films differs somewhat from the production technology of small pipes, of tubes, and of flaps. The production of thermosetting films[1,79,146] is shown schematically in Fig. 2. The best dose is 0.12 MGy.[79] Thermosetting pipes, tubes, and flaps can be produced by two methods.[147] In the first the tubes are produced by extrusion; they are then electron irradiated, their diameter is increased by orienting them above the melting point, and they are rapidly cooled, producing a new diameter. In the second method (called the tape method) a polyethylene tape is prepared by extrusion, is irradiated, exposed to oriented heating, and rapidly cooled; tubes are then produced from the heated tapes by winding them on a mandrel. It has been stated that the doses needed for the production of tubes and tapes could be 0.2-0.3 MGy[147] or 0.1-0.12 MGy[79-148] Obviously, the difference is due to differences in the state of the polymeric compositions used in the process.

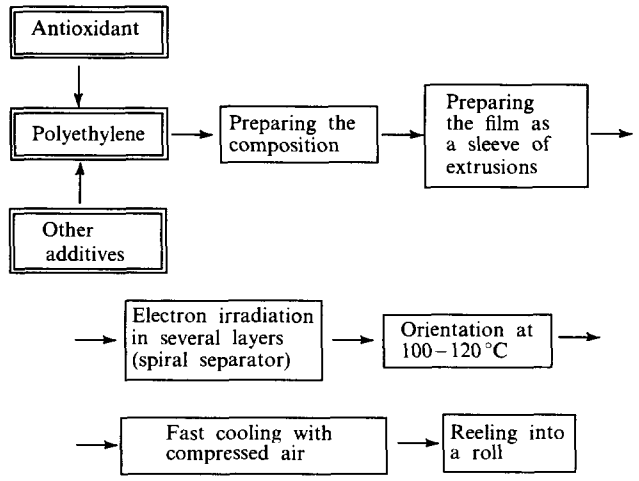


Figure 2. Scheme for the production of thermosetting films.

In the USA thermosetting films are used for packing cooled foodstuffs under vacuum.[146] The 'termoplen' film, produced in Russia, is also a packing material, whereas the 'agroplen' film is used in industrial hothouses to cover the soil before admitting overheated steam in order to eliminate harmful vegetable cultures.[152] Polyethylene tubes made of 'radplast T' are used for the insulation of connected wires and terminals in electric wiring, for the upkeep of damaged insulation, etc. 'Radlen' polyethylene films have been designed to protect gas and petroleum ducts from corrosion.[152]

3. Production of radiation-cross-linked foamed polyethylene

The production technology of radiation-cross-linked polyethylene foams was developed in Japan in the mid-1960s.[153,154] This material is produced in several countries at present.[154-156]

The production of radiation-cross-linked polyethylene foams includes the following main steps: the preparation of the initial composition, the production of the intermediate product (as a sheet) by extrusion at a temperature not above 125-130°C, the irradiation of this sheet by electrons in order to induce cross-linking (dose of 50-70 kGy), the foaming of the cross-linked item at 180-200 °C by the decomposition of a gas former (often known as a porofore) introduced into the composition. A commonly used porofore is diazodicarbonamide $H_2NCON{=}NCONH_2$, which decomposes at ~200 °C (giving 200-250 cm^3 of gaseous products per 1 g of porofore, including CO, CO_2, N_2, and NH_3. Foaming promoters (usually zinc stearate[155]) are added to the composition to lower the decomposition temperature of the porofore. Other additives are also used if necessary: antioxidants, cross-linking sensitisers, dyes, etc. The purpose of the irradiation is to increase the viscosity of the polyethylene melt as a result of cross-linking. An increase in density suppresses the emission of gas from the melt and thus greatly increases the volume of the polymer.

Radiation-cross-linked polyethylene foams have good cushioning and thermal insulation properties, low water absorption, and good elasticity.[154,156,157] In Russia polyethylene foams are produced from low-density polyethylene. It is available as foamed sheets with smooth surfaces (from 0.5 to 1.0 m wide, from 3 to 5 mm thick, up to 50 m in length).[157] These parameters of the radiation-cross-linked polyethylene foams allow them to be used in the building and automobile construction industry, in the production of sporting equipment, as a heating medium and a packing material, etc.

A method of producing cross-linked polyethylene foams with an improved surface was recently reported in Japan.[158] It consists in irradiating polyethylene containing diazodicarbonamide and dicumyl peroxide (initiators of chemical cross-linking) with electrons having an energy of 0.2–0.5 MeV, and then heating it to 220 °C. Cross-linking takes place in the bulk of the polymer as a result of the free radicals formed in the thermal decomposition of the peroxide: because of its low energy the electron beam can induce the radiation cross-linking of polyethylene only in a thin surface layer.

The technology for the preparation of radiation-cross-linked polypropylene foams was developed recently.[144] It is similar to the production technology of polyethylene foams, except for the higher temperature of the process. It was found that the dose should correspond to a gel fraction of 25%–45%. Radiation-cross-linked polypropylene foams have a much higher thermal stability (i.e. a smaller loss in volume when stored at a given temperature) than radiation-cross-linked polyethylene foams. The difficulty in preparing polypropylene foams arises from the rapid decrease in the viscosity of the melt with increase in temperature.[159] This disadvantage can be eliminated by adding polyethylene.[159]

4. Vulcanisation of elastomers and of items made from them

In the case of elastomers we replace the concept of 'cross-linking' by 'vulcanisation'. The radiation-induced vulcanisation of various elastomers and items made from them has found industrial application.

a. Vulcanisation of the components of tyres

It has long been considered (since the late 1950s) that the radiation vulcanisation of automobile tyre casings should be a promising area of application of ionising radiation. However, it was subsequently shown[77] that this process is undesirable because of the complexity of the configuraiton of the tyres, the variety of the chemical nature of tyres, and especially because of the presence of cord, whose strength is degraded by the irradiation. The idea of a combined thermal and radiation vulcanisation of tyres, for example by using ionising radiation for the final vulcanisation of the tyres after a partial thermal vulcanisation,[77] also failed to achieve industrial application because of lack of financial advantage.

A practically more successful approach was a preliminary irradiation of stocks of the individual components of tyres (protectors, carcasses, side walls, etc.) before assembly, formation, and thermal vulcanisation.[160,161] Electron accelerators with energies of 0.8–1.0 MeV were used as the source of radiation. The dose required for the treatment varies from 1 to 200 kGy, depending on the type of radiation. This preliminary treatment allowed the cohesive strength of the raw materials to be increased and some of the natural rubber to be replaced by synthetic rubber while keeping the total time of manufacture of the tyres constant to within ~20%.

The preliminary radiation treatment of the components of tyres has found industrial application in other countries (mainly the USA and Japan). For example, in Japan 9 electron accelerators with a total power of ~0.6 MW were used for this purpose in 1988.[116,162,163]

b. Production of thermally stable self-adhesive electrically insulating materials

In 1971 a radiation method of producing thermally stable self-adhesive electrically insulating tapes and rubber–glass cloths from polyheterosiloxane rubber was developed and introduced into industry.[66,164–166] The production of electrically insulating tape is achieved by using γ radiation from ^{60}Co, and that of rubber–glass cloth by an electron beam generated by an ELV accelerator. Assemblies of this type are now operating in a factory at Kazan'.[66]

The production of electrically insulating tape includes the following steps:[66] the preparation of the initial composition, consisting of polyheterosiloxane rubber with some additives, the addition of pigment to the composition in the rubber mixer at temperatures not above 50 °C, the preparation of stocks of the tape on a polyethylene substrate as rolls 13–15 cm in diameter, their radiation vulcanisation with a ^{60}Co γ source (dose of 0.10–0.13 MGy). Since the preparation of the tape is a batch process, blocks of 25 rolls of the tape are rotated during the irradiation in order to distribute the dose uniformly. The source of γ radiation has a projected activity of 0.75 MCi and an average dose rate of 2.2 Gy s^{-1}.

Siloxane rubber with an additive of a halogenated polymer containing boron is used for the production of the electrically insulating tape.[166] Its vulcanisate has the properties of autohesion and adhesion at room temperature, apparently due to the presence of B–O groups in the polymer chain. Tapes produced by this method are the leading electrically insulating material. They are characterised by a good autohesion, high stability towards water and ice, and long working life (at 250 °C they retain their properties for 200–300 days).[66]

The technological process of preparing self adhesive rubber–glass cloth consists in steeping the glass cloths in a solution of polysilosane, removing the solvent, depositing on the impregnated glass cloth the main layer of rubber mixture, and vulcanising the composite material with an electron beam (using a dose of 50–70 kGy).[66] A ^{60}Co source of γ radiation can also be used for the vulcanisation. In this case the cloth is irradiated in rolls. The operating characteristics of the cloth are approximately the same as in the tapes described above.

c. Other processes based on the vulcanisation of elastomers

Several other processes based on the radiation vulcanisation of elastomers have been described. In Indonesia a pilot plant based on a ^{60}Co γ source (with an activity of 225 kCi) is being operated for the vulcanisation of natural rubber latex.[167] The dose is ~30 kGy (with a dose rate of ~2.8 kGy h^{-1}). The operating speed of the assembly is 1000 t a^{-1}.

The radiation vulcanisation of the latex of natural rubber is one of the stages in the preparation of rubber gloves for handling radioactive preparations.[168] The γ radiation from ^{60}Co is used for this purpose (with a dose of 12 kGy).

It has been reported[169] that the vulcanisation of rubber based on butadiene–styrene copolymer under the influence of electron radiation generated by a linear accelerator can be used in the production of rubber 'cushions' for the tracks of tanks. A technology for the production of medical tubes from siloxane rubber, and roofing and water-repelling material with an atmosphere-resistant layer of ethylene–propylene or butadiene–styrene rubber by using electron radiation to vulcanise these elastomers has been proposed.[170]

5. Other processes based on the cross-linking of polymers

In addition to producing the insulation of wires and cables, thermosetting items, and polyethylene and polypropylene foams the radiation cross-linking of polymers is used to make other products and materials, such as polyethylene tubes for hot water installations,[79,171] matrices of filled polyethylene for concrete and reinforced concrete items,[172] protecting rings of low-pressure polyethylene for rubber packing in water apparatus,[173] insulators of ethylene–vinyl acetate copolymer filled with

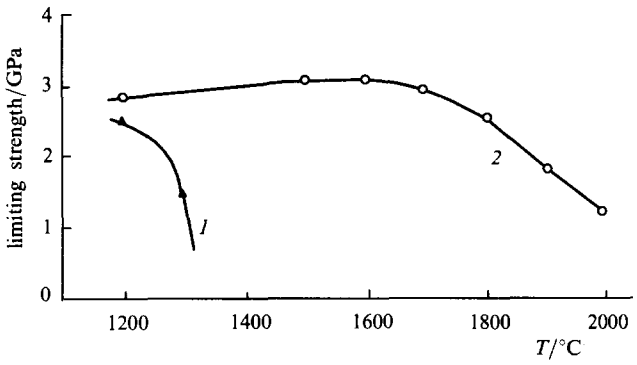


Figure 3. Temperature dependence of the limiting tensile strength of silicon carbide filament prepared by the usual method (*1*) and by using electron-beam treatment (*2*).[176]

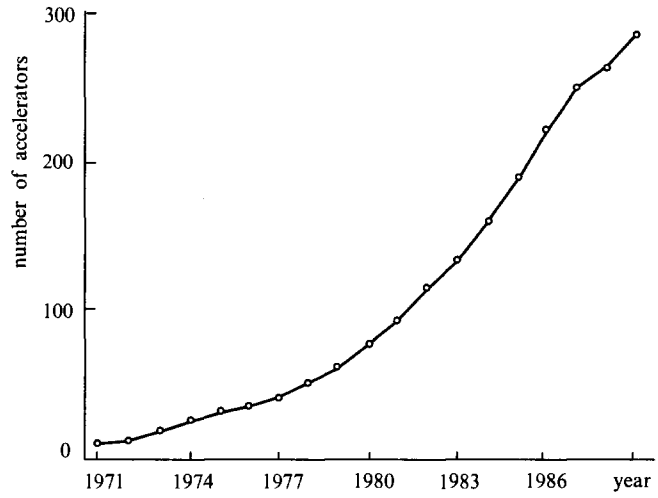


Figure 4. Increase in the number of assemblies with electron accelerators for hardening coatings.

aluminium hydroxide,[174] plastics [for example, of poly(ethylene terephthalate) and nylon] with improved thermal stability for use in modern electronics,[145] etc.

We shall briefly dwell on one new radiation process: the preparation of fibres of silicon carbide SiC.[175–177] This fibre is obtained by heat treatment at 1200 °C of radiation-cross-linked polycarbosilane fibre. It was found that the fibre has a higher thermal stability than the silicon carbide fibre prepared from thermally cross-linked polycarbosilane (see Fig. 3 and Ref. 176). The dose needed to achieve cross-linking is 10 MGy. In Japan a pilot plant is batch operated with an electron accelerator to treat 4.5 kg of polycarbosilane. A project for the commercial establishment of a production rate of 1 tonne of silicon carbide fibre per month in 1996 has been worked out in detail.[176,177]

IV. Radiation polymerisation

Many radiation processes realised on pilot plant and on industrial scales are based on the radiation polymerisation of monomers and their mixtures. These include primarily the radiation hardening of coatings (mainly under the influence of electron beams) and radiation graft polymerisation.

1. Hardening of the coatings

The radiation hardening of coatings has been introduced into industry in many countries.[1,67,98,101,102,116,178–195] In terms of the power of the electron accelerators this process occupies an intermediate place (coming after the radiation cross-linking of the polyolefin insulation of cables and wires). In 1990 ~350 laboratories, pilot plants, and industrial assemblies with electron accelerators for the hardening of coatings were operating throughout the world. Rates of development of this region of radiation technology are illustrated in Fig. 4, which shows the growth of the number of assemblies fitted with an electron accelerator (not including data for the former Soviet Union and for the People's Republic of China).[179]

The wide-ranging interest in radiation hardening was due mainly to its advantages over thermochemical hardening.[1,27,67,196] It was claimed to have a much lower (~85 times) energy consumption,[197] and to offer a gain in working areas, a reasonably high rate, the ability to operate at room temperature, and a lower consumption of reactants. It should specially be stressed that radiation hardening is a cleaner process from an ecological standpoint. Under thermal hardening the organic solvents in the hardened compositions are evaporated into the atmosphere. Industry produces approximately ~20 million tonnes of ordinary compositions every year [177] and, as a result, ~8 million tonnes of organic solvents are introduced into the surrounding medium. Radiation-hardened compositions contain no solvents. Unfortunately, these compositions (together with those obtained by photochemical hardening) account for only 1% of the total production. Obviously, in the interests of the protection of the ecological environment every effort should be made to replace the thermal method of hardening by the radiation (or photochemical) method.

Radiation hardening offers the following advantages over the photochemical hardening under the influence of UV radiation:[179,182] photoinitiators are not required, absence of sensitivity to pigments, uniform hardening even in relatively thick coatings, almost 100% conversion, and the possibility of grafting the monomer to the polymeric substrate. At the same time, the photochemical hardening offers a substantially lower cost (usually by 2–20 times) for the apparatus and instrumentation,[179] less attack on the sample, and lack of an oxygen effect. The high cost of hardening under the influence of electron radiation is often responsible for the preferential application of thermal or photochemical methods. For example, in Japan 29 090 photochemical assemblies were operating in 1988, as opposed to only 60 with electron accelerators.[116]

The doses needed to harden coatings depend on the state of the composition to be hardened and on the irradiation conditions, and usually lie between 20 and 200 kGy.[67] A high operating speed for these relatively high doses can be achieved by using sufficiently powerful electron accelerators. Since the thickness of the coatings is usually small mainly low-energy accelerators are used in this region of technology (electron energy between 0.15 and 0.35 MeV).

The most widely used accelerators are of the 'Electrocurtain' type (see Table 1): in 1991 ca. 200 of these machines were used for radiation hardening.

The power of the electron beams is expressed in kW, but the operating speed of the electron-beam assemblies is often measured in MGy m min^{-1}. For the low-energy accelerators made abroad whose parameters are listed in Table 1 the productivity in these units is 8.2, 3.75–15, and 2–12 respectively for EPS,[198] 'Electrocurtain',[199] and 'Broad Beam'.[100] These machines can be constructed with several accelerator tubes in order to increase the operating speed of the assembly. For example, accelerators of the 'Aurora' type are produced with 1–3 tubes, and accelerators of the 'Electrocurtain' type have between 1 and 4 tubes.[200,201] The power of an accelerator of the 'Electrocurtain' type with four accelerator tubes arranged in series is 100 kW m^{-1} (with an energy of 0.175 MeV).

Assemblies based on accelerators which generate electron beams of higher energy are sometimes used. This happens when the hardening of coatings is combined, for example, with the cross-linking of a polymeric substrate. In particular, electron accelerators of the ELV type (1.2–1.5 MeV energy) are used in

Russia for the production of artificial leather, in which the hardening of the decorative and protective coating is combined with the cross-linking of the polymeric material of the leather (see below).

The basis of hardening compositions are mixtures of unsaturated oligomers (oligoester maleates, oligoester-, polyester, polyurethane and epoxyacrylates and acrylates of organosilicon compounds) and vinyl monomers such as styrene, triethyleneglycoldimethacrylate, hexanediol-1,6-diacrylate, 2-ethylhexyl acrylate, tripropyleneglycol diacrylate, trimethylolpropane triacrylate, and pentaerythritol triacrylate.[67,202–205] In addition to oligomers and monomers the compositions may contain pigments, fillers, inhibitors, stabilisers, and other additives.

Irradiation produces copolymerisation of the oligomer and of the monomer with formation of a stable and insoluble three-dimensional cross-linked polymer. In the great majority of cases this 'thin-layer' radiation polymerisation is a free-radical process, strongly inhibited by the presence of oxygen. If the hardening is carried out in air the oxygen reacts with the free radicals in the surface layer of the coating, suppressing the polymerisation and producing an adhesive and insufficiently hard surface.

Several methods of overcoming the oxygen effect have been suggested.

(1) Irradiation in an atmosphere of inert gas (nitrogen, CO_2, combustion products of natural gas).[67]

(2) Closing the layer to be hardened with a polymeric film (for example, polyethylene or nylon), and removing the film after the irradiation.[206]

(3) Sequential irradiation with an electron beam and with UV light: also called the 'double hardening' method. The light dissociates the peroxidic compounds and induces additional polymerisation as a result of the free radicals created by the process.[184,207]

(4) Using additives which inhibit the oxidation (for example, amines) or which sensitise the hardening (for example, salts of transition metals),[208] or also 'floating' additives (for example paraffin wax).[67,209]

(5) Covering the composition to be hardened with a protective layer of water.[209]

(6) Using special compositions containing oligomers modified by phthalic anhydride, dicyclopentadiene, styrene, etc.[47,210]

(7) Irradiating at very high dose rates ($\sim 10^{11}$ Gy s^{-1}), generated by nanosecond pulses of electrons.[211]

(8) Polymerisation by a cationic mechanism (in this case the oxygen has practically no inhibiting effect).[208,209] This type of hardening is only seldom met.

Methods of suppressing the effect of oxygen were discussed in detail in a review by Fomina et al.[212] In practice only the first three methods have been realised (the second only once). The third method began to be used a few years ago. Nitrogen containing not more than 0.05%–0.1% of oxygen as an impurity is usually used as the inert gas.[209,213]

In recent years the technique of radiation hardening of various polymeric coatings has been developed and brought into industrial practice (paints and varnishes, adhesives, magnetics, metallised materials, printing dyes, etc.) on many surfaces (timber, metallic, ceramic, stone, paper, polymeric, on magnetic disks, etc.).[1] Table 4 shows a list of the materials with radiation-hardened coatings produced in Russia and the Ukraine. The list of the corresponding articles produced by the foreign industry is even wider.[1] In particular, it includes timber parquet tiles and massive rocket bodies.

Table 4. Products with radiation-hardened coating produced in Russia and the Ukraine.

Product	Location of equipment	Operating speed	Ref.
Wooden panels for television sets [a]	L'vov, Simferopol, Samara	11 m^2 min^{-1} (L'vov)	67, 214, 215
Wooden panels for furniture	Kiev, [a] Moscow	950 000 m^2 a^{-1}	67, 216
Artificial leather	Kirov [b]	1.3 $t\,h^{-1}$	217, 218
Gypsum–polymer plates with decorative coatings	Kolomna (Moscow region)	200 000 m^2 a^{-1}	219
Asbestos–cement plates with decorative coatings	Near Moscow	200 000 m^2 a^{-1}	67, 218
Ceramic lining plates with decorative coatings	Dnepropetrovsk	2–5 m^2 min^{-1}	220
Plenkosintokarton [c]	Moscow	—	221, 222
Premelts for the production of laminated glass textolite	"	—	221, 222
Polymeric pressure-sensitive thin-film adhesives	"	—	221, 222

[a] The apparatus is not functioning at present.
[b] The construction of a similar apparatus in Tver has been planned.
[c] A three-layer adhesive composition consisting of a poly(ethylene terephthalate) film and electrically insulating paper.

2. Grafting polymerisation

Radiation grafting polymerisation is used to improve the properties of materials (mainly polymeric). In practice this process is used for finishing textile items, for grafting acrylic acid to polyethylene (in order to increase its adhesion to aluminium), for producing ion-exchange membrane, etc. The most important region of application is radiation biotechnology.

a. Radiation biotechnology

Studies and technological developments in radiation biotechnology are proceeding in two main directions: the production of biocompatible materials and the immobilisation of bioactive substances in polymeric matrices.

Biocompatible materials. Synthetic polymers are often used as biomaterials.[223,224] However, they have several defects: the most important is the presence of toxic impurities (catalysts, stabilisers, plasticisers, dyes), which can be washed out in an aqueous biological environment. On the other hand if the polymer is produced by the radiation method it does not contain these harmful impurities and furthermore it is sterile. Among the most important radiation methods of preparing biocompatible materials we can include graft polymerisation, polymerisation in the bulk, in solution, in an emulsion, or in the solid state, and cross-linking.[223,224] The most widely used of these methods is the first.

One of the main requirements on biocompatible polymers is that they should be hydrophilic. However, hydrogels become mechanically weak when they adsorb large amounts of water (30%–95%), and therefore hydrophobic polymers are used as substrates in their production [silicone rubber, polyethylene, poly(ethylene terephthalate), polytetrafluoroethylene, polyurethanes].

The compounds mainly used to prepare hydrogels include 2-hydroxyalkyl methacrylates $CH_2=C(CH_3)CO_2ROH$ [where R is $-CH_2CH_2-$, $-CH_2CH(CH_3)-$, or $CH_2CH(OH)CH_2-$]; acrylic acid, acrylamide and their derivatives, the derivatives of aminoethyl methacrylate, *N*-vinyl-2-pyrrolidone, penta-2,4-dien-1-ol, *N*-vinyl-*N*-methylacetamide, sodium styrenesulfonate, etc. are used less often. The radiation grafting of these monomers (or of their mixtures) to various substrates produces neutral, anionic, or cationic hydrogels.[223–230] Let us consider some relevant cases.

The production of polyelectrolyte biomaterials having a good blood compatibility has been reported:[231] it uses the radiation grafting of acrylic acid (from an aqueous solution) to polyethylene, followed by the deposition of polyethyleneimine on the resulting copolymer. As reported,[228,232] the radiation grafting of acrylamide to blood vessel substitutes obtained from poly(ethylene terephthalate) fibres markedly improves their properties. Thromboresistant materials have been prepared by the radiation grafting of *N,N*-dimethylacrylamide on polytetrafluoroethylene and on the copolymer of ethylene with polytetrafluoroethylene. It was found that the biocompatibility depends on the dose rate used for the grafting.[233] An improved blood compatibility was obtained also by using other combinations of polymer and of grafted monomer, for example silicone tubes + *N*-vinyl-2-pyrrolidone,[234] polyurethane films and tubes + acrylamide or 2-hydroxyethyl methacrylate,[235,236] silicone rubber (silastic) + *N*-isopropylacrylamide or its copolymers with acrylamide,[237] poly[bis(trifluoroethoxy)phosphazene] or poly[bis(phenoxy)phosphazene] + *N*-vinyl-2-pyrrolidone,[229] or polyethylene tubes + acrylamide,[238] polyamide + a mixture of vinyl monomers (2-hydroxyethyl methacrylate, acrylamide, etc.),[230] and other combinations.

Polymerisation in the bulk and cross-linking are used much less often. Hydrogels obtained by these methods form solid systems or microspheres (without using polymeric substrates).[224] Studies of this type were carried out with 2-hydroxyethyl methacrylate,[239] poly(ethylene oxide),[240] *trans*-1,4-polyisoprene,[241] poly(vinyl alcohol),[242] poly-*N*-vinyl-2-pyrrolidone,[243–246] etc.

The biomaterials prepared in this way were suggested for use in the production of soft contact lenses,[239] of adsorbents for the separation of biologically important substances by the affinity chromatography method,[230] seamless thermosetting compounds for blood vessels,[241] indicators for bilirubin in the urine,[232] surgical dressing,[243,244,246] etc. (Surgical dressing material prepared by radiation cross-linking have been produced on a commercial scale in Poland since 1990 under the trade names HDR^R and AQUA-GEL^R).[244]

However, it should be stressed that these methods did not find wide application in practice. In particular, the use in medical implantation of any material produced by the radiation method has not so far been reported. According to one report[230] this is because of the loss of biocompatibility during lengthy in vivo trials. The explanation of this disappointing result lies in the monitoring (in most cases) of only one property, associated with the biocompatibility, whereas these materials call for a more complex study.

Immobilisation of bioactive substances. The greatest practical applications were achieved by radiation methods of immobilising bioactive substances (antibiotics, antibodies, antigens, anti-cancer preparations, bacterial cells, contraceptives, enzymes, hormones, immunodiagnostic substances, proteins, and others) in polymeric matrices in order to lower their mobility.[223,224,228,243,244,247–257] The main aims of immobilisation are the following:[247] fixing and lowering the solubility of a bioactive substance in order to extend its effectiveness, giving to a material of correct shape and size an enhanced stability towards heat and chemical reactants, and a controlled slow evolution for moderately high and local action. The main regions of application of radiation-immobilised biological materials can be classified into two groups:[250] (1) biochemical processes (of the fermentation type) with the participation of immobilised enzymes, yeasts, bacterial cells, etc.; (2) biomedical applications (systems with a controlled evolution of medicinal substances, immuno-logical systems, artificial organs, etc.), which involve immobilised medicinal preparations, enzymes, antibodies, and cells.

Two main methods of radiation immobilisation have been proposed: the formation of chemical bonds between a bioactive substance and the substrate, and the capture of the material by the polymeric matrix.[248] In the first method the biomolecules react with the functional groups of the polymer, radiation-grafted or radiation-cross-linked, or obtained by radiation polymerisation. It has been reported that heparin, trypsin, chymotrypsin A, L-aspartamine, papain, asparaginase, glucosooxidase, albumin, antibodies, antigens, etc.[251,252,258–260] can be immobilised by this method.

In the second method radiation polymerisation at room temperature or at low temperatures is used to immobilise the bioactive substance, in conjunction with cross-linking of the polymers.[223,247–249,261] The method has been used to immobilise antibiotics, bacterial cells, hormones, haemoglobin, polypeptides, ureases, and various medicinal preparations (pilocarpine, provital, cancer-fighting preparations, etc.). Let us examine some typical examples.

The radiation polymerisation of aqueous solutions of acrylamide in the presence of provital or pilocarpine hydrochloride yielded preparations with controlled additions of medicinal substances used in the treatment of burns and glaucoma respectively.[228] Polyvinylpyrrolidone rods containing prostalgin, prepared by radiation polymerisation and cross-linking, are useful for inducing births.[244] Thin polymeric membranes with a high enzyme activity were synthesised by the radiation hardening of a mixture of a hydrophilic polymer [for example, poly(ethylene glycol) dimethacrylate] and a solution of an enzyme (for example, glucoamylase).[262] Matrices with the cancer-fighting preparation narcyclazine, from which it can be very slowly evolved, were obtained by γ irradiation at -78 °C of a mixture of 2-hydroxyethyl methacrylate and trimethylolpropane trimethacrylate.[263] A promising application of the

chemotherapeutic treatment of cancer consists in implanting the immobilised anti-cancer agent within the tumour: in this way its effect is local and it does not penetrate into the blood stream, thus minimising undesirable side effects.[248,249]

b. Finishing of textile materials

The properties of natural and of artificial fibres and tissues can be improved by radiation grafting.[264–267] In particular, the grafting of *N*-methylolacrylamide significantly improves the crease resistance of tissues made from a mixture of polyester and cotton fibres.[196,265] At the end of the 1960s the firm 'Deering Milliken Corporation' (USA) demonstrated a combined method of finishing these tissues which included the radiation grafting of *N*-methylolacrylamide.[196] To this end they used several electron accelerators: the operating speed of the assembly was 4.5×10^6 m a^{-1}. Articles which do not need to be ironed for long times were produced from the modified tissue. This production was maintained for 10 years, but in the late 1970s the production of textiles by this method was abandoned because of its low profitability and of the introduction of the more economical photochemical method of grafting.[268,269]

Since 1976 a pilot apparatus including an accelerator of the 'Electron' type (energy 0.7 MeV, beam power 7 kW) has been in use for the finishing of tissues by the radiation grafting method at the Glukhovsk cotton and paper concern in the Moscow region.[270] The operating speed of the assembly was 10–100 m min^{-1} (for a dose of 10–20 kGy). One of the processes (the preparation of cotton and paper tissue with antibacterial properties, is achieved by the grafting of methyl-5-vinylpyridinium methylsulfonate followed by the addition of hexachlorophene.[264] Tissues with grafted acrylic acid, treated with a solution of a copper(II) salt, have similar properties. It was reported[271] that the industrial production of tissues having these properties has been prepared: the assembly is fitted with an electron accelerator of the 'Aurora' type.

Yet another pilot assembly (with an 'Aurora' accelerator) for the local finishing of textile materials (for example, polyamides) has long been operating in Dresden.[272,273] Irradiation simultaneously with grafting was carried out on given areas of the textile (outlined by using aluminium 'masks'); under these conditions the grafted and the nongrafted regions had different properties (in particular, a different depth of colour). The operating speed was 50–60 m min^{-1} (for a dose of 100 kGy).

At present, studies of the radiation finishing of cotton–paper materials by using an electron accelerator are also being carried out in India (see, for example, Ref. 274).

c. Other processes based on radiation grafting

Several other processes based on the radiation grafting of monomers to polymers have been developed. They include the preparation of polyethylene with grafted acrylic acid, which has a high adhesion to aluminium, the production of ion-exchange membranes, etc.

In 1968 an industrial assembly for the radiation grafting of acrylic acid to polyethylene, aimed at the preparation of material with a high adhesion to aluminium, began to operate in France.[275] Powdered polyethylene was irradiated with electrons (dose 7–10 kGy) in the air, and acrylic acid was then grafted to it by heating. The operating speed of the assembly was ~20 t d^{-1}. The material prepared in this way is used as a coating for aluminium foil. A technology for the production of grafted polypropylene has also been worked out.[275] Ion-exchange membranes are being manufactured in Japan on a pilot-plant scale by the radiation grafting of acrylic acid on polyethylene films.[276] These membranes are used as separators in alkaline batteries. An apparatus was constructed on the basis of a 'Dynamitron' accelerator (2 MeV energy). A part of the film (for tapes 100–300 m long) was irradiated in a nitrogen atmosphere: grafting was then carried out by inserting the sample for a prescribed time into a solution of acrylic acid saturated with nitrogen, washing the sample, and drying it.

There are reports[196] that battery separators manufactured from polyethylene films with radiation-grafted acrylic acid have been commercially distributed, but at the moment they are being sold only in the USA. The technology of preparing battery separators on the basis of polyethylene with radiation-grafted acrylic acid or acrylonitrile was developed also in Russia.[277,278] In China γ radiation from ^{60}Co is used for the manufacture of these separators (with an annual production of 10 km^2).[279]

The published literature contains a very large amount of other possible (or already feasible) applications of radiation grafting (see, for example, Refs 1 and 271). In the USA the radiation grafting of acrylamide on starch is used to produce flocculants.[196] In France radiation grafting of *N*-vinylpyrrolidone onto silicone rubber is used to prepare soft contact lenses:[196] this product is sold in China.[279] In Japan a pilot plant has been constructed (operating speed 1 t d^{-1}) with a ^{60}Co source of γ radiation (activity 6.5 kCi) for the gas-phase grafting of butadiene to poly(vinyl chloride); the product is characterised by an enhanced impact resistance.[280]

Pikaev et al.[281] have described the technology of the radiation grafting of acrylic acid, acrylonitrile, and of a series of other monomers to butadiene–styrene thermoelastic plastics and to rubbers based on the ethylene–propylene terpolymer which markedly improves the lubrication properties of the products and their adhesion characteristics. To carry out these processes they constructed a pilot plant assembly with a Cockcroft and Walton electron accelerator as the source of ionising radiation. The operating speed of the assembly was 4.2 t a^{-1} with a dose rate of 2.2 Gy h^{-1}.

Radiation gas-phase grafting polymerisation can be used to encapsulate fertilisers in order to extend their lifetime.[86] This is achieved by grafting acrylamide and then vinylidene chloride on the fertiliser (carbamide). The required dose is ~30 kGy.

Other important products obtained by radiation grafting include effective adsorbents for ammonia and acetaldehyde from the gas phase,[282,283] of uranium from sea water,[283] of metals from waste water,[283] water absorbents,[284,285] etc. A method of creating barrier layers from polysiloxane on polymeric packing materials by radiation grafting has recently been developed.[286] These layers protect the packed material from the penetration of oxygen, oil, etc. The grafting of phenylacetylene to polyethylene increases the thermal stability and improves the electric conduction properties of the polymer.[287] The radiation stability of polyethylene is substantially increased by the grafting of acenaphthene.[288] The ethylene–propylene terpolymer and chlorosulfonated polyethylene with radiation-grafted condensed bromoacenaphthalene have a relatively high radiation stability and fire resistance.[141]

3. Production of modified porous materials

The radiation method of modifying various porous materials (wood, cement, asbestos–cement materials, etc.) is now relatively widespread.[86] The method consists in impregnating these materials with monomers or oligomers and polymerising them under the influence of ionising radiation (usually γ radiation from ^{60}Co). It is most often used with wood and plastic materials.

a. Wood and plastics materials

The polymerisation of monomers impregnated in wood greatly improves the properties of the latter: its mechanical strength is increased, its stability towards decay is also increased, and the water absorption is decreased.[76] Methyl methacrylate is often used as the monomer. The dose required for the polymerisation is 10–20 kGy (depending on the dose rate).[76,289] Styrene, and a mixture of acrylonitrile with methyl methacrylate, butyl methacrylate, etc., are used more seldom.

The dose depends on the nature of the monomer. In the case of styrene it is 250–300 kGy.[76] At these high doses the process is complicated by the decomposition of the wood. For this reason the dose used to prepared wood–plastics materials should not exceed 50 kGy.[76] As a result, when monomers difficult to polymerise are needed (for example, styrene) sensitisers are used

(CCl_4, solutions of metal salts with a variable valency, tributylphosphate, etc.).

A high moisture resistance is achieved in wood by using compositions consisting of a mixture of acrylonitrile and methyl methacrylate with additives of ethylene glycol dimethacrylate and maleic anhydride.[290] The dose needed to polymerise this mixture is ~10 kGy. To polymerise butyl methacrylate with some additives 10–30 kGy are required at a dose rate of 8 kGy h^{-1} (see Khan et al.[291]). Radiation modification is used for both soft and hard timber species.[289,292] In the USA hard species are modified by the radiation method, more than 80% being oak timber.[289]

In many countries wood–plastic composites are prepared by the radiation method.[76] In the USA parquet flooring, sports goods, everyday objects, etc.[289,292] are manufactured. In 1975 a pilot plant with a ^{60}Co source of γ radiation (activity ~100 kCi) was produced in Russia (Solikamsk) and operated for a long time for the production of parquet flooring from birch timber impregnated with methyl methacrylate.[76,293] The operating speed was ~10^5 m^2 a^{-1}. A similar but smaller apparatus was assembled in Hungary (with an operating speed of ~200 t a^{-1}).[290,294]

Wood and plastics materials from wood of tropical origin (bamboo, rubber tree, red liana, etc.) prepared by the radiation method can now find practical application.[290,294–300] The original timber of these woods is not used because of its low stability towards rotting.

b. Other composite materials

Among other porous materials modified by polymers we should discuss the cements.[76,293] Cement–polymer materials prepared by the radiation method have a much higher stability than the initial concretes; they are also characterised by an improved stability towards external interactions. The operating characteristics of wood–textile materials, tufa, gypsum, cardboard, paper, etc. are improved as a result of the modification by polymers.[76,293] According to one report[301] composite materials usable in construction and in the production of ceramic articles can be made from the waste products of the cellulose and paper industry by drying them, introducing mineral additives, unsaturated esters, and vinyl monomers, followed by radiation polymerisation.

Radiation polymerisation has been proposed as a means of producing armoured plastics, consisting of a strength material (for example, glass cloth) and a polymeric binder.[302] Plastics of this type are produced by repeating the sequential electron-beam treatment of the cloth and the binder. The technique of polymerising a thin layer of monomeric composite additive on the surface of a moving polyethylene film under an electron beam was developed for the production of adhesion-active materials.[303]

The radiation polymerisation of polymers in porous materials allows us to preserve and strengthen items made of wood, stone, bone, ceramics, etc. having historical value.[304–308] To this end the eroding items (statues, clay vases, dishes, items of furniture, everyday objects, skeletons, gypsum objects, etc.) are saturated with the monomer in a vacuum (or the monomer introduced separately by diffusion), and the monomer is then polymerised by γ radiation from ^{60}Co. This polymerisation gives the item a high mechanical strength which cannot be achieved by ordinary methods. Methyl methacrylate is used most often, vinyl acetate and unsaturated polyester resins are used least often. When the colour of the article has become bleached, a hydrophilic monomer can be used (for example, 2-hydroxyethyl methacrylate) which 'develops' the colouring as a result of polymerisation. This method was developed in Austria, the former Czechoslovakia, France, Germany, Switzerland, the former USSR, and Turkey, and has found some practical applications.

Another application of the radiation polymerisation of monomers impregnated in porous objects has recently been described:[309] the restoration of old books kept in large libraries (like the British Library). A suitable mixture of monomers is deposited on the page, and irradiated when an appropriate degree of impregnation has been reached. The method has been validated on a pilot plant with a ^{60}Co source of γ radiation. The 'Nordion International Inc.' corporation in cooperation with the British Library has planned to assemble an industrial gamma source with an annual throughput of up to 5×10^5 books.

4. Other processes based on radiation polymerisation

There are reports of the practical use of several other processes based on radiation polymerisation. In the People's Republic of China (PRC) the radiation polymerisation method is used on a pilot plant scale to produce polyacrylamide, used in the petroleum industry.[279] The operating speed is 400 t a^{-1}. According to one report[310] polyacrylamide produced by the radiation polymerisation of acrylamide in an ethanol solution can be used as a coating for medical X-ray films: the product is available in China from many producers of photographic film.

Pilot plants with ^{60}Co sources of γ radiation for carrying out emulsion radiation polymerisation have been described.[68,311,312] In 1989 several types of latex were prepared in China by the radiation emulsion polymerisation method with a ^{60}Co γ source (operating speed up to 2000 t a^{-1}).[313] The products are used as a binder in the textile industry and as a thickener in the printing trade.

Various optical items (Fresnel lenses, contact lenses, prisms, etc.) can be obtained by the low-temperature radiation polymerisation of methyl methacrylate, 2-hydroxyethyl methacrylate, and some other monomers.[314,315] The monomer (or sometimes the prepolymer) is placed in a mold and cooled to a temperature close to its glass transition temperature (between −50 and −78 °C). After γ irradiation the resulting polymer is removed from the mold. Because the process has been carried out at a low temperature the compression of the product is relatively small, and the polymer emerges transparent and free from cracks and bubbles even with relatively large items: the method can be used to prepare Fresnel lenses having an area of 1 m^2 (see Kaetsu et al.[315]). The method has been used by the firm 'Nippon Kogaku Co.' (Japan) to produce lenses used in photolithography.[315] It consists of two stages: the preparation of the prepolymer and the polymerisation in the mold at low temperatures. The operating speed is several hundred lenses per annum.

V. Radiation degradation

Radiation degradation is not so widely used as radiation polymerisation. The most important processes based on the radiation degradation of polymeric materials are the production of fodder and of fodder additives from waste products containing cellulose, the control of the molecular mass of polymers, and the decomposition of PTFE and rubbers from butyl rubber.

1. Preparation of fodder for cattle from waste products containing cellulose

Waste products containing cellulose (sawdust, shavings, chaff, fine splinters, etc.) also contain large quantities of polysaccharides; therefore they can be treated as a potential source of fodder for cattle. Irradiation of these materials produces a marked change in their properties: they are amorphised, the recovery of polysaccharides from lignin is improved, the amount of cellular tissue decreases, and monomeric and oligomeric carbohydrates are formed.[41,85,316] For example, wheat chaff contains 36.8% of carbohydrates in the dry residue after γ irradiation to a dose of 1 MGy and acid hydrolysis.[317] It has been shown experimentally that these materials (in particular sawdust, chaff, or shavings) can replace 3%–10% of the normal fodder for oxen, pigs, sheep, and chickens when irradiated to a dose of 0.2–0.6 MGy.[85,316,318]

The dose needed for a substantial improvement in the quality of the fodder from waste products containing cellulose depends on the type of waste and on the class of cattle.[41,85,316,318] It lies between 0.1 and 1.0 MGy. Of course, this large dose can hardly be used economically. But it can be decreased by simultaneously irradiating and heating the waste products or by heating them after irradiation.[85]

A large-scale series of experiments with these fodders has been planned by building a pilot-plant assembly with an ILU electron accelerator.[85,318] Its operating speed is 0.2–0.3 t h^{-1} (see Ershov[85]). The use of the irradiated product as a 5% addition to the feed in an aviary with an annual production rate of ~7 million hens has been reported.

2. Degradation of PTFE waste products

The radiation degradation of polytetrafluoroethylene (PTFE) waste products converts them into a powder or into products having a low molecular mass which are useful in practice.[269] Relatively high doses are required (0.5 MGy or even higher), and at sufficiently high dose rates the heat evolved within the polymer produces a simultaneous thermal degradation (observed at temperatures above 360 °C).[319,320] Under these conditions the nature of the resulting substances depends on the temperature, the dose, and the presence of oxygen. Irradiation in an inert atmosphere produces perfluoroolefins (up to 60%) and perfluoroparaffins. In the presence of oxygen fluoroanhydrides of perfluorocarboxylic acids are formed. The resulting compounds can be used in the synthesis of other substances containing fluorine.

In Russia and in the former German Democratic Republic (GDR) two pilot plants with electron accelerators have been assembled. The annual production of one of these plants is 12 t a^{-1}.[319,320] The Japanese firm 'Sumitomo Heavy Industries, Ltd.' carries out this process on a commercial scale, using a high-power 'Dynamitron' accelerator. In the People's Republic of China three assemblies have been built for the same purpose:[279] the product is used mainly as a high-quality lubricating material.

3. Regeneration of rubbers based on butylrubber

In most cases items made of rubber based on butylrubber cease to perform satisfactorily after a relatively short period of operation. However, many substances present in their composition remain almost unchanged. Therefore it should be possible to exploit them for a second time after a suitable regeneration. One regeneration method which has been used in practice is a radiation treatment which leads to degradation of the polymer.[321–324]

Butylrubber is a copolymer of isobutylene and isoprene. The process consists in breaking up the degraded vulcanised rubber, irradiation (both ^{60}Co γ radiation and an electron beam can be used), crushing, etc. The optimum dose is 50–100 kGy. The product can be added (in 10%–15% quantities) to various rubber mixtures.

The radiation method of regeneration of rubber made from butylrubber is used in the PRC on a commercial scale. The assembly (including an electron accelerator) has a productivity of 200 tonnes per annum,[279] and more than 400 tonnes of rubber were regenerated up to the middle of 1992 in an apparatus using a ^{60}Co source of γ radiation.[324]

4. Other processes

Among the other processes of this group we should include the control of the molecular mass of polymers. It is difficult to obtain a polymer with a prescribed molecular mass by polymerising the monomer: this aim is much more simply achieved by subjecting the polymer to degradation by radiation. The process was realised in practice with poly(ethylene oxide) in the USA[196] and with cellulose (in Russia).[325] In the latter case a pilot plant with an electron accelerator (energy 0.3–0.6 MeV, power 40 kW) was used to irradiate a cellulose bed (1–5 layers, 0.8–1.0 m in width) with a dose of 50 kGy.

Many workers have reported that a previous irradiation of waste products containing cellulose (wood shavings, paper spoilage, waste material from the production of palm oil, etc.) increases the yield of final products even for relatively low doses. We shall quote some examples.

It was stated[78,196] that the irradiation of wood waste in air with a dose of 5–20 kGy increases its storage life and improves the yield of cellulose when the material is subsequently treated by traditional methods (for example, by boiling in acid). Thus, in the case of Christmas tree residues the yield of final product is increased by 5%–9% even for a dose of 5 kGy.[78] The reason for this large effect is not clear.

Brenner[326] has proposed a combined method of treatment of waste paper and other waste containing cellulose aimed at the production of glucose. The method consists in the preparation of a fibrous mass, irradiating it with a dose of 10 kGy, and subjecting it to a brief high-temperature (232 °C) acid hydrolysis. The yield of glucose is 50% of the amount of cellulose in the initial mass, i.e. 10% higher than the amount obtained in treatment without irradiation. A similar effect was observed in the fermentative hydrolysis of previously irradiated sawdust, fine chaff, and other waste products.[327,328]

Let us also consider the methods of increasing the yield of the final products from waste containing cellulose obtained from the irradiation of food products used in the treatment of this waste. It was shown (see, for example, Refs. 85 and 316) that the irradiation of the hydrolysate produced by thermocatalytic hydrolysis of vegetable stocks increases the yield of nutrient yeasts when grown on this hydrolysate. The yield increases by 8%, 16%, and 20% for γ radiation doses of 1, 5, and 10 kGy respectively. This effect is explained by the radiation-chemical decomposition of furfural and other compounds, known to be inhibitors of the growth of yeasts. According to Kume and coworkers[329–331] the irradiation of fermentation media used in treating the waste from the production of palm oil so as to obtain from them fodder for animals and to use them to grow edible fungi (dose 10 or 25 kGy), gives satisfactory results.

VI. Radiation sterilisation of medical articles

The radiation sterilisation of medical articles (in most cases, used only once) is one of the most important industrial processes which uses ionising radiation. It follows from Brinston's paper[332] that in the late 1980s about 30% of the medical production items for once-only usage were sterilised by the radiation method. We note a tendency for an increase in the amount of medical production sterilised by the radiation method. At present the fraction amounts to 40%–50%.[176,177] It has been forecast[332] that in the year 2000 more than 50% of the production of once-only medical items will be sterilised by this method.

γ-Radiation from ^{60}Co and electron beams are used for the sterilisation. The possible advantages of using bremsstrahlung X-radiation generated by powerful electron accelerators have been pointed out. An apparatus of this type based on an accelerator of the Cockcroft and Walton type (electron energy 5 MeV, beam power 150 kW) has already been built[121] (see also Section II.3). In 1992 about 120 large γ sterilisers using ^{60}Co were functioning throughout the world (see also Woods and Pikaev[1]). These assemblies are located in more than 40 countries. Of course, γ radiation from ^{137}Cs is also used for sterilisation, but only relatively seldom.[50]

About 30 sterilisers based on electron accelerators (mainly linear accelerators and accelerators of the 'Dynamitron' type) are operating throughout the world. The energy of their electron beams, used for the sterilisation, is mainly 5–10 MeV. Beams with a lower energy may find application[333,334] in the sterilisation of the packing of medical items. Of course, an assembly with an accelerator of the ILU-6 type (electron energy up to 2.5 MeV, beam power up to 20 kW) has already been tested.[335] It has been suggested that hypodermic syringes should be located in a vertical plane and irradiated from both sides.

It should be noted that in recent years the use of electron accelerators has been increasing as compared with γ sources. This is because of the greater safety offered by working with accelerators as well as because of the greater powers, resulting in shorter times of treatment. Thus, linear electron accelerators specially designed for radiation sterilisation have recently come onto the market (in particular, from the American firm 'Varian Associates Inc.').[336]

Table 5. Characteristics of industrial radiation sterilisers in Russia and the Ukraine with ^{60}Co sources of γ radiation (A) and with linear electron accelerators (B).

A. ^{60}Co source.

Location of the steriliser	Activity/MCi
St. Petersburg	0.93
Belgorod-Dnestrovskii (Ukraine)	0.36
Moscow region	0.12
Kaluzhsk region	0.67
Kazan'	0.17
Tyumen'	0.47
Dimitrovgrad [a]	1.5

B. Linear electron accelerator.

Location of the steriliser	Number and type	Energy/ MeV	Power/ kW
Kurgan[b]	2, LUE-8-5V	8	Both 10
Kostroma[a]	1, UELV-10-10	10	10
Moscow[a]	1, LEU	10	10
Leningrad region[a]	2, LUE-8-15S	8	Both 15

[a] The steriliser is in the building stage.

[b] Improvements are being carried out on the steriliser. Two LUE-8-15S linear electron accelerators will be brought into operation (energy 8 MeV, power 15 kW, annual production from each machine 1400 t).[337]

In Russia the last ten years have seen a large increase in the number of once-only items (mainly syringes). In 1995 it is planned to produce 6×10^9 syringes for once-only use, 190×10^6 containers for the storage of blood, and 320×10^6 blood transfusion units.[337] At the same time we observe an intense development in the radiation sterilisation of these products. In Table 5 we quote some data on the industrial radiation sterilisers in Russia and the Ukraine.[98] In addition to industrial sterilisers, equipment based on linear electron accelerators is located in research institutes. The total number of assemblies, including those functioning in institutes, is ~ 30 (see Khrushchev et al.[338]).

In addition to medical items for once-only applications (syringes, needles, surgical items, materials and tissues to be implanted, anaesthetic and obstetric kits, equipment for inhalation, dialysis, and blood transfusion, dressings, gloves, Petri dishes, masks, bandages, pipettes, etc.), some pharmaceutical preparations are also subjected to sterilisation by radiation (eye ointments and drops, ointments for burns, salt solutions, veterinary products, etc.), as well as packing materials. In some countries radiation sterilisation is applied to various solid medicinal preparations, ointments, and suspensions of pharmaceutical stock.[339] This method is used also in the sterilisation of tissues and organs of humans and animals needed in implantation surgery.[340,341] The radiation sterilisation of cosmetic materials (bentonite, gelatine, starch, talc, etc.) also offers attractive prospects.[324-344] The sterilising dose adopted in many countries is 25 kGy. In the Scandinavian countries it is much higher (35 kGy for electron radiation and 32 kGy for γ radiation).[57,345] In some countries (in particular the USA and Canada) there is no fixed sterilising dose: it is determined by the initial number of microorganisms in the product to be sterilised, by their nature, and by their sensitivity to the action of the radiation.[346] Therefore it may vary from 10 to ~ 40 kGy. The dose may be decreased by a careful control of the production conditions of the medical items. In Russia the dose used for sterilisation is 15–25 kGy.[337,338,347]

These doses are relatively high, and therefore in parallel with the sterilisation we must solve the problem of the radiation stability of the preparations and materials from which the item is manufactured. It was found (see, for example, Refs 348 and 349) that many polymers used in the preparation of medical articles are stable enough towards radiation to 'endure' the sterilising dose, but the degradation (especially, post-radiational) of polypropylene, which is widely used as a material for syringes, produces a coloration and makes the material brittle.[350-352] Therefore polypropylene stabilised by various additives has now begun to be used for the production of syringes.

Most of the solid medicinal preparations retain their properties after irradiation with sterilisation doses (see, for example, Ref. 341). This is also true of a series of preparations in the form of concentrated aqueous solutions.[353] However, most medicines in the form of aqueous solutions suffer large changes (dissociation with formation of new substances, changes in pH, etc.). These include some new radiopharmaceutical preparations[354-356] vitamin B_{12},[357] insulin,[357] etc. For these preparations the use of protective additives has been suggested (for example, thiosulfate for a solution of ^{131}I sodium iodide),[354,358] or alternatively irradiation in the frozen state,[357,359-362] when as a result of phase separation only a very small fraction of the energy of the ionising radiation is absorbed by the dissolved substance. Neither of these methods has been applied in practice so far.

An analysis of the economics of these processes has shown that the cheapest method of sterilisation is treatment with steam, and the dearest is the use of ethylene oxide: the radiation method occupies an intermediate place.[363,364] However, at high production rates the radiation sterilisation may compete with the steam method.[364] Obviously, in future the sterilisation with ethylene oxide will continue to be applied in the case of medicinal products unstable towards heat and ionising radiation. For many other items intended for once-only application the radiation method will be the predominant method of sterilisation.

VII. Use of radiation for the protection of the environment

The first studies of the use of ionising radiation for the protection of the environment were carried out in the 1950s.[11] At present studies and technological developments in this region of radiation technology are proceeding in the following main directions:[365] the radiation treatment of natural water, the radiation purification of domestic, industrial, and agricultural waste waters, the radiation treatment of deposits from waste waters, the radiation purification of discharge gases, and the radiation treatment of solid refuse.

1. Natural water

Natural water (from rivers, lakes, reservoirs, artesian wells, etc.), which is used to feed the population, may be contaminated by harmful impurities and contain pathogenic microorganisms and parasites. Often the concentration of these impurities and the level of contamination are small, and relatively low doses are needed for the radiation treatment of the water.

It was found (see, for example, Refs 11, 366, 367) that doses of ~ 1 kGy are sufficient for the purification and disinfection of natural water (in particular, for the removal of organic compounds of the humin type, which produce colour, smell, etc.). It was recently shown[368] in studies of water strongly coloured by natural organic compounds and by finely divided particles, taken from a river in northwestern Russia, that doses of the order of several kGy can lower the coloration to the required level. The dose required for decoloration depends on the season in which the sample was taken from the river. For example, the dose for autumnal water is higher than for the winter.

One of the important problems still awaiting solution is the purification of natural water from toxic and carcinogenic organic compounds containing chlorine. These substances are introduced into the water from the contaminated surroundings, and are formed during the chlorination of water containing several

organic compounds. It has been shown[365,369–378] that the irradiation of water contaminated with organic substances containing chlorine (1,2-dichloroethane, 1,1,1-trichloroethane, trichloroethylene, tetrachloroethylene, chlorobenzene, 4-chlorophenol, 2,4-dichlorophenol) leads to their decomposition. On the basis of these data we may conclude that small amounts of these substances (10^{-4} mol dm^{-3} and below) may decompose upon exposure to relatively small doses (1 kGy or less). In these systems the use of radiation methods seems promising.

However, it should not be forgotten that in the radiolysis of chlorinated aromatic compounds the dechlorination may be accompanied by the formation of other toxic substances. For example, in the radiolysis of chlorobenzene solutions isomeric hydroxycyclobenzenes [sic. Ed. of Translation] and phenol compounds are formed. Furthermore we observe a marked dependence of the yield of decomposition products upon the strength of the dose (especially at low concentrations).[378]

The irradiation of contaminated water in conjunction with ozonisation produces a synergistic effect (see below). Thus, ozonisation of water contaminated with trichloroethylene and tetrachloroethylene[376,377] also eliminates almost completely the dependence on dose strength in dilute solutions, and also protects the irradiated water from a second appearance of the microorganisms and parasites during its transport along conduits.[377]

Radiation treatment gives good results also in the treatment of ground waters. Firstly, it can be used successfully to regenerate water boreholes contaminated by the products of biological processes.[379–381] Ionising radiation kills the bacteria responsible for the redox reactions of the ions Fe(II), Mn(II), etc., and for the subsequent precipitation of insoluble hydrolysis products, which lead to 'clogging' of the water separators and 'ageing' of the boreholes. The doses needed for this are 0.25 – 0.4 kGy.[379] This method was widely used in the GDR.[273,379] 372 Boreholes were fitted with ^{60}Co sources of γ radiation (total activity 132 kCi). However, after the union of the German Democratic Republic and the Federal Republic of Germany all sources were removed from the boreholes because in the FRG the irradiation of food products is not allowed, and drinking water is classified as such. Interest in this method has been shown in the Czech state[380] and in the USA.[381]

Secondly, in situ irradiation of contaminated water in underground reservoirs leads to its purification. For example, it has been shown[380] that the concentration of cyanide ions in underground water is much decreased if the reservoir is fitted with a ^{60}Co source of γ radiation and activated carbon is added to it. After a 6 years use of the installation the concentration of cyanide ions in the reservoir had fallen by more than an order of magnitude.[382]

In spite of the promising results of studies and technological developments the purification of natural water to produce drinking water has still not found large-scale application. Of course, in Austria it is planned to build an assembly for the purification of drinking water having a production rate of 1000 m^3 h^{-1} (see Ref. 376). The details of its future operation are being planned with a prototype having an operating rate of 3 m^3 h^{-1}.

2. Sewage

It has been found (see, for example, Refs 369, 383 – 385) that for the radiation treatment of domestic sewage after its biological purification doses from 0.4 – 0.5 kGy to several kGy are required. For example, the doses needed for disinfection and for the decomposition of harmful impurities (detergents, organic sulfides, dyes, etc.) in the sewage of Tokyo amounted to several kGy.[385] The use of radiation treated water for industrial purposes has been recommended. Kurucz et al.[369] give the same doses, and point out that they are higher for nonchlorinated than for chlorinated water. In the latter case the study was carried out in an apparatus based on an IST electron accelerator (operating rate 460 dm^3 h^{-1}).[369,386]

Industrial sewage differs from contaminated natural water in containing more impurities at much higher concentrations. In most cases higher doses are required for the purification of these effluents (some tens of kGy or more). As a result combined methods of purification have been developed in recent years, in which the radiation treatment is carried out in conjunction with a conventional method (chemical, biological, thermal, flotation, etc.). A brief description of the combined methods is given in Table 6.

Table 6. Combined methods of purifying sewage waters.

Method	Basic processes	Removed impurity[a]	Ref.
Radiation – flotation	Flotation, γ irradiation, secondary flotation	Mercury	387, 388
Radiation – biological	Electron irradiation, additional biological purification	Mixture of isobutyl naphthalenesulphonates	389
Radiation – polymerisation	Irradiation of the sewage containing the monomer	Monomers	26
Thermo – radiation	Irradiation of the waste products while heating	Bacteria, parasites, etc.	390
Radiation – electrodialysis	Combination of radiation and electrodialysis	Various organic substances	391
Radiation – coagulation	Irradiation in the presence of a coagulant	Polyoxyethylene-n-nonyl phenyl ether etc.	392, 393
Radiation – adsorption	Irradiation in the presence of activated carbon	Pesticides	394 – 396
Oxyradiation	Irradiation of the waste while passing oxygen through the solution	Parasites, bacteria, etc.	397
Ozonoradiation	Irradiation of the waste saturated with ozone	Various organic substances	392, 393, 398

[a]These impurities are quoted as an example.

A radiation-biological method is used to purify the discharge waters of the Voronezh synthetic rubber factory from the emulsifier. The latter material (Nekal) is a mixture of isomeric butyl naphthalenesulfonates of the general formula $C_{10}H_6(R)SO_3Na$, where $R = (CH_3)_3C-$, $(CH_3)_2CHCH_2-$ or $CH_3CH_2CH(CH_3)-$, predominantly the first two butyl groups;[399] the alkyl and the sulfonate group are in the same ring in a pair of positions relative to each other. Nekal is classified as a 'hard' surface-active substance and does not dissociate biologically. However, it was shown[389,399] that the removal of the alkyl of the sulfonate group (or both) from its molecule produces biodegradable substances. Dealkylation and desulfonation take place at relatively low doses. The dose needed to decompose $\sim 100-150$ mg dm^{-3} of Nekal is 2–3 kGy. A study by pulse radiolysis has shown[400] that OH radicals contribute to these processes, and to a smaller extent the hydrated electrons produced in the radiolysis of water also make a contribution.

An apparatus for purifying waste waters has two ELV electron accelerators (0.7 MeV energy, total power 70 kW). The waste water is irradiated as a foam (density 0.02–0.03 g cm^{-3}). The operating rate of the assembly is $\sim 12\,000$ m^3 d^{-1}. After the electron beam treatment the water passes to the biological purification arrangement. The degree of removal of Nekal can be as high as 99.5%. At present this apparatus is used to purify underground water contaminated with Nekal.

We should briefly mention the problem of the disinfection of manure discharge in connection with the building and operation of large pig farms. Many workers[41,401,402] have shown that this problem can be solved in principle by using radiation methods. Four pilot plants (three with electron accelerators, one with a ^{60}Co source of γ radiation) were developed for the disinfection and purification of waste waters in large amounts in the Minsk, Moscow, and Omsk regions and operated for a long time. However, the process was never used in practice.

In our country several projects for the production of large assemblies including electron accelerators (total power ~0.9 MW) were considered for the purification of domestic and industrial sewage.[403–405] The largest of these projects was aimed at the radiation treatment of the domestic sewage of one of the towns in the Leningrad region. Its designed operating rate was 110 000 m^3 d^{-1}.[405] However, none of these projects has yet been realised.

3. Sedimentation of sewage

When domestic sewage is allowed to settle (the first stage in their normal purification) deposits containing insoluble solid particles (5%–8%) and water (92%–95%) are formed. In the biological treatment deposits of another type, called the excess active silt (which consist mainly of microorganisms) are formed at the aeration stage. The deposits can be used as fertilisers and as additives to animal fodder. However, they are loaded with bacteria, viruses, and parasites, and they may contain harmful substances. Obviously, they should be disinfected before being used. As can be seen from many published reviews (see Refs 28 and 401) this problem can be solved successively by radiation methods.

It was found that disinfection is achieved at doses of 2–10 kGy. Furthermore irradiation often accelerates the filtration and the sedimentation of deposits, and therefore also their dehydration. At present the technology of the radiation treatment of deposits from sewage waters is being applied in many countries on pilot plant or on industrial scales. The corresponding equipments are based on sources of γ radiation or on electron accelerators. Some data on these assemblies are listed in Table 7. It is intended to build similar apparatus in Canada, Poland, and the Argentine. The system proposed in Canada is based on a ^{60}Co source of γ radiation (with a planned production rate of 80 t d^{-1}).[416,417] The planned production of the Polish system with a linear electron accelerator (energy 10 MeV) is 50–70 t d^{-1} (for a dose of 5 kGy).[418]

Table 7. Apparatus for the radiation treatment of deposits from sewage waters.

Location of apparatus	Period of operation	Source of radiation	Energy/MeV	Power or actvitiy	Operating rate/m^3 d^{-1}	Dose/kGy	Ref.
Heiselbullach (FGR)	1973–1993	^{60}Co and ^{137}Cs	1.25 and 0.66	135 kCi of ^{60}Co + 55 kCi of ^{137}Cs	180 (1981)	2	397, 406, 407
Grosslappen (FGR)	1974– mid-1980s	^{60}Co	1.25	—	30	3	407
Albuquerque (USA)	1978–1985	^{137}Cs	0.66	~0.9 MCi	8 [a]	10	408, 409
Baroda (India)	Since 1989	^{60}Co	1.25	150 kCi	110	5	410
Boston (USA)	1976–1980	ICT electron accelerator	0.8	50 kW	379	4	383, 411
Boston (USA)	1980– late 1980s	"	1.5	75 kW	654	4	383, 411
Near Miami (USA)	1984–1985	"	1.5	75 kW	648	4	409, 411
Takasaki (Japan)	Since 1987	Cockcroft–Walton electron accelerator	2.0	60 kW	7.2[a]	5	412, 413
Near Minsk (Belorussia)	In the 1980s	ILU electron accelerator	1.6–2.0	30 kW	~150	5	41, 414, 415

[a] Quoted in tonnes per day.

4. Gaseous emissions

At present the most intensively studied area in radiation technology includes the work on one of the most important ecological problems: the purification of gaseous emissions from harmful substances (mainly SO_2 and the nitrogen oxides NO_x, where $x = 1, 2$). Many workers have demonstrated the promise of using electron beams for the purification of these gases. It was clearly shown that the electron-beam treatment of gases containing SO_2 and NO_x removes both impurities at the same time.

A pioneering contribution to this problem was made by Japanese research workers and engineers in the early 1970s.[419,420] It was subsequently found[420–423] that the addition of ammonia to the irradiated gas results in the formation of a powdery product of composition $(NH_4)_2SO_4$ and NH_4NO_3 which can be used as an agricultural fertiliser. At present the process goes under the name of the 'Ebara process', after the Japanese organisation 'Ebara Co.' which built and operated the first pilot plant for the purification of gases.

At present studies and technological developments in this area of work are being carried out in Japan, the USA, Germany, Poland, Russia, Italy, China, Belorussia, and South Korea. The method is realised on a large pilot plant scale. Table 8 shows some information on the pilot and demonstration assemblies. Furthermore, in some countries large experimental plants with electron accelerators are being operated for the development of new methods of radiation purification of gas discharges from various sources.[436]

From the results obtained during studies, technological developments, and extended trials it may be concluded that effectiveness of removing SO_2 exceeds 95%, and in the case of NO_x it can reach 80%–85%.[436] The doses needed for purification are between ~10 and 20 kGy (depending on the concentrations of SO_2 and NO_x); the energy of the electorn beam should lie between 0.3 and 0.8 MeV.

The mechanism of the reactions proceeding during the irradiation of gas discharges containing SO_2 and NO_x has been studied by several workers (see, for example, Ref. 371). The electron beam, interacting with the main components of the gas discharges, produces secondary electrons, ions, free radicals, atoms, and excited particles, which react with SO_2, NO_x, and other possible constituents, as well as taking part in dimerisation, neutralisation, and other reactions. The extent of these processes is not large. For example, in one reported computer modelling[437] 181 reactions of this type were considered. Not only are the nitrogen oxides in these processes oxidised, but they can also be reduced (25%–30%) to N_2O and N_2. Whereas the NO_x is removed entirely by radiation-chemical reactions, the SO_2 is oxidised both in radiation-chemical processes and in thermal reactions involving oxygen and ammonia.[438–440] Up to 70%–90% of the SO_2 can be removed by thermal reactions.[440]

Electron-beam treatment is used also in the purification of exhaust gases from thermal electric power stations operating with coal, fuel oil, etc. and also for the removal of harmful impurities from the exhaust gases from furnaces for the heat treatment of sweepings (SO_2, NO_x, and HCl), from tin treatment plants, (SO_2), and from automobile subways (NO_x). Recently a mobile apparatus with an electron accelerator (0.15–0.3 MeV energy) was constructed in the FRG for the removal of harmful volatile organic compounds from the gases of industrial undertakings, and of nitrogen oxides and benzene from the gases of automobile subways.[441] It was mounted on a trailer, and its operating speed was 1000 $m^3\ h^{-1}$. Sometimes the purification technology differs

Table 8. Large pilot and demonstration scale apparatus with electron accelerators for the purification.

Location	Operating period	Source of gases	Number of accelerators	Energy/MeV	Total power/kW	Additive	Operating rate under normal conditions/$m^3\ h^{-1}$	Ref.
Vakamatsu (Japan)	1977–1978	Furnace for firing iron ore	2	0.75	90	NH_3	10000	421, 423, 424
Indianapolis (USA)	1984–1989	Thermal power station	2	0.8	160	NH_3	16000–32000	425, 426
Karlsruhe (FGR)	1985–1989	Thermal power station	2	0.28–0.3	180	NH_3	10000–20000	426, 427
Kaveshchin (Poland)	Since 1991	Thermal power station	2	0.7	100	NH_3	20000	428, 429
Novosibirsk (Russia)	Since 1991	Tin refining works	1	0.5–0.7	50	None	—	430, 431
Matsudo (Japan)[a]	1992–1995	Furnace for roasting refuse	1	0.95	15	$Ca(OH)_2$	1000	432, 433
Nagoya (Japan)[b]	Since 1993	Thermal power station	1	0.4–0.8	108	NH_3	12000	434, 435
Tokyo (Japan)[c]	Since 1992	Automobile subway	1	0.5	25	—	50000	436

[a] Apparatus designed for the removal of SO_2, NO_x and HCl. [b] The accelerator has three irradiators. [c] The accelerator has two irradiators.

from the Ebara process. Thus, in the purification of gases from the furnace for the heat treatment of sweepings the additive $Ca(OH)_2$ is used; in general this additive is not used in the gases from tin treatment plants (where the SO_2 is removed as sulfuric acid).

In Russia the studies in this area of radiation technology are carried out in several scientific and technological development centres.[442,443] In addition to the equipment already functioning in Novosibirsk (see Table 8) pilot plants are also planned for Moscow, Lipetsk, and Orenburg.[403,430,443] It has been suggested[443] that one of the installations should be fitted with a many-aperture electron accelerator of the 'Finval' type (see Table 1).

However, even the largest of the assemblies built so far allow the removal of the gases produced by only one relatively small generating block (with an electric power of 5–8 MW) of a thermal power station. This limitation is due first of all to the inadequate power of currently available electron accelerators. Accelerators with beam powers of 0.5 MW (in Russia[108]) and even 0.8–1.8 MW (in the USA[109,436]) are now being built. We should stress the importance of a Polish project aimed to build an assembly with a productivity of 270 000 $m^3 h^{-1}$ (for a total electron beam power of 1.2 MW).[444,445]

A lowering of the dose required for the removal of harmful impurities (i.e. an increase in the radiation-chemical yield of the decomposition) should accompany the large-scale applications of the radiation methods of purifying exhaust gases. Different methods of solving this problem have been reported. The effectiveness of the removal of NO_x increases if the technique of repeated (or band) irradiation is used.[434,446,447] As can be seen from Ref. 442 the introduction of an aqueous aerosol into the gas to be purified (in the absence of ammonia) produced a marked lowering of the dose.

Another possible path is to use catalysts as additives. Injecting a solution containing (for example) Mn^{2+} ions into the gas before the electron-beam treatment stage can increase the efficiency of the process. The evidence for this statement[72] is that gases are very effectively purified from SO_2 (oxidation yield up to 10^4 molecules for 100 eV) when passed through a dilute sulphuric acid solution of Mn(II).

Increased efficiency can be achieved also by combining the irradiation with other methods of treatment. It has been reported[448,449] that combining γ irradiation with the application of an electric field produces a marked increase in the radiation-chemical yields of the oxidation of SO_2 in the gas phase (up to 100–150 molecules per 100 eV). According to Zimek et al.[450] the purification efficiency is increased by the simultaneous application of an electron beam and of a stream of microwave energy.

From the economic point of view the Ebara process can compete with the conventional methods of purifying discharge gases.[436,438,451] Its cost effectiveness increases with the SO_2 content of the gases to be purified.

5. Solid waste

There are published reports that radiation methods can find practical applications in the decontamination of waste from hospitals and from airports, in the regeneration of active carbons, and in the purification of contaminated soils. The importance of using γ radiation for the disinfection of hospital waste has been pointed out.[452] At present only one assembly with a ^{60}Co source of γ radiation is being operated (in the state of Arkansas, USA),[453] to treat infected hospital waste. As reported,[452] one relatively small source can disinfect this waste for all the hospitals in a town with a population of 1 million, and a large source can provide for the needs of the hospitals in a town with a population of 5 millions.

The technology of the radiation treatment of hospital wastes has been developed also in Russia.[454] It consists of four stages: (1) the separation of the liquid and the solid phase, (2) the radiation disinfection of the liquid wastes, (3) the radiation disinfection of the solid wastes, (4) the purification of the emitted gases. A suitable assembly with a ^{60}Co source of γ radiation was constructed ('Gammatok-100'); its productivity is 65 $m^3 d^{-1}$. However, the method has not yet been used on a commercial scale.

Another promising application of γ radiation is the treatment of wastes for international airports.[452] 20–30 t (or even more) of waste are produced annually in large international airports. This amount of waste can be treated by a gamma-apparatus of intermediate size. The Canadian company 'Nordion International Inc.' plans to construct an irradiator of this type.[452]

The next possible application is the regeneration of the activated carbon used in the purification of natural and of waste waters by using electron irradiation.[455] Samples of carbon with adsorbed sodium lauryl sulfonate were subjected to radiation treatment. The dose required for regeneration was 1 MGy. An economic assessment showed that the radiation method is ~8–10 times cheaper than the usual high-temperature steam method.

Radiation methods can be used to purify contaminated soil.[456–458] Two methods have been developed. The first consists in mixing the contaminated soil with water and a nonionic surface-actant substance and treating the mixture with γ radiation.[456] This method was used to purify soil contaminated with chlorinated dioxins. In particular it was shown that 2,3,7,8-tetrachlorodibenzo-*p*-dioxin is converted by successive oxidative dechlorination into the nonchlorinated dibenzo-*p*-dioxin, characterised by a negligibly small toxicity. The radiation-chemical yield of the decomposition is $\sim 10^{-6}$ molecules per 100 eV. This means that the breakdown takes place mainly as a result of the 'direct action' of the ionising radiation on the dioxin molecule.

The second method was developed for soil contaminated with volatile organic substances (for example, trichloroethylene).[457,458] It consists in the vacuum extraction of impurities from the soil followed by their electron-beam treatment in the gas phase.

VIII. Radiation treatment of food products

The history of the radiation treatment of food products spans an interval of about 50 years. Many important data on the useful effects of ionising radiation on these products have been obtained. These effects include the suppression of the growth of potatoes and onions during storage, the extension of the storage time of meat and fish in the frozen state, the disinfestation of grain and fruit, the sterilisation of meat products in order to achieve long lifetimes in the non-frozen state, etc.[1] Up to 1994 the irradiation of food products was permitted in 38 countries, and pilot and production plants were operating in 27 countries for the radiation treatment of food products:[459] potatoes, onions, garlic, tomatoes, beans, seasonal vegetables, spices, strawberries, citrus fruit, apples, mangoes, dried fruit, grains, rice, poultry, fermented sausages, shrimps, dried fish, frozen frog's legs, etc. Data for spices and seasonal vegetables (Fig. 5) show that the quantity of products treated by ionising radiation increases from year to year.[459]

Careful chemical and biological studies and also tests on the nourishing properties of the irradiated products reported from specialists in many countries have shown that the radiation treatment has no harmful effect on the products. International organisation have stressed[1] that the irradiation of any foodstuff is safe up to doses of 10 kGy: under these conditions higher doses can be used for food products which account for a small part of the human diet (for example, spices). It has been decided that the following types of ionising radiation can be used: γ radiation from ^{60}Co and ^{137}Cs, bremsstrahlung X-rays generated by electron accelerators with an energy not greater than 5 MeV, and electron radiation with an energy not greater than 10 MeV. The setting of an upper energy level for electrons and X-rays aims to avoid any substantial induced radioactivity. This has been confirmed by many theoretical and experimental studies (see, for example, Refs 460–462).

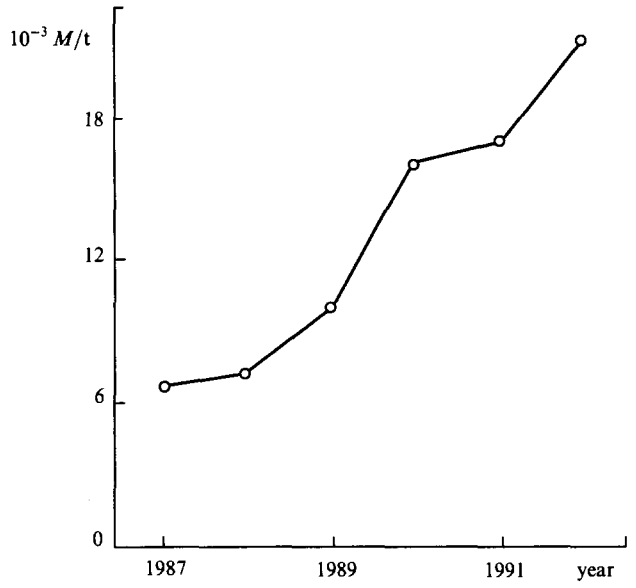


Figure 5. Increase in the number of species and seasonal vegetables (M) treated by radiation.

At present both γ radiation and electron beams are used for the treatment of food products. The possibility of using bremsstrahlung radiation is being considered. The suggested doses are relatively small:[1] 0.05–0.15 kGy (for inhibiting the growth of potatoes, onions, etc.), 0.15–0.50 kGy (for the disinfestation of grain, fruit, etc.), 0.5–1.0 kGy (to slow the ripening of fruit, vegetables, etc.), 1.5–3.0 kGy (for increasing the lifetime of strawberries and other fruit), 2.0–5.0 kGy (for the destruction of pathogenic parasites and microorganisms in fresh and in frozen poultry, shrimps, frog's legs, etc.), 2.0–10 kGy (to improve the technological properties of several food products), 10–50 kGy (for the decontamination of food additives and ingredients, especially spices), 30–50 kGy (for the sterilisation of meat, meat products, dietary products for the sick, etc.). Some establishments have a relatively high operating speed. let us consider some examples.

In 1973 an apparatus with a ^{60}Co source of γ radiation (activity 0.3 MCi) began to function for the treatment of potatoes (productivity 15 000–20 000 tonnes per season).[463] In 1986 a pilot plant with a ^{60}Co activity of 0.24 MCi was constructed in the GDR for the irradiation of onions (operating speed 18 t h^{-1}).[464] The largest apparatus ever used in this region of radiation technology, with two electron accelerators, was assembled in Odessa in the early 1980s for the disinfestation of imported grain (operating speed 400 000 t a^{-1}).[465] It was planned to build an apparatus of this type in the Rostov region, but the project could not be realised. From 1986 until 1990 the French firm 'Société des Protéines Industrielles' used an electron accelerator (energy 7 MeV, power 5 kW) to treat chicken's fillets (operating speed ~3 t h^{-1}). A more powerful accelerator (energy 10 MeV, power 10 kW) has been in use since 1990: this change has made a 2-fold improvement in the operating speed.[466–467] Since the end of 1991 the 'Vindicator Inc.' company (USA) has treated strawberries and citrus fruit with γ radiation from ^{60}Co.[468,469] In the USA two demonstration equipments with linear electron accelerators were built (energy 5 MeV, power 20 kW, or energy 10 MeV, power 10 kW) to irradiate strawberries, fruit, poultry, and other products.[470] In Poland an apparatus based on a linear electron accelerator of the 'Elektronika' type (energy 10 MeV, power 10 kW) was built for the treatment of spice, mushrooms, etc.[471] In the late 1980s the radiation treatment of spices had been established in 17 countries (for example, in Belgium, France, the Netherlands, the UAR, and the USA).[472] Garden strawberries are another product now being treated in large quantities. This is specially true of France, the Netherlands, the USA, and several other countries. For example, in the UAR 4–8 tonnes of strawberries were irradiated per annum.[473] In the early 1990s the total amount of food products treated by radiation methods was 500 000 t a^{-1}.[468]

An important problem in this field of radiation technology is the identification of food products which have undergone radiation treatment. The identification of irradiated products is essential for the information of the buyer and for proper sales control. This is a difficult problem, because the effects produced by the ionising radiation are usually small; furthermore they lead

Table 9. Chemical changes used to identify irradiated food products.

Change	Product	Ref.
Formation of volatile compounds from lipids	Fish, meat	474–476
Changes in DNA (for example, formation of thymidineglycols)	Meat	474,475
Changes in proteins (for example, formation of *o*-tyrosine)	Meat, prawns	474–477
Formation of hydrocarbons from fatty acids	Meat, prawns, frogs' legs	476,478
Formation of 2-alkylcyclobutanones from fatty acids	Poulty, eggs	476,479
Formation of CO from fatty acids	Meat	476,480
Formation of 2,3-butanediol	Alcoholic drinks	481
Hydroxylation of aromatic compounds	Fruit, vegetables	482
Decomposition of starch	Spices	483,484
Formation of free radicals	Strawberries, fruit, meat with bones, fish and sea foods containing bones, shells, etc., spices	474–477, 485,486

to changes similar to those produced by storage. Useful results have nevertheless been obtained.

A universal method for the detection of irradiated food products has still not been developed, though all types of radiation effects have been examined (chemical, physical, and biological). They include changes in the histological and morphological characteristics, in the physical properties (electric impedance, viscosity, wetting properties, etc.), in the chemical changes in the components of the food products (carbohydrates, lipids, proteins, nucleic acids, vitamins, etc.), and in the formation of free radicals, detected by chemiluminescence, thermoluminescence, and ESR methods.[474-476] Some chemical changes used to identify irradiated food products are shown in Table 9.

Clearly, the most promising are the methods based on the formation of free radicals. These species are retained in bones, shells, membranes, grains, skins, etc.; they can exist for relatively long times, and therefore they can be detected by luminescence methods and by ESR. It has been claimed[476] that routine analyses can already be done by the ESR method (for the analysis of meat including poultry, with bones), by the thermoluminescence method (for spices and herbs), by the gas chromatography method (for meat, including poultry), and by the determination of long-chain hydrocarbons.

The level of industrial application of radiation treatment is strongly dependent on the ratio of consumers to the number of irradiated food items. Many questionnaires have shown that this ratio is usually large (see, for example, Refs 459 and 472).

IX. Radiation-physical processing

The changes in the physical properties of materials (mainly solids) after irradiation have been used as a basis for several practical applications. They include ion implantation, the doping of semiconductors, the modification of semiconductor materials and articles, the preparation of polymeric membranes and resists for photolithography, changes in the colour of glass and of precious stones, the thermal effect of powerful electron beams, etc.

Ion implantation is the introduction of additional atoms into the surface of a solid by bombardment with accelerated ions. Ion energies greater than 1 keV are often used.

Ion implantation is used for the doping of semiconductors, for modifying solid surfaces (to generate anticorrosion coatings on metals and alloys, to clean surfaces, to improve optical surfaces, to deposit films, etc.)[14,29,30,43] We note that for high ion fluxes (greater than $10^{17} - 10^{18}$ cm^{-2}), when the concentration of implanted ions is comparable with the concentration of atoms in the surface layer of the target, new compounds are formed (or, in the conventional language, ion synthesis takes place). For example, when silicon is bombarded with nitrogen, carbon, and oxygen ions the compounds Si_3N_4, SiC, and SiO_2 are formed respectively.[43] This process is used to form protective films and insulating layers in integrated circuits. Ion implantation is also used to produce alloys and solid solutions, including metastable alloys: the process is often called ion metallurgy.

The next region of radiation-physical processing is the radiation doping of semiconductors with the help of nuclear reactions.[35] The reactions can be initiated by thermal neutrons, which are characterised by large ranges, so that by using this method semiconductors can be doped evenly over their entire volume. The most important application of the method is the doping of silicon by phosphorus, based on the $^{30}Si(n,\gamma)^{31}Si$ reaction in a nuclear reactor.[35,487] Silicon-31 has half-life of 2.62 h: by undergoing a β decay it is converted into phosphorus-31.

The first large-scale production of radiation-doped silicon was set up in 1983 in the RBMK-1000 reactors of the Chernobyl atomic power station;[488] 54.5 t of this material were prepared (including 12.8 t in 1991). Methods of producing it in other atomic power stations with reactors of the RBMK type are being examined.[488] The doping of silicon is carried out also in an experimental reactor in Obninsk (with a production rate of several tonnes per annum). In foreign countries radiation-doped silicon is almost wholly produced in research reactors.[488]

Attempts are also being made to dope GaAs, InAs, InP, InSb, etc. by using n,γ reactions.[488] The most widely used of the materials prepared in this way is doped gallium arsenide. We note that doping can be carried out also by using other nuclear reactions. Thus the irradiation of silicon with protons of 20–25 MeV energy in order to dope it with aluminium has been suggested.[489]

X-Radiation, and electron and ion beams, are used in photolithography. The first two forms of radiation offer a high resolution (up to $\sim$0.1 μm) in the preparation of silicon integrated circuits.[490,491] The separation of the device from the SiO_2 in these circuits (as one of the stages in the lithographic process) can be achieved by ion beam etching.[43] Polymers having high radiation-chemical yields in their cross-linking or degradation reactions can be used as resists when ionising radiation is used. For example, chloromethylated polystyrene and poly-α-methylstyrene,[492] and also poly(glycidyl methacrylate),[493] are cross-linked by irradiation and act as negative resists. Poly(methyl methacrylate) and its derivatives, poly-1-butenesulfones, and some polysilanes are decomposing polymers: they behave as positive resists.[491] Polymers usually undergo cross-linking and decomposition simultaneously. It has been suggested[491] that a polymer acts as a negative resist if G (decomposition) $< 4G$ (cross-linking), where G is the radiation-chemical yield, measured as the number of molecules, atoms, bonds, etc. formed (or dissociated) by the absorption of 100 eV of energy of ionising radiation.

The irradiation of high-power semiconductor devices (for example, power diodes and thyristors) with electrons in relatively high doses improves their high-speed performance and some other operational characteristics.[30,494-498] This irradiation is practiced in several countries (Italy, the Czech republic, China, Japan etc.).[279,494,499] For example, in China and in Italy up to 100–150 thousand semiconductor devices are subjected every year to electron-beam treatment.[279,494]

Low-energy focussed electron beams (0.25 eV and below) can be used to heat the irradiated objects to high temperatures. These beams can be used for melting, evaporating, cutting, and welding various materials.[43,500,501] According to several workers (see, for example, Refs 502–504) electron irradiation can be used for the high-temperature synthesis of materials such as portland cement, sodium aluminate, barium and strontium ferrites, lead molybdate, etc. Simultaneous radiation and thermal treatment can lead to reactions with a higher rate, a higher yield, and at a lower temperature. A project has been reported[505] for the construction of an apparatus with an electron accelerator of the ELV type (energy 1.5 MeV, power 20 kW), aimed to treat cement so as to improve its performance. An apparatus has been built in Novosibirsk on the basis of an ELV electron accelerator (energy 1.5 MeV, power up to 100 kW) with the aim of creating a radiation-thermal technology for the production of cement and other similar materials.[506]

The formation of cylindrical tracks in materials (usually in polymeric films) irradiated with beams of heavy ions has been used for the production of membrane filters.[43,507] In most cases poly(ethylene terephthalate) films 1–10 μm thick are used, with ion beam energies (argon, nitrogen, xenon, etc.) above 100 MeV. The damaged parts of the irradiated film are removed by etching with a suitable solvent. This treatment produces pores with a diameter dependent on the mass, charge, and energy of the ions and on the time and temperature of the etching.[507-509] By controlling these parameters pores of a diameter dependent on the mass and charge (from a few nanometers to tens of micrometers) can be prepared. Filters prepared by this method are used in medicine, biology, and in the food industry.[43,507]

The ability of ionising radiation to form colour centres in solids is used in practice. It is used to change the colour of some

glass items, precious stones (for example topaz, diamond, and others), and pearls.[499] One of the metro stations in Prague is decorated with γ-irradiated glass tiles (in which a brownish tint was produced by irradiation).[499] This project required the irradiation of about 10 000 tiles with γ radiation (dose 2.7 kGy).

X. Other applications

Other applications of ionising radiation are known. First we should mention radiation synthesis. This has long been thought to be one of the most promising sections of radiation-chemical technology. Thus it was widely believed that ionising radiation (in particular, the radiation from a nuclear reactor) can be successfully used also for large-scale synthesis. Only a few processes using γ radiation and electron beams have been realised in practice (see Table 10). At present these studies have been almost completely discontinued, and they are carried out only in a few centres on a laboratory scale. For example the preparation of 2,3-dimethyltartaric acid by the γ irradiation of aqueous solutions of pyruvic acid,[515] of 1,2,3,4-butanetetracarboxylic acid by the γ radiolysis of aqueous solutions of succinic acid,[516] and of hexafluoropropylene oxide by the low-temperature liquid-phase oxidation of hexafluoropropylene,[517] etc. have been described.

As reported,[518,519] high-temperature electron-beam treatment can be used to regenerate catalysts and sorbents used in the oil and gas industry. Tests with large samples (up to 2 t) of irradiated catalysts showed that this treatment leads to almost 100% regeneration of the initial catalytic activity.

The possibility of using electron beams for the treatment of mineral deposits[520] and for the gasification of coal[521] has been studied, but these processes are still far from practical realisation. Paths towards the use of radiation from a nuclear reactor for the synthesis of hydrogen from water and CO_2 (through the formation of carbon monoxide and its subsequent conversion) were studied in the 1970s and 1980s, and considered to be an important problem in hydrogen energetics.[522,523] However, studies in this direction were subsequently abandoned.

Some problems in atomic energetics and in radiochemical production are directly related to applied radiation chemistry. They include accounting for special features of radiolytic transformations in aqueous solutions of actinide and of trace elements, establishing the features of the radiolysis of extractants and diluents, studying the radiation-chemical processes in highly radioactive waste, the radiation capacity of heat-transfer agents (in particular, water) and other reactor materials, the radiation corrosion of construction materials, etc. A discussion of these problems goes beyond the scope of the present work. Relevant information can be found in published monographs[1,47,53,60,71,524–528] and reviews.[529–533]

XI. Technological dosimetry of ionising radiations

In the development of the technology of a radiation process the best control of the operation of the assembly and of the creation of a high-quality product requires carrying out various dosimetric measurements, including the determination of the dose and of its strength, establishing the distribution of the dose in the irradiated sample, etc. The absorbed doses used in radiation technology cover a wide range (from ~50 Gy for the inhibition of the growth of potatoes and onions to >1 MGy for experiments with the radiation); the same is true of the strength of the dose. The irradiated samples include gases, liquids, and solids; they can be homogeneous or heterogeneous. It follow that dosimetry in radiation technology is required to solve many complex problems.

A large set of parameters needing to be measured can be 'overlapped' by using a relatively large number of dosimeters. Obviously, for each range of doses characterising the various processes there should be a particular dosimeter. To a large extent

Table 10. Radiation syntheses realised on pilot plant and on production scales.

Country and period of functioning of the apparatus	Process	Type of radiation	Product	Operating rate/t a^{-1}	Ref.
USA, 1962–1970s	$CH_2=CH_2 + HBr$	^{60}Co γ radiation	C_2H_5Br	~450	510
USA, 1960s	Alkanes + SO_2 + O_2	"	Sulfonic acids	—	511
USSR, 1966–1970s	Alkanes + SO_2 + Cl_2	"	Sulfonyl chloride	0.36[a]	27,512
USSR, 1967–1990s	$CH_2=CH_2 + CCl_4$	"	Tetrachloropropane, tetrachloropentane	175	513
USSR, 1974–1980s	H_2 + Cl_2 (removal of H_2 from Cl_2 prepared by electrolysis)	Electrons, 0.65 MeV	HCl	—	74
USSR, 1980s	2 C_4H_9Br + Sn	γ Radiation from ^{60}Co	$(C_4H_9)_2SnBr_2$	20	319
USSR, 1980s	Synthesis of organochlorosilanes	Electrons, ~0.3 MeV	$CH_3SiCl_2C_6H_5$, $C_6H_5SiCl_3$, etc.	—	87
Germany, 1980s	Poly(vinyl chloride) + Cl_2	γ Radiation from ^{60}Co	Chlorinated poly(vinyl chloride)	—	514

[a] Quoted in t h^{-1}.

Table 11. Dosimeters for different dose ranges.

Type of dosimeter	Method of measurement	Range of dose/Gy
Alanine	ESR	$1 \times 10^0 - 2 \times 10^5$
Solution of ferrous sulphate (Fricke dosimeter)	Spectrophotometric	$2 \times 10^1 - 2 \times 10^2$
Solution of dichromate	"	$5 \times 10^2 - 1 \times 10^5$
Solution of Ce(IV) sulfate	"	$1 \times 10^2 - 1 \times 10^5$
Solution of chlorobenzene in aqueous ethanol	Titration of H^+ or Cl^- (potentiometric, or high-frequency conductimetric)	$5 \times 10^1 - 1 \times 10^6$
Thermoluminescent, based on LiF	Measurement of the luminescence on heating to 195 °C	$< 1 \times 10^0 - 1 \times 10^3$
Crystalline LiF	Spectrophotometric	$2 \times 10^2 - 2 \times 10^6$
Solutions of dyes	"	$2 \times 10^0 - 2 \times 10^5$
Coloured polymer films and plates	"	$2 \times 10^0 - 2 \times 10^5$
Colourless polymer films and plates	"	$1 \times 10^4 - 4 \times 10^5$
Glucose solution	Polarimetric	$5 \times 10^4 - 2 \times 10^6$
Glass (silicate, activated with nickel)	Spectrophotometric	$1 \times 10^2 - 1 \times 10^4$
Glass (metaphosphate, activated with manganese)	"	$3 \times 10^3 - 1 \times 10^5$
Quartz	"	$1 \times 10^5 - 5 \times 10^7$
Nitrous oxide	Change in pressure, gas chromatographic, mass spectrometric	$5 \times 10^2 - 2 \times 10^4$

this problem is already solved. Table 11 shows the chemical dosimeters available for different ranges of doses.[19,33,50,57,97,534]

Among the recent developments we may quote the dosimetric systems based on aqueous solutions of rhodamine dyes with additions of selenate[535] and of solutions of tetrazolium salts.[536,537] The former system is suitable for dosimetric measurements in the radiation treatment of food products. The latter system can be used, depending on the composition, to determine doses over a wide range of compositions.

In Russia several dosimetric systems have been developed, including practically the whole range of doses used in radiation technology.[33,81,538] They include glucose solutions, plates of poly(methyl methacrylate), polymer films containing a dye, glasses with various additives, etc.

In several radiation processes (for example, the radiation sterilisation of medical products) we use light indicators of the dose in the form of labels attached to the item being irradiated. The labels contain a radiation-sensitive dye or the leuco-base of a dye. The irradiation produces a change in the colour of the indicator. This indicates that the item has been irradiated. Some data on these dose indicators can be found in various publications.[538-545]

A direct determination of the dose can be made with a calorimeter. Several forms of calorimeter, differing in the simplicity of their design and used in routine measurements and for the calibration of chemical dosimeters, have been developed in recent years.[1,545-548] They include water, graphite, and polystyrene calorimeters. The first two consist of Petri dishes filled with water or containing a graphite disk; changes in temperature are measured with thermistors. They can be used to determine doses in the ranges of 1 – 50 and 0.1 – 20 kGy respectively. The polystyrene calorimeter is designed to measure the power of the dose of γ radiation.

In Russia a special equipment including precision calorimeters has been produced for the accurate preliminary testing and calibration of dosimeters.[33,538]

Another important problem is the international comparison of dosimetric mesurements. It is essential, so as to ensure that radiation processes are carried out on a single world dosimetric basis. The International Atomic Energy Agency plays a leading role in this international effort.

XII. Conclusion

This discussion of the present state of radiation technology leads to the following conclusions. In addition to the expanded use of some well known processes, new processes have been developed (for example, the production of silicon carbide fibre). The use of electron accelerators as a source of ionising radiation safer and more power-ful than sources of γ radiation has been greatly developed. Bremsstrahlung X-radiation has begun to be used in radiation technology. It should be noted that the use of ^{137}Cs as a source of γ radiation has almost completely ceased because it is less safe than ^{60}Co. Interest in ion beam problems has increased considerably, especially in Japan, where ion beams are now used in studies of their influence on semiconductors and on constructional materials for cosmic technology, on the radiation defects in materials for thermonuclear reactors, in radiation biotechnology, etc.[176]

At present radiation technology is finding increasing applications in ecology. This is specially seen in radiation methods of purification of rejected gases from SO_2, NO_x, and other harmful impurities. Evidently, a substantial outbreak in the radiation treatment of food products can be expected in the near future. This will be assisted by the recent commissioning of the first appropriate commercial assembly in the USA.[468,469]

In spite of the general commercial recession we find (in Russia) an increase in the production of medical items sterilised by the radiation method. This is accompanied by an extension in the use of electron accelerators. Ecological applications of radiation technology are also being successfully developed. Definite improvements were made also in the region of the radiation hardening of coatings.

More and more countries are now using radiation technology, which is being transferred from the developed to the developing countries. The International Atomic Energy Agency maintains both a financial and a scientific and technical support of the various programmes, and as a result of this support radiation assemblies have been constructed in Bangladesh, Vietnam, Syria, Iran, Peru, Ecuador, Ghana, and other countries. The main field of application of these assemblies is the radiation sterilisation of medical items and the treatment of food products.

One of the main advantages of radiation technology is the lowering in the level of contamination of the environment produced by its use. In particular, no harmful gases (of the ethylene oxide type) are used in radiation sterilisation. As has already been pointed out, the compositions used in radiation hardening, unlike the compositions used for ordinary, thermal hardening, do not contain organic solvents. Undoubtedly, all this will stimulate further developments in radiation technology.

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Molecular modelling of the chemical interaction of atoms and molecules with a surface

A A Valuev, A S Kaklyugin, G E Norman

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Abstract. The modelling of a surface as an assembly of moving atoms interacting with one another and with an incident particle is examined. Both dynamic methods for the modelling of a surface (for short times) and probability methods (for long times) are analysed. The Massey adiabaticity criterion has been used to determine the regions of applicability of the methods of molecular dynamics. Within the framework of probability methods, the chemical bond is described with the aid of Harrison's generalised periodic system of the elements. Together with the general modelling problems, the reconstruction of the surface, physical and chemical sorption, as well as the modification of the surface and of its morphology as a result of the multiple repetition of elementary processes (precipitation, etching, corrosion) are discussed. The bibliography includes 169 references.

I. Introduction

The molecular modelling of the chemical interaction of atoms and molecules with a surface is based on the concept of the surface as an assembly of moving individual atoms or molecules interacting with one another and with the incident particle.[1–6] The central problem is that of the description of the chemical bonds, including the situation where the incident particle interacts with the surface, at a level ensuring the reconstruction of the surface, the generation of electronic surface states, etc. Problems involving the selection of the laws of motion arise: the Newton and Schrödinger equations, the stochastic approximations of the type of Langevin equations, and the specification of the interactions between the particles. The next problem is that of the selection of the number of atoms, the geometry of their arrangement in the cell, and the boundary conditions representing the interaction of these atoms with the surrounding medium.

In the classical method of molecular dynamics (MMD), Newton's equations are solved numerically. The principal problem is that of selecting the interaction potential. In the quantum MMD, the interaction energy for each configuration of the heavy particles is found in the course of the calculation by solution of the Schrödinger equation. The observed forces acting on the ions are used to determine the classical trajectories of the latter.

Both the classical and the quantum MMD are valid only for a particular electronic state (the adiabatic approximation). Such approaches are suitable for the determination of equilibrium characteristics of different states and for modelling the dynamics within the framework of only one electronic state.

The adiabatic approximation is inapplicable in the region of the intersection of the potential surfaces of different electronic states. In these regions, the motion of the heavy particles may induce electronic transitions and their trajectories permit branching. The main problem involves the search for an effective solution of the nonstationary Schrödinger equation.[5] Modern computers permit calculations for times many orders of magnitude shorter than those required for the description of the dynamics of the modification of the surface in terms of real length and time scales. However, such problems generally require the consideration of nonadiabatic chemical reactions. This inevitably introduces a probability element into the dynamics. Furthermore, the dynamic memory of the initial conditions is retained only over periods of the order of magnitude of several relaxation times, after which the trajectories become stochastic, as happens in nature.[7–11]

For this reason, it is necessary to resort to probability modelling methods as well as dynamic methods, particularly since in many cases the result of a specific dynamic process and not the process itself is important. Discrete probability

A A Valuev, A S Kaklyugin, G E Norman The Moscow Physical Society, Leninskii prosp. 53, 121019 Moscow, Russian Federation. Fax (7-095)135 79 95. E-mail: gribkov@sci.fian.msk.su.

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approaches and the Monte Carlo method† are based on lattice models of the surface. The simpler studies are limited to the geometrical modelling of the morphology (cellular automata). In the continuous models, the surface is assumed to be a continuous function of the spatial coordinates and time. The principal problem in probability methods involves the inclusion in the latter of a universal description of the chemical bond on the surface which could be chosen for modelling the multiple repetition of elementary steps. The use of the method based on Harrison's generalised periodic system of the elements (GPSE) is very promising.[14]

The authors of the present review have confined themselves to the consideration of the simplest systems permitting modelling by the most sophisticated methods, and endeavoured to consider all the fundamental problems which determine the further development of the molecular modelling of chemical processes on the surface.

II. Classical molecular dynamics

The method of molecular dynamics (see, for example Refs 9, 15, and 16)‡ in its traditional formulation consists in the numerical solutions of Newton's classical equations for a system of N particles with a known interparticle interaction potential Φ and with specified initial conditions:

$$\frac{m_i \mathrm{d}^2 r_i}{\mathrm{d}t^2} = \nabla\Phi(r_1,...,r_N), \quad i = 1, 2, ..., N, \tag{1}$$

where m_i and $r_i(t)$ are the mass and the coordinate of the ith particle respectively. The calculated phase trajectories $\{r_i(t), v_i(t)\}$ [here $v_i(t)$ are the velocities] are used to calculate the quantities $X[r_i(t), v_i(t)]$, which depend on microscopic variables. In order to obtain the macroscopic average quantities $< X(t) >$, all these quantities are averaged either with respect to time or with respect to a set of initial states of the system. The method of molecular dynamics makes it possible to calculate the time correlation functions, the relaxation to equilibrium, etc. and also the characteristics of the equilibrium states.

Eqns (1) model a nearly microcanonical assembly (the total energy of the system remains constant on average).[7-9] In other cases, described by assemblies differing from the microcanonical assembly, the MMD equations may contain additional terms. These can represent, for example, the Langevin forces, which model the heat exchange with the external medium, or the reactions of the bonds, imposed on the system and ensuring the constancy of the thermodynamic quantities (kinetic energy, pressure) or of the spatial gradients of the macroscopic parameters (temperature, velocity).[17,18]

Depending on the problem being solved, different boundary conditions are applied to the system (periodic conditions, rigid or 'stochastic' walls, a subsystem of stationary particles, etc.).

The interaction potential Φ is frequently represented approximately by the sum of the interaction potentials of all the pairs of particles and use is made of simple analytical formulae of the Lennard-Jones, Buckingham, etc. types. The necessary number (two-three) of parameters included in them is selected on the basis of empirical data.

However, such an approach is not always applicable even to the description of the properties of condensed inert gases.[13] The situation is even more complex in the case of the atoms of other elements, between which the formation of chemical bonds, for example covalent bonds (like those between Si or Ge atoms), is possible. No pair potential ensures the stability of a tetrahedral structure of such a system because it does not give rise to even a local energy minimum for this configuration.

A somewhat different picture is observed in the case of metals.[19] With the aid of pair potentials, it is possible to describe in this instance the regular structure and energy of the equilibrium crystal. For the modelling of, for example the elastic properties, it is necessary to introduce into the total energy of the system additional terms which clearly depend on the volume of the system (i.e. which take into account the interaction of the lattice site ions through the electron gas). This approach is applicable only to 'regular' structures, where the concept of volume is unambiguously defined. For 'defective' structures (vacancies, microcracks, surfaces), the volume is not defined unambiguously and such a simple model becomes inapplicable because the dependence of the results on the volume is very marked. The problem of the formation of a chemical bond between the metal atoms and the chemically reactive impurity introduced into the metal, for example hydrogen, which was mentioned above, also remains unsolved.

Many attempts have been made to overcome the above difficulties by introducing multiparticle (ie. not reducible to the sum of pair interactions), empirical (or semiempirical) potentials.[19-35] Following the procedure of Baalamane et al.,[36] we shall divide these approaches into three main groups: the cluster potentials, cluster functionals, and inserted atom methods.

The cluster potentials[20,25,28,29,31] include the following terms, after the pair interaction terms, in the expansion of the total energy in terms of the multiplicity of the interaction:

$$\Phi = \sum_{i>j} \Phi_2(r_i, r_j) + \sum_{i>j>k} \Phi_3(r_i, r_j, r_k) + \sum_{i>j>k>l} \Phi_4(r_i, r_j, r_k, r_l) + ... \tag{2}$$

Each term represents the sum of the interaction energies $\Phi_n(r_i, r_j, ..., r_n)$ of a n-particle 'cluster', which do not reduce to a combination of the preceding terms. The series (2) usually terminates at the Φ_3 term.

Such a potential makes it possible to specify around each atom, on a sphere having a radius equal to the distance to the nearest neighbour in the crystal, four potential wells located at the vertices of a tetrahedron. This idea was first applied to the MD modelling of crystalline and liquid silicon by Stillinger and Weber (the SW potential),[20] who represented Φ as the sum of pair and three particle interactions. The pair potential has the usual form with components corresponding to attraction and repulsion and a minimum at a distance equal to the distance to the nearest neighbour in a diamond-like lattice.

$$\Phi_2(r_{ij}) = \begin{cases} A(Br_{ij}^{-p} - r_{ij}^{-q}) f_c, & r_{ij} < a, \\ 0, & r_{ij} > a, \end{cases} \tag{3a}$$

where r_{ij} is the distance between the atoms i and j and $f_c = \exp[(r_{ij} - a)^{-1}]$ is a function which smoothly cuts off the interaction at distances equal to the distance between the first and second nearest neighbours.

The three-particle potential has the form

$$\Phi_3(r_i, r_j, r_k) = h_i + h_j + h_k , \tag{3b}$$

$$h_i = \lambda \exp[\gamma (r_{ij} - a)^{-1} + \gamma (r_{ik} - a)^{-1}] \left(\cos\vartheta_{ijk} + \tfrac{1}{3}\right)^2,$$

and includes a function of the angle ϑ_{ijk} between the ij and ik bonds which in fact ensures its relative rigidity. The parameters p, q, A, B, a, λ, and γ are chosen in order to satisfy the empirical data on the structure, energy, and elastic properties of the silicon crystal.

† The Monte Carlo method, used for the molecular modelling of the structure and thermodynamic properties of equilibrium states,[12,13] has not been included in this review but is mentioned in those cases where it is employed.

‡ The importance of this method for chemical physics has been emphasised in A L Buchachenko's review [*Uspekhi Khimii* **56** 1593 (1987); *Russ. Chem. Rev.* **56** 907 (1987)].

The structure and melting point of the diamond-like silicon,[20] its phonon spectrum,[37] and even the formation of the dimers on the Si (100) surface [(2 × 1) reconstruction][38] are modelled satisfactorily with the aid of the SW potential. However, the other crystalline modifications of silicon and amorphous and liquid silicon at temperatures remote from the melting point as well as more complex reconstructions § of surfaces with different orientations are not described by potential (3).[38,39] This is not surprising, since a potential with a rigidly specified angle between the bonds does not permit the formation of a structure with a coordination of the atoms other than tetrahedral.

Nevertheless, owing to its relative simplicity, the SW potential has been used widely in calculations (see, for example, Refs 40–46). The potentials of the interaction of silicon atoms with oxygen atoms and fluorine (Si–F and Si–O) have been derived from the SW potential. They are used, for example, in the study of the chemical reactions of the silicon surface with fluorine[44,45] or of the structures and vibrational spectra of crystalline and amorphous SiO_2.[46]

The cluster functionals[18–21,23,27,29,30] have the form

$$\Phi = \sum_{i>j} \Phi_n(i,j;k \in a_n) \ . \tag{4}$$

Here each pair of interacting particles i and j in an instantaneous configuration enters into the composition of the cluster a_n comprising n particles, including those selected. The configuration of the cluster depends on the structure of the test substance (crystal, glass, etc.) and on the law governing the interparticle interaction. The energy of the interaction of a pair of particles i and j depends not only on their coordinates but also on the coordinates of all $n-2$ particles k included in the cluster a_n. The more complex form of Eqn (4) arises from the desire to construct a universal potential, i.e. to describe the greatest possible number of structures with different coordinations using a single functional form and as far as possible a single set of parameters.

The most characteristic attempt on these lines has been undertaken by Tersoff.[21–23] The main idea was to incorporate the weakening of the bonds with increase in the number of nearest neighbours of the atom participating in the formation of the bonds. The total energy of the system has the form characteristic of the pair interaction approximation.[22]

$$\Phi = \sum_{i>j} f_c(r_{ij})\left[f_A(r_{ij}) + b_{ij} f_R(r_{ij})\right] \ , \tag{5a}$$

where $f_c(r_{ij})$ is the cut-off function which determines the radius of action of the potential and $f_A(r_{ij})$ and $f_R(r_{ji})$ are the pair attraction and repulsion potentials. The coefficients b_{ij} are functions of the local environment of the particles i and j:

$$b_{ij} = \left\{1 + \beta^m \left[\sum_{k \neq i,j} f(r_{ij}, r_{ik}, \theta_{ijk})\right]^m\right\}^{-1/2m} , \tag{5b}$$

where β and m are adjustable parameters and f is a function of the coordinates of the three particles i, j, and k; the summation was carried out over all the atoms k within the radius of action of the atoms i and j. Thus the depth and position of the potential minimum for the atom i in the vicinity of the atom j depend on the instantaneous positions of all the remaining atoms of the system, which renders potential (5) in essence a multiparticle potential. This imparts to it a fairly high flexibility, which makes it possible to describe structures with different configurations when the adjustable parameters (there are 13 of these altogether) are selected successfully.

§ Reconstruction is defined as the change in the structure (and symmetry) of the near-surface layers of the crystal compared with the bulk-phase structure.

Indeed the Tersoff potential models almost all the crystalline modifications of silicon,[22] its phonon spectrum,[23] and many reconstructions of the surface.[22,37] Liquid and amorphous silicon are less successfully modelled.[23] For an appropriate parametrisation, this potential makes it possible to describe multicomponent systems[24] (which need not contain silicon), including simple chemical reactions occurring on detonation of explosives of the type $A_2 + B \rightarrow A + AB$.[47] Nevertheless, potential (5) is not fully universal, since for the calculation of different properties and structures it requires different parametrisations.[22,23] For example, when the parameters of Eqn (5) are selected for the best description of the dependence of the energy on the specific volumes of different crystalline modifications of silicon, the accuracy of the calculation of the phonon spectrum is lost, and conversely.

The inserted atom method (IAM).[19] The total energy of the system assumes the form

$$\Phi = \sum_{i>j} \Phi_2(r_i, r_j) + \sum_i F(\rho_i) \ , \tag{6}$$

where Φ_2 is the energy of the pair interaction of ionic cores, $F(\rho_i)$ is the energy of the atom i 'inserted' in a medium having at the site of insertion an electron density ρ_i, which is generated by the electrons of all the remaining atoms of the system and is assumed to be additive, i.e.

$$\rho_i = \sum_{j \neq i} \rho(r_{ij}) \ , \tag{7}$$

$\rho(r)$ being the density of the electrons in the atom of the test element at a distance r from the nucleus. The last function is determined either from quantum-mechanical calculations or from empirical data. The functions Φ_{ij} and $F(\rho)$ in the initial formulation of the inserted atom method were selected by adjustment for consistency with empirical data for the crystal (the lattice constant, the elastic constants, the sublimation energies of various crystalline modifications, the formation energy of a vacancy).

It is seen from Eqns (6) and (7) that there is a relation between the IAM and the method of cluster potentials. Thus, if the function $F(\rho)$ is linear, then the IAM is equivalent to the approximation of pair interaction potentials, since the force acting on the atom i is proportional to the sum of functions which depend only on r_{ij}. For a quadratic variation of $F(\rho)$, we arrive at the triple potentials approximation, etc. This approach has been assigned[36] to the method of cluster functionals. We segregated it in a separate group because different physical considerations are employed in constructing the right-hand sides of Eqns (4) and (6). This is associated with the fact that initially these two methods developed in relation to different groups of elements: to Group IV semiconductors and metals respectively.

The relation[34]

$$F(\rho) = -c\rho^{-1/2},$$

which is universal for all metals, has been largely used recently for $F(\rho)$. This is based on the possibility of interpreting $\rho(r)$ in Eqn (7) as the square of the overlap integral of the wave functions of the atoms i and j.

The IAM has been applied successfully to the study of the structures and diverse properties of metals and alloys (including liquid ones): defects, the structures of the surfaces, various reconstructions, the phase structures of alloys, the bulk-phase and surface phonons, the structures of the interfaces, and the hydrogen on the surface (see, for example, Baskes et al.[35] and the references quoted therein).

The attempt to extend the IAM to systems with covalent bonds (Si and Ge)[35] has not been very successful. In particular, it leads to the 'external relaxation' of the surfaces on

reconstruction, i.e. the distance between neighbouring crystalline planes increases near the surface and does not diminish as would be expected from experimental data and which has been confirmed by other theoretical models. The IAM method[35] has been extended[48] to 26 elements (mainly metals). Certain deficiencies of the potentials[35] have been corrected, but a radical improvement could not be achieved for silicon and germanium.

III. The regions of applicability of the adiabatic approximation

As early as 1988, Tersoff,[22] who proposed one of the most successful cluster functionals, expressed doubts concerning the possibility of constructing a fully universal empirical potential. Having compared the results obtained with the aid of six potentials from different groups, the authors of a critical review[36] concluded that they are not universal and that no potential has decisive advantages which would lead to its being preferred to others. It was concluded that a universal potential cannot be constructed.

The causes of the relative failure of the group of methods employing the interaction potentials of the particles in calculations of their motion (the potential approach) have been specified as "...the general inability to model the formation of π-bonds" and "...the inadequacy of the description of angular forces", i.e. there is a direct indication that many quantum-mechanical effects cannot be described with the aid of classical potentials.

We shall now consider the limits of the applicability of approximation (1).

The use of the potential Φ is valid only in terms of the adiabatic approximation. In this case, the potential $\Phi(R_i)$ is a solution of the problem of the determination of the eigenvalue of the equation

$$\left(-\frac{\hbar^2}{2m}\sum_{i=1}^{n}\nabla_i^2 + V(R,r)\right)\varphi_R(r) = \Phi(R)\,\varphi_R(r)\ , \qquad (8)$$

where the summation is carried out over all the electrons. The term ∇_i denotes differentiation with respect to the electronic coordinates r_i and V denotes the interaction of all the charges [R and r are the sets of coordinates of the ions and electrons and $\varphi_R(r)$ is the wave function of the electron subsystem, which depends parametrically on the ionic coordinates R].[99]

The wave function in Eqn (8) refers to a specific state of the electron. For example, the ground state of crystalline silicon corresponds to the diamond lattice and is described by the wave function φ_0, which represents a linear combination of the sp^3 orbitals for each atom. The potential curve *1* in Fig. 1*a* corresponds to this structure. Another wave function and hence another potential curve (curve *2*) correspond to any metastable crystalline modification of silicon (for example, the simple cubic modification). We may note that, depending on the average distances between the ions, the ground states of the lattice may prove to be the states of structures of different symmetries. Strictly speaking, different structures should be modelled by different potentials.

Nevertheless, with the aid of the same empirical classical potential, it is possible to model not only the global but also certain local energy minima in the configuration space. The explanation for this is that the potentials examined in Section II do not follow from Eqn (8). They contain a large number of adjustable parameters, the successful selection of which permits the construction of a potential surface similar to that illustrated by a dashed line in Fig. 1*a*.

In order to understand the possibilities and limitations of this approach, it is necessary to apply Massey's adiabaticity criterion:[5,99]

$$\frac{a\Delta\Phi}{\hbar v} \gg 1, \qquad (9)$$

where a is the characteristic distance over which $\varphi_R(r)$varies, $\Delta\Phi$ the distance between the adiabatic potential surfaces, and v the characteristic velocity of the heavy particles. Thus the adiabatic approximation is valid over the entire range of values of R, except in the regions of the intersections (or the pseudo-intersections) of the adiabatic potential surfaces.

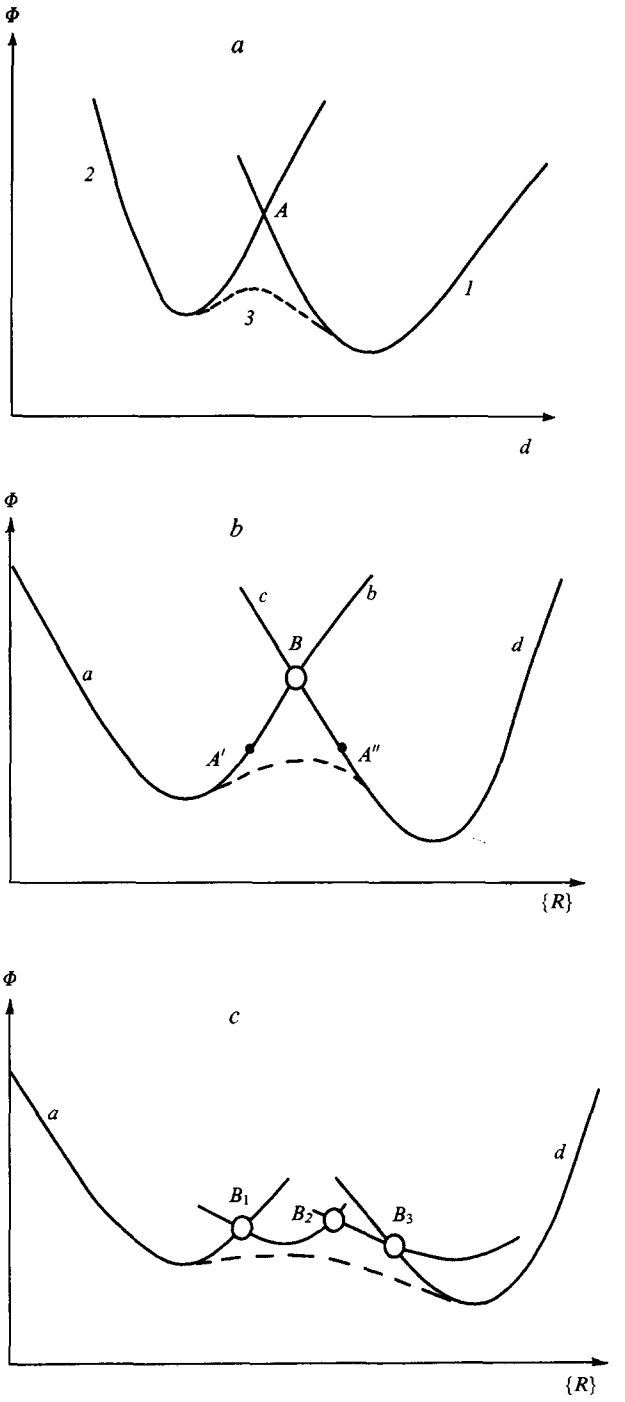


Figure 1. Conventional schematic illustration of adiabatic potential surfaces and nonadiabaticity regions: (*a*) potential curves for different regular crystalline structures as a function of the distance (d) to the nearest neighbour: continuous lines *1* and *2* — exact quantum-mechanical calculation, dashed line *3* — model potentials; (*b*) potential surfaces in the configuration space; the circle B represents the region of nonadiabaticity; (*c*) schematic illustration of numerous potential surfaces.

In the vicinity of such intersections, the motion of ions may induce nonadiabatic electronic transitions, the representation of the wave function for the system in the form of the product of the electronic anionic components becomes impossible, and approximation (8) loses its physical significance. The solution of

the dynamic problem in this (nonadiabatic) case must involve the study of electronic transitions.

In other words, the adiabatic approximation is by no means valid over the entire range of the possible values of R for a polyatomic system and the use of Eqns (1) with $\Phi(R)$ is possible only in the regions of the configuration space R (hypervolumes) separated from one another by hyperlayers, where approximation (1) is in principle impossible. The thickness of such layers may be estimated with the aid of Eqn (9).

Fig 1*a* does not illustrate this situation, since the point A does not correspond to the intersection of the surfaces $\Phi(R)$ in the space $\{R\}$ (Fig. 1*b*). The points A' and A'' in Fig. 1*b* correspond to identical distances to the nearest neighbour, i.e. to the point A in Fig. 1*a*, but they are completely different points in the configuration space. The potential surface for the ground state (the aBd curve) is divided into the adiabatic regions $aA'B$ and $BA''d$ corresponding to different electronic states (which in turn correspond to different symmetries), the adiabatic approximation breaking down in the vicinity of the boundary between them (the region of the point B).

Fig. 1*b* illustrates highly schematically the principal idea, although it does not in fact correspond to reality — the potential surfaces for the diamond and simple cubic lattices in the configuration space cannot intersect anywhere. Any path in this space, connecting the points corresponding to these structures, passes in succession through the points B_i at which there are intersections with the potential surfaces of the excited states (there are only three such points in Fig. 1*c*). The degeneracy of these points can be removed by taking into account any of the interactions disregarded previously, but in this case Massey's criterion necessitates a quantum treatment of the region B_i, although this is not in fact important.

The motion of the atoms within the adiabatic regions (aB and Bd in Fig. 1*b* and aB_1, B_1B_2, B_2B_3, and B_3d in Fig. 1*c*) obeys Eqns (1). On the other hand, when the regions intersect at the points B_i, Eqns (1) lose their significance — the potential $\Phi(R)$ cannot describe the interaction of heavy particles. Electronic transitions may occur in these regions and the trajectories may undergo branching. The choice of the type of extension of the trajectories must be made with the aid of statistical modelling based on the quantum-mechanical calculation of the amplitudes of the transition probabilities. Such an approach is valid if the nonadiabatic regions B_i in the phase space are much smaller than the regions corresponding to classical motion. In this section, we shall confine ourselves to the consideration of the quantum effects associated with the interaction and will not be concerned with cases where the de Broglie wavelength of the heavy particles becomes comparable to a and interference effects appear.

Thus the empirical potentials (the dashed lines in Figs. 1*a* – 1*c*) may describe the properties (including the time correlations) of the stationary state of the system in the vicinity of several (but not all!) local minima. However, the transitions between these states, obtained by the MMD, are not transitions with a real dynamic process occurring in the course of the correct time. For this reason, the processes accompanied by electronic transitions, for example the kinetics and times of the reconstruction of surfaces, are difficult to describe with the aid of the MMD in its classical formulation.

Example. We shall analyse a study[42] in which the temperature dependence of the velocity of the phase transition front (solidification or fusion) in silicon was investigated with the aid of the SW potential. The calculation was performed as follows. A rectangular parallelepiped was examined; 24 crystal planes, containing 18 silicon atoms each, passed through it parallel to its bases. Periodic boundary conditions were applied in the directions parallel to the planes. The atoms in two planes closest to one of the bases are stationary and occupy the crystal lattice sites. The atoms in the third and fourth layers are used to supply or remove heat (a constant temperature is maintained for these atoms with the aid of a scaling recalculation of the velocities). The remaining atoms of the system obey the usual MD [Eqns (1)] and are referred to as MD atoms.

In the initial instant, the MD atoms are either in positions corresponding to a specially prepared melt (in the modelling of crystallisation) or at the crystal lattice sites (in the modelling of fusion). The distribution of the velocities of these atoms corresponds to a certain initial temperature. The required phase transition temperature is then specified for the atoms of the third and fourth layers and is subsequently maintained constant. The heat exchange front gradually spreads towards the MD layers and leads to a structural rearrangement of the atoms (the phase transition).

Any layer is regarded as having become crystallised when its particles have become stably localised in the vicinity of lattice sites. Conversely, a layer is regarded as having fused when the particles have moved away from the vicinity of the lattice sites.

The results of the calculation are compared with experimental data in Fig. 2, which also presents the curves for the classical transition state theory. We may draw attention to a significant scatter, increasing on passing to fusion [$V(T) < 0$], which indicates a less satisfactory description of the fusion process. From our point of view, this scatter does not reduce to a statistical scatter but can be accounted for by the following causes:

On crystallisation, the particles 'roll down' into the potential well, the depth and position of which are determined beforehand by the particles of the preceding, already 'solidified', layers. In this case, the process activation energy is low (if it exists at all) and the results of the classical and quantum calculations may be similar.

On the other hand, on fusion such potential wells are not prepared beforehand. The atoms must 'collectively' seek the energy minimum. Such a process may be accompanied by the overcoming of high potential barriers, as a result of which the system may be fixed at local (metastable) minima, with which the scatter of the results may in fact be associated. In this case, the results of the classical and quantum-mechanical calculations will not agree and the possibility of determining the velocity of the fusion front within the framework of the adiabatic approximation (1) is open to doubt. The discussion of these questions will be continued in Sections IV, V, and VI.

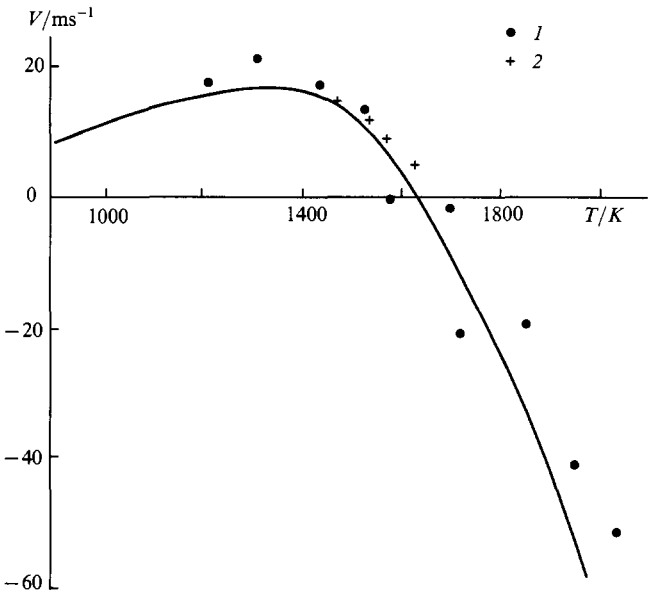


Figure 2. Temperature dependence of the velocity of the phase transition front. The positive velocities correspond to hardening and the negative ones to fusion. The curve was obtained by means of the transition state theory: (*1*) calculation; (*2*) experiment.

IV. Adiabatic quantum molecular dynamics

Approaches, which are frequently referred to as quantum MD, have developed in recent years in parallel with the potential approach. The scheme of Car and Parrinello (CP)[49] and the tight-binding method,[50,51] genetically related to the first procedure, are the most popular and will be briefly discussed in this Section.

1. The method of Car and Parrinello

The CP method involves the simultaneous calculation of the dynamics of valence electrons and ions (ionic cores),[52] the ions being considered in terms of the classical approximation and the electrons in terms of the quantum-mechanical approximation. Suppose we have a system of N ions with a mass M, described by the coordinates R_i ($i = 1, \ldots, N$) and the velocities $\dot{R}_i$, and N_1 electrons in the ground state and characterised by a set of wave functions (orbitals) $\psi_j(t)$ ($j = 1, \ldots N_1$). The latter may be expanded in terms of a set of basis functions $\chi_1, \ldots \chi_m$.

$$\psi_j(t) = \sum_k C_k^j(t)\chi_k .$$

The significance of coordinates and velocities of the electron subsystem is attributed to the amplitudes C_k^j and their derivatives with respect to time $\dot{C}_k^j$. Thus if the dependence of the potential energy E_{tot} of the system on R_i and C_k^j is known, it is possible to construct the pseudo-Lagrangian

$$L = \frac{\mu}{2}\sum_j\sum_k(\dot{C}_k^j)^2 + \frac{M}{2}\sum_k\dot{R}_i^2 - E_{tot}(C_k^j, R_i) .$$

Here the first term is the fictitious kinetic energy of the electronic component and μ the fictitious mass of the electron, the choice of which will be discussed below. Having supplemented the pseudo-Lagrangian by the condition that the functions ψ_j are orthonormalised

$$\sum_k C_k^{j*}C_k^j - \delta_{ij} = 0, \tag{10}$$

it is possible to obtain the equations of motion of the electrons and ions.

$$\mu\ddot{C}_k^j = -\frac{\partial E_{tot}}{\partial C_k^j} - \sum_l \lambda_{jl}C_k^l , \tag{11a}$$

$$M\ddot{R}_i = -\frac{\partial E_{tot}}{\partial R_i} . \tag{11b}$$

The last term in Eqn (11a) represents the response to the 'binding' [Eqn (10)] and λ_{jl} are undefined Lagrange multipliers, which are found simultaneously with the solution of Eqns (11).

The energy of the system E_{tot} is determined by the density functional method (see, for example, Yin and Cohen[53]). A system of planar waves is generally chosen as the basis system. Eqns (11) are solved numerically by methods analogous to those employed for the integration of classical MD equations. The scheme used in the solution, the minimisation of the initial electron energy (the adjustment of the energy of the electron subsystem to the Born–Oppenheimer surface, i.e. to the ground state) for fixed initial positions of the ions, the choice of the number of basis functions, etc. have been discussed in detail in a review.[52]

The theoretical justification of the CP method[49] consists in the fact that the solution of Eqns (11) under conditions where the trajectories reach equilibrium and in the temperature limit $T \to 0$ ('annealing') makes it possible to find the states of the electron and ion system (wave functions and coordinates) which gives rise to a minimum in the density functional. The $T \to 0$ annealing procedure is an important element of the CP method.

The principal difficulty in the application of the CP method (the maintenance of the constancy of the overall kinetic energy of the ions and E_{tot} at finite temperatures) is associated with the presence of the fictitious kinetic energy of the electrons, which depends on the fictitious mass μ. In choosing μ, it is necessary to seek a compromise. On the one hand, in order to diminish the oscillations in the 'real' energy, μ must be reduced. On the other hand, μ determines the minimum permissible time step in the integration and, in order to decrease the computational time, it is desirable to increase μ. This question as well as other procedures for the attainment of adiabatic conditions have been examined in a number of studies.[52,54,55]

The CP method has been applied successfully in the calculation of the structures (including the electronic structure) and properties of systems such as the protons in crystalline silicon,[56] liquid and amorphous silicon[54,57,58] and carbon,[59,60] liquid metals,[61] crystalline ice,[62] and liquid water.[63]

The fundamental limitation of the CP method in its current formulation is that the electrons exists only in the ground state, i.e. are on the Born–Oppenheimer surface, which is different for different characteristic structures (crystalline, liquid, and amorphous). Being capable of describing each of these structures, the CP method is not in principle designed to calculate the transitions between them. In this respect, the CP method is even more limited than the potential approach.

Thus, by resorting to CP quantum dynamics, we cannot solve the problem of the description of transitions between different electronic states.

The CP method proved to be extremely powerful, but it requires an enormous expenditure of computer time. This is associated with the simultaneous numerical integration of the equations of motion of the ions and electrons. The small time step in the integration is determined by the low fictitious mass of the electron, but the overall time is determined by the characteristic times of the dynamics of the ions. The total number of steps proved to be very large. The second cause is the enormous number of planar waves necessary for the calculation (several hundreds for semiconductors and several thousands for metals).

These factors limit the number of atoms involved in the calculation to ~ 100, whereas the number of particles required in calculations for complex reconstructions, dislocations, and real surfaces is much greater.

2. The tight-binding method

The wish to reduce the requirements for computer resources associated with the CP method led to the appearance of its simplified versions — the so called tight-binding methods (TBM). These methods make it possible to accelerate the computations by factors of tens and hundreds at the expense of accuracy.

In the most radical version[50] of the TBM, the following principal simplifications, compared with the CP scheme, are introduced:

(a) The abandonment of the explicit calculation of the electron dynamics.

(b) The choice as basis functions of only a small number of valence electron orbitals in the consideration of the crystal structure (four sp^3 orbitals per atom for diamond-like Si).

(c) The forces F_i acting on the ions from the electrons are calculated in accordance with the Hellmann–Feynman theorem

$$F_i = \sum_j < \psi_j|\frac{\partial\hat{H}}{\partial R_i}|\psi_j > ,$$

where $\hat{H}$ is the Hamiltonian of the electron subsystem (the summation is carried out over all occupied electronic levels).

(d) Interionic pair potentials are introduced in accordance with the equation

$$\Phi_2(R) = E_{tot}(R) - E_{BS}(R) , \tag{12}$$

where E_{tot} is the total potential energy of the system determined by the density functional method[64] and E_{BS} is the energy of the band structure calculated in accordance with the tight-binding empirical scheme.[65] The quantities $E_{tot}(R)$ and $E_{BS}(R)$ are found for a regular crystal structure per atom of the crystal.

Thus the equations of motion of the ions assume the form

$$M\ddot{R}_i = F_i - \nabla_i \sum_j \Phi_{ij}.$$

They are solved according to the following scheme: (1) adjustment of the energy of the electrons to the Born – Oppenheimer surface for the initial positions of the ions; (2) calculation of the forces F_i; (3) calculation of a single time step for the ions; (4) recalculation of the wave functions and return to step 2.

The phonon spectra of diamond-like silicon,[50] the fine anharmonicity effects (thermal expansion, the shift and broadening of the phonon lines with increase in temperature) in diamond-like silicon,[66] the degree of adsorption of hydrogen on the (100) surface of diamond,[67] etc. have been calculated with the aid of the TBM.

The attempts to apply the TBM to the modelling of different Si and Ge surfaces demonstrated its nonuniversality,[68] analogous to the nonuniversality of the classical potential approach. The reason for this is that a system of basis wave functions specific to a tetrahedral structure is employed. This system is unsuitable for the description of electronic structures with symmetries other than tetrahedral, which have other wave functions.

These considerations led Mercer and Chou[68] to the conclusion that the TBM must be parametrised for Si and Ge. Here $E_{BS}(R)$ is again calculated for the sp^3 orbitals, while $E_{tot}(R)$ is calculated separately for each of the large number of crystalline modifications. Thus the interionic pair potential $\Phi_2(R)$ is found to be different for different crystal lattices, i.e. its dependence on the coordination appears. This dependence was in fact parametrised in such a way that $\Phi_2(R)$ was a function of the local environment of the given atom, i.e. of the local coordination number. This procedure is fully analogous to that employed by Tersoff[22] in the classical potential approach. In this approach, $\Phi_2(R)$ is a cluster functional.

The parametrised TBM is extremely flexible, i.e. it makes it possible to describe successfully virtually all reconstructions of the Si or Ge surfaces with the aid of the same (for each element) set of adjustable parameters.[69]

Thus the situation illustrated schematically in Fig. 1 is also repeated in the TBM. By using this method, it is possible to construct a potential surface having local minima close to the real minima for different electronic states (terms). On the other hand, it is clear that the dynamics of the transitions between these states cannot be reproduced by such procedures. The CP and TBM methods operate only with stationary solutions of the Schrödinger equation. On the other hand, the description of the electronic transitions requires the solution of nonstationary quantum-mechanical equations.

V. Reconstruction, adsorption, surface diffusion, clusters

1. Modelling of the surface

The block of mobile particles in the MMD is referred to as the basic cell (BC). For the surface of a crystal, it consists of a certain number of layers of particles and is bounded 'from below' by a layer (or several layers) of stationary particles. When necessary, the deeper layers can be replaced by a continuous medium, which acts on the BC in accordance with the Mie or Steele potentials.[6] We select a cell with a height h and a length and width l [in the horizontal directions, the BC is either also bounded by layers of stationary particles or periodic boundary conditions (PBC) are used in these directions]. The number of particles in the BC is $N = nl^2h$, where n is the average concentration of particles.

The choice of the dimensions of the cell. Modelling a section of the surface, is made in such a way that the motion of individual atoms reproduces characteristics of the phonon spectrum important for the given problem; the reconstruction and relaxation of the cell surface are reproduced.

In the modelling of equilibrium processes (desorption, surface diffusion, incidence of thermal particles) at a certain temperature, the size of the cell is chosen on the basis of the conditions l, $h > k_{min}^{-1}$, where k_{min} is the minimum wave vector of the phonons which still contribute to the energetics of the process investigated.

In the modelling of nonequilibrium processes (incidence of fast particles), the size of the BC must be chosen so that the interaction time t_1 (the computation time) is much shorter than the time t_2 required for the return to the surface of the nonequilibrium excitation reflected from the BC boundary:

$$t_1 \sim \frac{\sigma}{v_{inc}} \ll t_2 \sim \frac{l}{c} \left(\text{or } \frac{h}{c}\right), \tag{13}$$

where σ is the characteristic dimension of the potential, v_{inc} is the velocity of the incident particle, and c the speed of sound.

There exists a procedure for softening condition (13) by introducing the removal of heat into the calculation. The Langevin terms (the δ-correlated random force and friction linked in accordance with the fluctuation-dissipation theorem) are then introduced into the equations of motion (1) for the boundary particles in the BC. They model thermal conduction, quenching the nonequilibrium excitations arriving at the cell boundary. The inequality (13) is replaced by the condition $t_1 < t_2$.

The above conditions are useful for the estimation of the characteristic dimensions, because the quantities involved in them are frequently known only in terms of order of magnitude. It is desirable that the choice of the final BC dimensions (and boundary conditions) should be made on the basis of the results of trial calculations.

Boundary conditions. The reconstruction and relaxation of the surface can be modelled only with the aid of PBC. On the other hand, if the structure of the surface is already known, then the corresponding geometry can be specified for a bounded cell. Nevertheless it appears that an equal degree of uniformity of the BC along the horizontal plane is attained for PBC when the BC size is smaller than for a bounded cell.

The removal of heat is more naturally modelled for a bounded BC, because it can be achieved in all directions, whereas for PBC it is possible only in the 'downward' direction. The reproduction of the removal of heat for PBC requires an increase in the size of the BC compared with the bounded cell.

Averaging. The result of the interaction of an incident particle with the surface depends on the position of the target point relative to the surface atoms. Therefore, if interaction coefficients averaged with respect to the surface are required, the averaging must be carried out with respect to all the positions of the target point within the limits of the projection of the unit cell of the crystal (or the BC for a noncrystalline body) on the surface. Naturally, for a reconstructed surface the averaging region is greater than for a nonreconstructed surface. The statistical error increases owing to the motion of the surface atoms, which in fact never occupy equilibrium positions.

2. Reconstruction

Flat surface. An attempt at the classical modelling of the dynamics of the initial stage of the reconstruction (dimerisation) of the Si(100) and Ge(100) surfaces and of their equilibrium struc-ture has been undertaken[70] with the aid of potentials of the SW type.

In the initial instant, all the atoms occupy the sites of a tetrahedral structure and have velocities with a Maxwellian

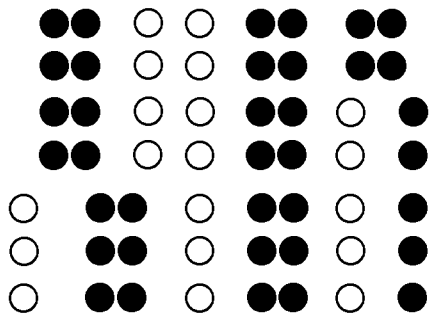


Figure 3. Schematic illustration of the first layer of a reconstructed silicon surface.

distribution at the temperature considered. In the course of the computation, the nonequilibrium initial structure evolves to a reconstructed structure containing ordered rows of dimers (Fig. 3). The reconstruction takes place as follows: the formation of a dimer at any surface site induces the rapid dimerisation of two adjoining atoms, etc., i.e. a growing row of dimers appears. Two rows of dimers, growing in opposite directions, can meet and form a single long row. If the rows are displaced relative to one another when they meet, then 'free' atoms are formed at the meeting point.

The properties of the equilibrium structure obtained correspond to the available experimental data. The average distance between the atoms in the dimer proved to be 2.42 Å (the experimental values range from 2.36 to 2.47 Å). The qualitative explanation of the experimentally observed transition from the $c(4 \times 2)$ structures (inclined asymmetric dimers) and $p(2 \times 2)$ structures (inclined symmetrical dimers) at low temperatures to structures with the (2×1) symmetry (noninclined dimers) at high temperatures is one of the most interesting results.[70] From the standpoint of the MD experiment at finite temperatures, the inclined dimers are always present owing to the thermal shift, i.e. the 'instantaneous photograph' always reveals their presence. However, at low temperatures the slopes of neighbouring dimers are correlated — they exist in the counterphase. This in fact yields an instantaneous picture of type $c(4 \times 2)$ reconstructions. Owing to the intensification of thermal motion, at high temperatures the inclinations of the dimers become noncorrelated, which corresponds (on average) to the (2×1) symmetry.

The attempt to apply the more complex Tersoff potential showed that the latter yields a force of attraction between the atoms in the dimer which is too large (Fig. 4).

Calculations have also been made[70] of the reconstruction times, but these results may be open to doubt (see Section III).

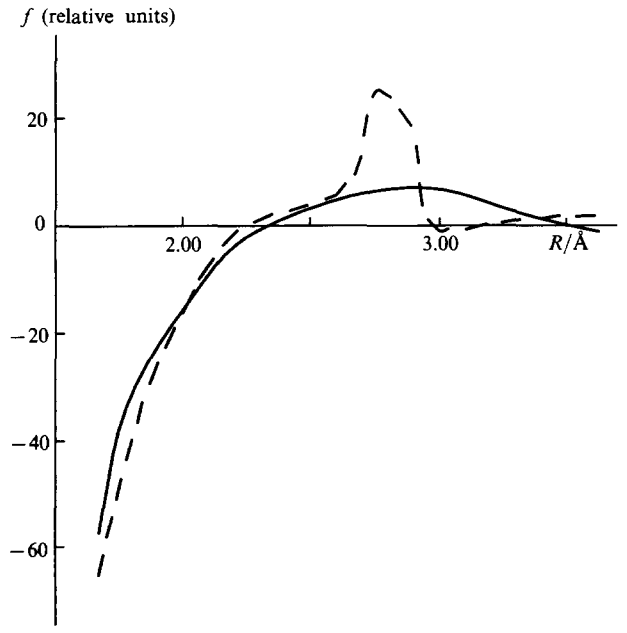


Figure 4. Forces acting in the direction between the atoms in the dimer for different potentials. Continuous line — calculation employing the SW potential; dashed line — calculation employing the Tersoff potential.

Steps. In a study of the atomic and molecular structures of monomolecular steps on the Si(001)−(2 × 1) surface, the Car–Parrinello method was employed.[71] A cell comprising seven layers was considered. The free bonds of the lower layer of silicon atoms were saturated by 48 oxygen atoms.

For a flat surface, it was found that symmetrical dimers, i.e. those in which both atoms have the same coordinate z, are unstable. Compared with $s(2 \times 1)$, the $b(2 \times 1)$ reconstruction (inclined dimers in which the difference between the levels of the atoms is $\Delta z = 0.51$ Å) lowers the overall energy by 0.10 eV dimer^{-1}. The ground state of a flat surface proved to be the $c(2 \times 4)$ reconstruction (the directions of inclination of neighbouring dimers in one row and on passing from one row to another alternate, $\Delta z = 0.72$ Å, and the decrease in energy is 0.24 eV dimer^{-1}). The $p(2 \times 2)$ reconstruction with $\Delta z = 0.72$ Å is inferior to the latter only to the extent of 8 meV dimer^{-1}.

The geometry of a monomolecular step may be extremely varied. Fig. 5 illustrates three configurations: S_A — the upper terrace dimers perpendicular to the edge of the step (Fig. 5*a*), S_B — dimers parallel to the edge of the step whereupon the step may be terminated by the row of atoms of the lower terrace, the corresponding dimer pair which is ahead of the upper terrace (Fig. 5*b*) or under it (Fig. 5*c*) (the nonrebonded and rebonded edges). The combination of the inclinations of the dimers, the

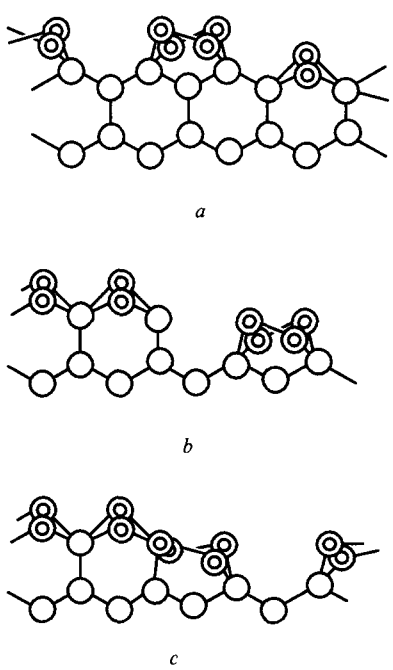


Figure 5. Schematic illustration of a step on the surface of silicon for three configurations: (*a*) S_A; (*b*) S_B (nonrebonded edge); (*c*) S_B (rebonded edge). The double circles denote the atoms of surface dimers. Apart from the atoms of the dimers, which are in the plane of the figure, the atoms in the next plane (in depth) are also shown.

different reconstructions of the upper and lower terraces, and the edges of the step decrease by a large factor the number of possible configurations. Boguslawski et al.[71] modelled only eight principal cases, including those variants of the S_A and S_B steps which had been observed experimentally.

Calculation of the electron dynamics enabled the authors[71] to reproduce the specimens observed in a scanning tunnel microscope and to compare them with the results of measurements. The qualitative features of experimental data could be explained on the basis of the shape of the wave functions of the surface states without additional hypotheses concerning the reconstruction induced by the blade.

3. Sticking, accommodation, adsorption, and scattering

The elementary sticking and accommodation steps have been widely investigated by the MMD, for example in Refs 41 and 72–74. We shall consider the study[41] where the sticking and energy accommodation coefficients for the atoms X (helium, neon, and argon) on falling on the Si(100) surface were calculated in the range of energies of the incident particles from 0.1 to 1 eV and at surface temperatures from 300 to 1000K. The Si–Si interaction was described in terms of the SW potential. The interaction of the X atoms with the Si atoms was described with the aid of the Lennard–Jones potentials.

The X atoms were projected towards the surface and at right angles to it from a certain distance z_0, selected at random, over which the X–Si interaction is virtually nonexistent. The initial position of the atom relative to the region of mobile surface particles was also selected at random. The distribution of the initial velocities of the moving surface particles was of the Maxwellian type at a temperature T_s in the range from 300 to 1200 K. The trajectories of all moving particles were calculated.

A particle was regarded as having been reflected when the condition $z > z_0$ (z being the current distance between the atom and the surface) was fulfilled, i.e. if the particle intersected the plane of projection in the opposite direction. This criterion of reflection leads to prolonged calculations, but it is necessary for the accurate calculation of the energy accommodation coefficient.

The atom is regarded as sticking if the direction of its velocity changes four times. Sometimes the first return of the particle to the surface is regarded in the literature as sticking.[74] However, visualisation of the calculations shows that the particle is in many cases reflected after the second collision with the surface atoms. On the other hand, instances of reflection after the third collision during the residence time of the X particles within the confines of the modelled block have not been observed.

After the completion of the calculation in each attempt, the surface particles return to the initial position with a new Maxwellian velocity distribution. The total number of attempts N for each energy E_i was 100. The sticking coefficient k_{st} is defined as the ratio of the number of attempts with sticking M_{st} to the total number of attempts M.

Fig. 6 presents the results of the MD calculations of the coefficients of sticking to the nonreconstructed Si (100) surface. The sticking coefficients diminish with decrease in the mass of the incident particles, with increase in their energy, and also after an increase in the temperature of the surface. A procedure has been proposed[41] for reconciling the results of the calculation with the analytical rigid cubes model[75] by introducing into the latter an effective angle of incidence ϑ.

A dependence on the mass of the incident particles is manifested also in interaction with the surfaces of polymers; we shall return to this question at the end of this section.

Methods in which the sticking of a gas to the surface is considered within the framework of the approximation where the incident atom is classical (quasi-classical) but the phonons are treated quantum-mechanically have been analysed.[76] A model example of the sticking of He, Ne, and Ar atoms to the surface of copper has been quoted.

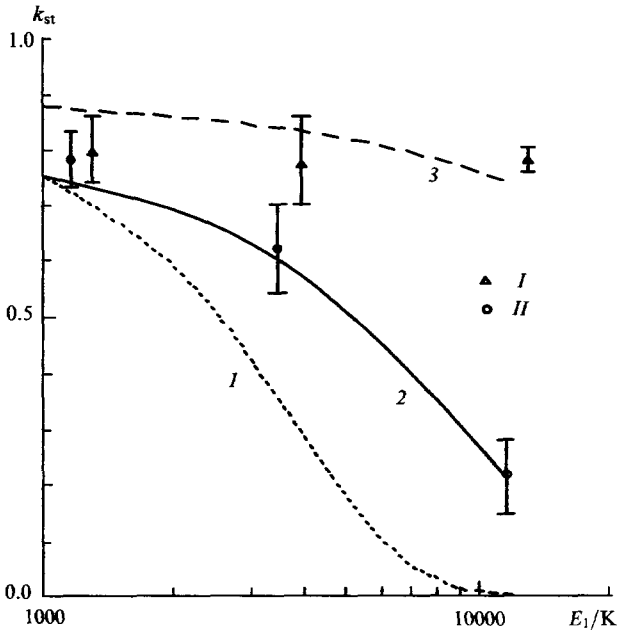


Figure 6. Dependence of the sticking coefficient on the energy of the incident particle. MD calculation: (*I*) Ne, surface temperature $T_s = 640$ K; (*II*) He, $T_s = 1160$ K. Rigid cubes model: (*1*) He (angle of incidence $\vartheta = 0$); (*2*) He ($\vartheta = \pi/6$); (*3*) Ne ($\vartheta = 0$).

The enthalpies of adsorption of 13 hydrocarbons (pentane, cyclohexane, 2-methylbutane, decane, etc.) on a mineral smectic clay have been calculated with the aid of the classical MMD.[77] The significant sensitivity of the results to the choice of the parameters of the Lennard–Jones potential used for the description of the interaction of the nonbonded atoms with one another was elucidated. None of the sets of potentials known in the literature made it possible to achieve agreement with experimental data.

Various equilibrium states of hydrogen adsorbed on the (001) surface of diamond have been considered by the tight binding method.[67] The method of molecular dynamics has been used only in the gradient descent method, i.e. as a procedure for the fastest determination of the location of the energy minimum for a system which was initially close to the configuration of the system under consideration. The structures of the clean C(001) surface and two structures with adsorbed hydrogen — monohydrogenated (001)—(2 × 1):H (phase *1*) and dihydrogenated (001)—(1 × 1):H (phase *2*). The structures of the electron bands and the density of the electronic states were calculated. It was found that there are no electronic states in the forbidden band gap in phase *2*, while in phase *1* they do exist. Yet another qualitatively explained effect is the repulsion of the surface electronic states in phase *2* into the conduction and valence bands. In the latter case, the surface electronic state is in resonance interaction with the electronic level of the C atom, which actually leads to an increase in the conductivity of diamond by several orders of magnitude after its treatment in a hydrogen atmosphere. This effect is apparently of a purely surface type.

For high energies of the incident particles, the treatment is restricted to the simplest interaction potentials. The individual trajectories of the incident Ne^+ ion (2 and 4 keV)[78] were modelled by a sequence of pair collisions with surface atoms. Account was taken of the collective effects when the Ne^+ ion interacts almost simultaneously with a group of atoms arranged in a nearly symmetrical configuration around the trajectory of the ion (chanelling is a typical example).

The scattering of ions on different Ni faces on the reconstructed Pt(110)–(1 × 2) and –(1 × 3) surfaces as well

as the dislodgement of the oxygen atoms adsorbed on Ni were investigated. The results agree satisfactorily with experiment.

4. Surface diffusion

The diffusion of rhodium and nickel adsorbed atoms on the (111) and (001) surfaces of rhodium and nickel respectively has been considered.[79] The Morse and inserted atom potentials were used. The distributions with respect to energies and the relation between the rotational and translational energies in the diffusion of a CO molecule on the Ni(111) surface have been determined in another study.[80] Tully's stochastic dynamics was used. The non-Arrhenius temperature dependence of the calculated diffusion coefficients is noteworthy. A comparison was made with Kramers theory.

Wang et al.[81] carried out calculations for the diffusion of a CO molecule on the Pt(111) surface at temperatures in the range 100 – 500 K. The surface was specified by a potential which depends on the coordinates of the stationary platinum atoms. The CO molecule was oriented mainly at right angles to the surface. The dependence of the diffusion on the rotational and vibrational states of CO was noted. The diffusion coefficients obtained agreed with the available experimental data within the limits of the scatter of the latter. An attempt was made to model the energy exchange between CO and the surface by including the interactions of the molecule with phonons. In view of the increase in the required computation time by a factor of 100, only two trajectories were calculated. They showed that the energy exchange influences the diffusion.

Engdahl and Wahnström[82] investigated the nonequilibrium diffusion of hyperthermal adsorbed oxygen atoms arising on dissociative chemisorption of the O_2 molecule on the Al(111) surface. In view of its complexity, the chemisorption process was not considered. The initial condition chosen was such that the bond in the O_2 molecule had already been ruptured and the atoms had moved apart so much that the interaction had been neglected. The initial energies of the O atoms were chosen to be 3.5 eV, which corresponds to the energy of the chemisorption of O atoms, and 9.5 eV (for comparison). The inserted atom potentials and Tulley's model were employed. In the model, the Langevin equations were used for the atoms of the third layer, while the atoms of the fourth and deeper layers were fixed in the equilibrium positions.

It was shown that the atoms are mainly displaced in the ballistic stage over a period less than 0.5 ns. Further thermalisation requires a longer time (> 5 ns) but takes place without a directional shift. The ballistic shift is 16 Å for an initial energy of 3.5 eV and 52 Å for 9.5 eV. The latter shift (and not the former as one would wish) agrees with measurements by means of scanning tunnel microscopy. The penetration of atoms into the bulk of the support takes place in the first 0.2 ns, whereupon the number of inserted atoms proved to be approximately twice as great as the number observed experimentally. The possible role of nonadiabatic transitions in the diffusion of adsorbed atoms on the surface was not discussed in the above studies.[79–82]

MD studies on surface diffusion have not yet received due recognition. Thus, in a review[83] where the results obtained with the aid of scanning tunnel microscopy for the motion of atoms on different surfaces are analysed, no mention whatever is made of molecular dynamics. It was actually claimed that "surprisingly little is known about the mechanisms of the motion of atoms on the surface". Yet one of the main purposes of MD is in fact the study of such mechanisms of dynamic processes.

5. Interaction of clusters with surfaces

Recently much attention has been devoted to the MD modelling of the processes involving the incidence of atomic and molecular clusters on the surfaces of solids.[84–92] Studies have shown that the cluster–support collisions are not described by simple analytical models, since no account is taken in the latter of the collective effects of interatomic interaction. This is the reason why MD modelling is required.

The scheme used in such modelling does not in essence differ from that described above for the incidence of individual atoms (molecules). On the other hand, the choice of the interparticle interaction potentials depends on the energy of the incoming clusters and the energies of the particles in the final state. The entire range of energies investigated is arbitrarily divided into two regions: high energies (> 1 keV atom^{-1}) and low energies (< 1 keV atom^{-1}).

In the first case, problems such as that of the possible appearance in the collision zone of conditions for an appreciable release of neutrons[84,85] or for the excitation of the internal electron shells of the atoms[86] are investigated. Here the relatively short times after the incidence of the cluster are important, during which the highest concentrations of energy are attained and the result is determined by close pair collisions of the atoms. Comparatively simple pair repulsion potentials are therefore selected.

In the case of low energies of the clusters, the formation and structure (epitaxial, amorphous) of the films arising in the interaction of the clusters with the surface,[87,88] the dependence of the appearance of different structures (films, blobs, craters, insertion zones) on the energy and size of the incident clusters,[89] are investigated as are the angle, size, and velocity distributions of the small clusters dispersed from the surface when ions are incident on it.[90] Here it is necessary to trace the energy relaxation process, sometimes up to the thermal level, so that more realistic and complex, multiparticle interaction potentials are needed.

We shall consider in greater detail the processes of this group in relation to the study of Hsieh et al.[89] The incidence of Cu, Ni, and Al clusters with dimensions ranging from 4 to 92 atoms and energies from 92 to 1000 eV atom^{-1} on the surfaces of the same metals in various combinations was investigated. The inserted atom potentials, modified for short distances in order to take into account correctly the collisions of atoms having high energies, were employed.

Depending on the size and energy of the clusters, the elastic and chemical properties of the materials, and the ratio of the atomic masses of the cluster and the support, significantly different results were observed for the interaction. The cluster consisting of 92 copper atoms, incident on the copper surface at low energies, can form a blob, whereas at high energies it penetrates the support, inducing its marked deformation. If the energy of the cluster exceeds 25 eV atom^{-1}, surface defects arise in the support. A cluster consisting of 92 aluminium atoms hardly deforms a nickel support, spreading on the latter epitaxially despite the 15% discrepancy between the Al and Ni lattice parameters. For an energy of 1 keV atom^{-1}, several Al atoms break away from the cluster and are either deflected into a vacuum or are scattered on the surface. Ni clusters with an energy of 326 eV atom^{-1} are almost fully incorporated in the aluminium support and form local amorphous zones.

Fig. 7 presents a diagram illustrating the mechanisms of the interactions of clusters with a surface,[89] showing what results should be expected depending on the kinetic energy of the incoming cluster and the bond energies for an atom in the cluster and in the support.

It is essential to note that, in the MD modelling of certain cluster processes by using the potential approach, it is also necessary to exercise caution (see Section III). Thus it has been found[90] that numerical data agree qualitatively with experimental data and with data derived by means of the analytical theory of the energy distributions of the atoms and dimers dislodged from the surface of the copper crystal when an argon ion is incident on the latter. On the other hand, in order to achieve a quantitative agreement with the theory, it is necessary to choose a copper sublimation energy which is much smaller than the experimental value. The authors[90] explain this discrepancy by the 'loss' of some of the dislodged low-energy atoms due to the characteristics of the methods used in the MD experiment.

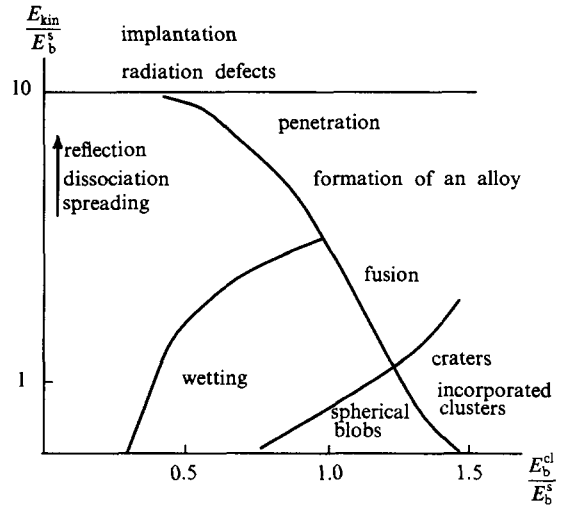


Figure 7. Diagram illustrating the mechanisms of the interaction of clusters with the surface. E_{kin} = kinetic energy of the cluster per atom; E_b^{cl}, E_b^s = the bond energies of the atoms of the cluster and the surface respectively.

However, another interpretation is also possible. If one considers surface + bound atom and surface + free atom states as different electronic states, then the sublimation energy corresponds to the height of the potential barrier between them. As noted in Section III, the interpolated potential surface can model incorrectly the potential barrier between different electronic states. One cannot rule out the possibility that this was in fact the reason for the discrepancy between the qualitative and experimental sublimation energies in the above study.[90]

Insepov et al.[91] investigated the dispersion of the gold surface atoms by argon clusters comprising 87, 141, and 201 atoms. The energy of the cluster was 100 eV atom^{-1}. A method was developed for the removal of the excess pressure arising on impact. The dispersed material of the target consisted of small gold clusters; lateral dispersion was observed.

The limiting case of the spreading of the involatile microblob, present initially on the surface, has been modelled by isothermal MD.[92] Both one-component blobs comprising Lennard-Jones particles and two-component blobs were considered. The second component consisted of a very simple polymer model: a flexible elastic chain consisting of two, four, or eight Lennard-Jones atoms. The total number of atoms in the microblob was $\sim 10^3$. The polymer concentration varied from 0% to 100%. The surface was modelled by a uniform half-space acting on the atoms of the blob via the Mie potential. The initial form of the microblob was specified as a comb periodically extended along its entire length.

The formation of the precursor film was investigated: its width increased initially almost linearly as a function of time and then its growth became diffusional. Its thickness could correspond to the thickness of one or several stepped layers. In the case of polymer solutions, the layers began to mix, which led to their shape approaching hemispherical. The nature of the mixing was investigated for different polymer models and different parameters of the potential. The results agree qualitatively with experimental data.

6. Processes on the surfaces of liquids and polymers

The surface of a liquid differs from that of a solid, apart from lack of order (which incidentally is also characteristic of amorphous solids), also by the fact that it is not as a rule sharp. The density of the surface layer of a liquid gradually decreases from the density of the liquid to the density of the saturated vapour over several intermolecular distances in the liquid.

The scattering of Ne atoms on the surface of glycerol has been modelled[93] for collision energies ranging from 25 to 60 kJ mol^{-1}. The glycerol molecule was described by a nine-centre model, which makes it possible to take into account the torsional flexibility. The hydroxyl hydrogen atoms were included explicitly in the model, i.e. the hydrogen bonds appeared directly. The intramolecular potential energy was expressed approximately by the sum of the Coulombic and Lennard-Jones pair interactions and also by torsional terms. The intermolecular interaction was represented by the sum of Coulombic and Lennard-Jones pair-additive terms. The Ne-glycerol interaction involved only the Lennard-Jones interaction. The glycerol surface at $T = 300$ K was modelled by a cubic cell comprising 343 glycerol molecules with two free surfaces along the z axis. A vaporised glycerol molecule was not observed (the melting point is 291 K).

The sticking, reflection and desorption coefficients of the Ne atoms after several collisions were calculated. The energy losses and the energy and angular distributions were found for the reflected Ne atom. The results agree satisfactorily with experimental data. When an attempt was made to describe the results with the aid of a simple binary collisions model, a decrease in the effective mass with increase in the collision energy was observed. This has been explained by the influence of multiple collisions and by vibrations of the liquid. Data on the energy transfer in the liquid were obtained. The collision energy passes to translational and rotational modes and, to a lesser extent, torsional modes. The energy is then rapidly distributed among the neighbouring glycerol molecules.

Ahlström and Berendsen[94] modelled a L-didecanoyllecithin (an example of an amphiphilic molecule) monolayer on the surface of water. The area of the surface was chosen so that 42 lecithin molecules were accommodated on it. The thickness of the layer of water molecules was 4 nm. The water layer was covered by lecithin from below and from above. The density profiles, the surface tension, and the electrostatic surface potential were found. Local penetrations of water molecules into lecithin were observed. The water-lecithin contact surface is very large and disordered. The results proved to be extremely sensitive to the form of the potential energy for lecithin.

Computer modelling of the dynamics of light gases in a 'rigid' dense polymer matrix exhibits apparent discrepancies with experimental data. Modelling shows that light atoms and molecules (H_2, He) easily attain the diffusional regime, whereas the mobility of heavy atoms and molecules proves to be low. The authors[95] conclude that the 'rigid' matrix is an inadequate representation of the dense system comprising polymer molecules. A qualitative agreement with experimental results can be attained by taking into account the influence of the thermal vibrations of the polymer molecules on diffusion.

VI. Chemical reactions in terms of the adiabatic approximation

1. The use of potential surfaces.

Etching. The chemical interaction of fluorine atoms[45] and molecules[96] with a reconstructed Si(100)-(2 × 1) surface has been modelled. The temperature of the surface of the incident atoms was 300 K. Use was made of the SW type interaction potentials (Si-Si, Si-F, F-F), the parameters of which were chosen in order to achieve agreement with independent experimental data. Sticking, the dissociation of molecules on the surface, the formation of various compounds between fluorine and silicon, etc. were investigated. Hypotheses concerning the etching mechanisms were put forward.

It was observed[45] that, when there is less than one monolayer of F atoms on the surface (surface coverage $\theta < 1$), three outcomes of the incidence of a F atom on the Si surface are possible:

(1) recoil (30%);

(2) chemisorption (the capture of a F atom at the site of rupture of an Si–Si dimer bond or capture by a free bond (60%);

(3) physical sorption (the capture of a F atom by the surface as a whole with retention of the mobility of the F atom along the surface) (10%).

When the coverage of the Si surface by F atoms ranges from $\theta = 1$ to $\theta = 1.25$, the structure of the Si–F surface layer is ordered and stable. There is then no chemisorption, i.e. the physically adsorbed atoms do not penetrate into the bulk of the surface layer and do not form chemical bonds with silicon atoms.

For $\theta > 1.25$, the ordered state of the first adsorbed F layer (illustrated schematically in Fig. 8) becomes unstable. The mutual repulsion of the F atoms distorts the structure. The surplus F atoms can penetrate into the bulk of the surface layer and can break the bonds between the silicon atoms with formation of the complexes SiF, SiF_2, and SiF_3. Subsequently the complex SiF_3 can combine with yet another F atom to form the volatile SiF_4 (etching).

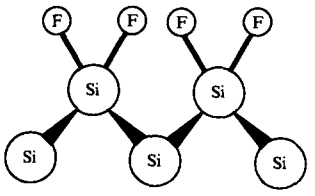
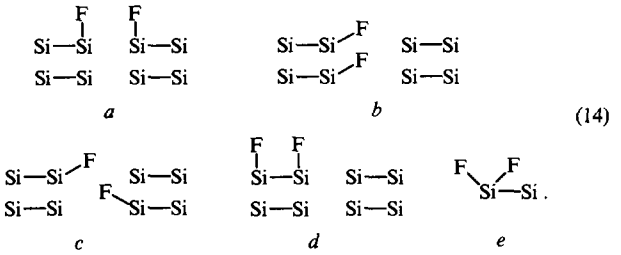


Figure 8. The ordered state of the adsorbed fluorine atoms on silicon.

The overall conclusion of the above study[45] is that, in order to attain the highest rate of etching, the greatest possible disorder of the initial surface is required.

Two main paths in the interaction of an F_2 molecule with the Si surface have been observed[96] — the chemisorption of one of the F atoms and the recoil of the other or, more rarely, the chemisorption of both atoms of the dissociated F_2 molecule. In addition the formation of the Si–F–F complex, where the second F atom is weakly bound to the rest of the complex, has been noted. Rare instances of the reflection of F_2 molecules have also been detected (10^{-3}).

Two chemisorbed F atoms form different combinations of chemical bonds with the Si atoms of the dimers. These bonds can be illustrated schematically as follows:



(14)

Evidently the F atoms can be linked to neighbouring Si atoms belonging to two dimers of different rows (*a*) 'opposite' configuration), two dimers in one row (*b*) 'adjacent' configuration), two dimers in different rows with a displacement by one dimer (*c*) 'diagonal' configuration), one dimer only (*d*) 'the same' configuration). Case (*e*) corresponds to the complex SiF_2.

The numerical probabilities calculated by the MD method can be questioned (see Section III), but the dry etching model agrees qualitatively with experimental data. The study of the role of the removal of heat in the interaction of fluorine molecules with a silicon surface has been initiated.[97]

Surface photochemistry. The dynamics of the surface photochemistry in the system comprising HBr molecules adsorbed on the LiF(001) surface and $\hbar\nu$ quanta has been investigated.[98] The interaction on the surface of the product of the photolysis (H atoms with an energy of 2.6 eV) with H′Br molecules (H and H′ denote simply different hydrogen atoms) has been investigated by the method of classical stochastic Tully trajectories.

$$\mathrm{H'} + \mathrm{HBr} \longrightarrow \begin{cases} \mathrm{H'Br} + \mathrm{H} \\ \mathrm{HH'} + \mathrm{Br} \end{cases} \qquad (15)$$

The interaction energy was specified by the London–Eyring–Polanyi–Sato potential supplemented by the electrostatic and nonelectrostatic potentials of the interaction of the adsorbed atoms with the surface and with one another.

The probabilities of the occurrence of the reactions via paths (15) were investigated, the energy and angular distributions of the H′ atoms were found, and the dependences of these quantities on the surface coverage and temperature were determined. A decrease in temperature increases the probability of the reaction at low coverages and diminishes it at high coverages ($\theta > 0.5$). This effect has been attributed to the formation of a cellular structure of the adsorbent.

Discussion. In the studies considered above and many similar ones, both the results of the dynamic process and the process dynamics itself were investigated. There are no grounds for doubting the reasonableness of this approach to the determination of equilibrium properties — energies, configurations, structures, etc. The process dynamics also has a physical signifiance when one investigates processes occurring on the same potential surface, as specified, for example, in formula (15). As regards processes in which the initial and final stages of the system belong to different electronic states and their wave functions cannot be obtained from one another by any adiabatic alteration of the coordinates of heavy particles, the MMD constitutes for such processes a computational procedure for the determination of the properties of the system in the final equilibrium states. On the other hand, the correspondence of the dynamic process itself to real quantum dynamics requires at least a careful discussion. However, such processes are not even considered in these investigations.

2. Quantum adiabatic calculations

The Car–Parrinello method has been used[100] to investigate the vibrations of hydrogen atoms chemisorbed on the Si(111)–(1 × 1) surface. Fourier analysis of the MD trajectories made it possible to determine the frequencies of the surface phonon mode and to observe an anharmonic relation between the Si–H vibrations and the lower-frequency mode of the surface phonons. The calculated frequencies agree well with the experimental values (except one). The dispersion curves are also close to the experimental ones.

Since the publication of the Car–Parrinello method, investigators made considerable efforts to reduce the expenditure of computer time. One approach involves the improvement of computational schemes (see, for example, Gibson and Carter[101] and Tuckerman and Parrinello[102]). In another approach the number of particles treated quantum-mechanically is reduced and they are surrounded by classical atoms, i.e. a special selection of boundary conditions is made. As an example, we shall discuss a study[103] where the adsorption of the ethyne molecule on the Si(100)–(2 × 1) was modelled.

The basic cell consisted of 360 silicon atoms arranged in ten layers (Fig. 9). The first six layers of atoms moved in accordance with Newton's equations, the seventh, eighth, and ninth layers modelled the removal of heat, and the tenth layer, comprising stationary atoms, bounded the cell from below. Periodic boundary conditions were imposed along the x and y axes. The central group of atoms (quantum cluster), comprising 35 silicon

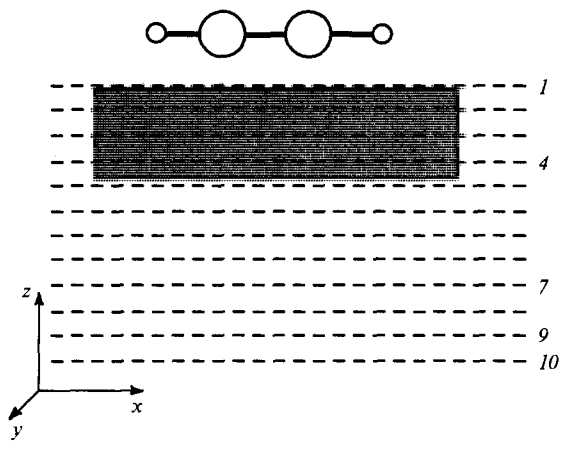


Figure 9. Schematic representation of the basic cell. The quantum cluster is shown shaded: (*1*) – (*10*) numbers of the layers.

atoms in the first four layers (the shaded region in Fig. 9), was examined quantum-mechanically, whilst the remaining atoms interacted with one another in accordance with a potential of the SW type (classical approximation). The problem of the interaction of the "quantum-mechanical" atoms with the "classical" atoms surrounding them was specially solved.

Two configurations of the quantum cluster were considered. The surface layer in a planar projection for the first configuration is illustrated in Fig. 10*a*, while the second layer is show in Fig. 10*b*. The crosses denote the region of incidence and the possible orientations of the C_2H_2 molecule. The first configuration modelled the incidence of C_2H_2 on the dimer or within a row of Si dimers, while the second modelled the incidence between the rows of dimers.

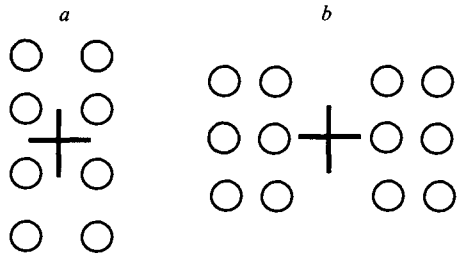


Figure 10. The surface layer of a quantum cluster in plane form. Incidence on a row of dimers (*a*) and between rows (*b*).

The dynamics were considered as follows. With the aid of one of the semiempirical quantum-mechanical methods, the ground electronic state of the system was found: a quantum cluster of Si atoms + C_2H_2 molecule, i.e. a system consisting of 35 Si atoms, two C atoms, and two H atoms. (Additional hydrogen atoms were actually introduced in order to eliminate surface effects — in order to "close" the free valence bonds). The forces found from the quantum-chemical calculations and from the SW potential were then used in Newton's equations, the new positions of all the atoms in the nine layers were found (Fig. 9), and the procedure was repeated. The dynamics of the physical and chemical sorption was investigated in this way, the time characteristics of the interaction were found, and the bond energies and the geometries of the resulting equilibrium configurations were determined.

In the case of a coaxial incidence of the C_2H_2 molecule on the silicon dimer in the geometry presented in Fig. 10*a*, the formation of chemical compounds between C_2H_2 and the silicon surface containing both one σ-type Si – C bond (Fig. 11*a*) and two such

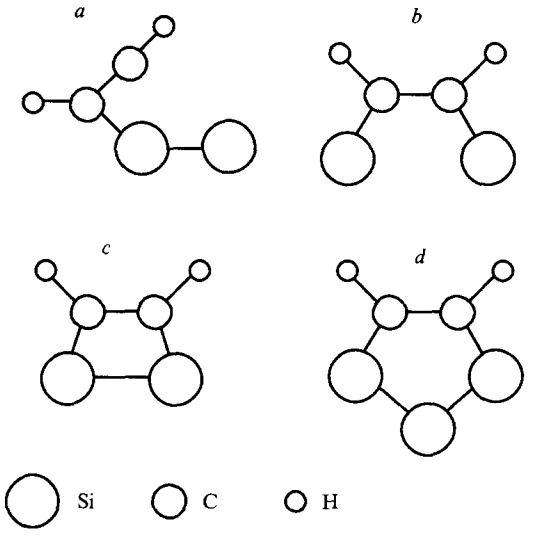


Figure 11. Schemes explaining the formation of chemical compounds between C_2H_2 and the Si surface: (*a*) the formation of one bond with the Si – Si dimer; (*b*) the formation of two bonds with dissociation of the Si – Si bond of the dimer; (*c*) the formation of two bonds without the dissociation of the Si – Si bond of the dimer; (*d*) the formation of a bridged compound.

bonds (Fig. 11*b*) was observed. In the case of the configuration shown in Fig. 11*b*, the Si – Si bond in the dimer was broken. This bond could then be restored without the dissociation of a Si – C bond, but this configuration (Fig. 11*c*) proved to be unstable. After several transitions from the configuration 11*b* to 11*c* and conversely at 100 – 400 fs intervals, the collision configuration 11*b* was established.

The result of the incidence of C_2H_2 depended strongly on the site of incidence. On incidence between neighbouring dimers of the same row, when the axes of the dimer and C_2H_2 are mutually perpendicular (Fig. 10*a*), the bridged configuration 11*d* may be formed. On incidence of C_2H_2 between neighbouring rows of dimers (Fig. 10*b*), bridging configurations were not observed. Only physical sorption was noted and the axis of the C_2H_2 molecule was arranged almost parallel to the surface of silicon. In the case of the migration of C_2H_2 onto the row of dimers, the configurations already considered in Figs. (11*a*) and (11*b*) were formed. The dependence of the outcome of the incidence on the orientation of the molecular axis of C_2H_2 relative to the axes of the dimers was no less marked. For a nonparallel arrangement, the ethyne molecules were reflected.

The criticisms expressed in the previous subsection retain their force in this case too. Indeed, the authors themselves[103] present a plot analogous to that shown in Fig. 1. The physical and chemical sorptions are described by different potential curves (curves *2* and *1*) corresponding to different electronic states. In fact, the calculations[103] are performed for curve *3*, joining both local minima. Thus the dynamics of the transition from physical to chemical sorption within the framework of the above approach[103] is described with the aid of Newton's equations for a single potential surface. However, in actual fact this transition is electronic and should be described by the nonstationary Schrödinger equation. We may note that it is seen from Fig. (11) that a whole series of chemisorption states are possible, i.e. there should be several type *2* curves in Fig. 1 in this case.

However, these questions were not even mentioned in the above study.[103] Thus the time characteristics obtained[103] may not correspond to reality. On the other hand, the equilibrium characteristics of the final state do not give rise to such doubts — the formulation of the problem of their determination is correct and the error may be due only to the approximate nature of the computational procedure or $\Phi(R)$.

VII. Nonadiabatic quantum molecular modelling

Sections II – VI led to a paradoxical conclusion: both the classical and quantum MMD may prove to be inadequate precisely in those applications for which they have been in fact generally speaking designed — for the calculation of the dynamics of the transitions between different states. Such calculations require the solution of the nonstationary Schrödinger equation. The numerical methods for the integration of this equation have been the object of intense investigation (see, for example, Refs 5 and 104 – 110 as well as the references contained therein). By themselves, these methods have no bearing on the MMD, which is based on the calculation of trajectories, although they can be combined with it in order to solve quantum problems, as will be shown below.

Molecular dynamics with electronic transitions. A series of studies associated with Tully's name have been devoted to this question.[5,104–106] We shall explain the idea of the method by means of a schematic example (Fig. 12). Suppose that a particle is reflected during adiabatic motion along trajectory *1*. If the particle causes the excitation of the surface of a solid, it loses part of the energy, a nonadiabatic electronic transition takes place, and the particle trajectory (curves *2*) changes, in particular sticking may occur.

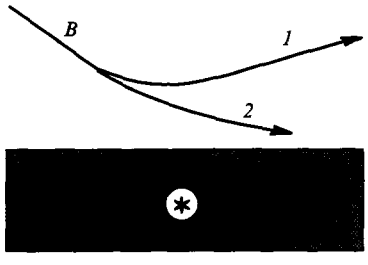


Figure 12. Scheme explaining the splitting of the trajectory in electronic transitions. The star denotes the excitation of the surface.

It is clear from the foregoing that the branching of the trajectories is a distinctive feature of MD with electronic transitions, which has already been discussed in Section III (the potential picture in Fig. 1*b* corresponds to Fig. 12). No jumps in space occur under these conditions, the concept of the trajectory is retained, and the latter remains smooth, but at point *B* the trajectory no longer satisfies Newton's equation. Since the electronic transition has a probability, it is necessary to generate a family of trajectories with the same initial conditions. The frequency of the appearance of points *B* and their spatial distribution are then modelled.

In the general case, the problem involves the nonstationary Schrödinger equation for a quantum particle or a subsystem of particles, the transitions between different adiabatic potential surfaces, and Newton's equations for heavy particles. The Schrödinger equation can be approximately reduced to ordinary differential equations for the expansion coefficients of the wave function in terms of stationary states, the coefficients being time-dependent in the given instances. Newton's equation includes the response of heavy particles to electronic transitions in the quantum subsystem.

In view of the complexity of this problem, solutions have so far been found only for certain special cases. Thus one-dimensional two-level methodological examples have been considered.[5] In other studies,[104,105] a series of results have been obtained for the solvated electron. The study of Webster et al.[106] was devoted to further development of the method and to a methodological two-level example.

In order to illustrate the role of nonadiabatic effects, Dodson[4] carried out the MD modelling of the incidence of silicon atoms onto a silicon support for a single energy (12.5 eV) and two interaction potentials of the incoming atom with the surface atoms: a type SW potential described the adiabatic case and the Ziegler – Biersack – Littmark potential described the case of the complete rupture of Si – Si bonds. The results proved to be very different: thus the depth of penetration of the Si atoms into the surface layer was 2.8 Å in the first case and 10.5 Å in the second.

Tunnelling. It has been noted[5] that this process can be investigated separately from electronic transitions, since the probability of the latter decreases, according to Massey's criterion, with increase in the velocity and is independent of the mass of the particles, whereas the role of tunnelling increases with decrease in velocity and in mass. The object of study was the dissociation of hydrogen molecules on a surface.

The dissociation of H_2 on copper has been considered.[107] In view of inadequate computer capacity, the quantum calculations were restricted to the case of a two-dimensional potential surface. Although the influence of quantum effects on the sticking coefficient was in fact noted, a satisfactory agreement with experiment was attained only on passing to a six-dimensional description of the potential surface within the framework of quasi-classical molecular dynamics.

The grid method was used for the numerical integration of the time dependent Schrödinger equation.[107] In this case, the computation time is proportional to N_g^D, where N_g is the number of points in the grid and D is the dimensionality (the number of degrees of freedom). The nonstationary problem has been solved[108] with the aid of the multiconfiguration Hartree approximation with a natural choice of one-particle states. The computation time proved to be proportional to $N_g^{D/2}$. However, only a two-dimensional model of the dissociation of H_2 on the surface of a generalised transition metal was considered as an example.

An approximate approach, which made it possible to model the dissociation of the hydrogen molecule when it is incident on the Cu(110) surface, has been proposed.[109] The interaction surface of the $H_2 - Cu(110)$ system was six-dimensional. It was found by using the inserted atom method and for H_2 it was brought into correspondence with the LEPS surface. The probability of sticking (α) and the free energy activation barrier (ΔF) were found in terms of the approximation of the quantum theory of the transition state (TTS):

$$\alpha = \exp(-\beta \Delta F) , \tag{16}$$

$$\Delta F = -\int_s f \mathrm{d}s , \tag{17}$$

where s is the trajectory of the hydrogen molecule and f the average force acting on this molecule taking into account the quantum dispersion. The principal TTS approximations are as follows: (1) the inequality $\alpha \ll 1$ must hold for Eqn (17) to be valid; (2) in the phase space of the $H_2 - Cu(110)$ interaction there must be a narrow place which would make it possible to determine clearly the hypersurface separating the region of the initial state (the H_2 molecule) from the region of the reaction product (the H + H atoms); (3) (the main approximation) when the trajectory s of the H_2 molecule intersects the separating hypersurface, determined on the basis of the preceding assumption, the dissociation of H_2 is assumed to have occurred. Thus the integration in Eqn (17) is carried out from the distance where the $H_2 - Cu$ interaction can be neglected up to the intersection by the separating hypersurface.

For the calculation of ΔF by Eqn (17), the following approximate procedure has been proposed.[109] The minimum energy path which smoothly and continuously transfers the system from the initial to the final state is found. This is carried

out by a novel method, developed by Mills and Jonsson,[109] whereby the trajectory s is obtained. Five-dimensional hypersurfaces perpendicular to s are determined in succession along this trajectory. For each surface, the average force f acting on the H_2 molecule located on this hypersurface is found. The calculations are repeated until the hypersurface with $f = 0$ is reached. After this, the integral (17) and then α are found.

All the quantum effects are contained in the force f. In order to determine the latter, the formal treatment involving integrals along the trajectories, already mentioned earlier in connection with molecular modelling, is resorted to.[12,111] The representation of the partition function, proposed by Feynman, in the form of a Wiener integral along the 'trajectories'¶ is employed. Its finite-dimensional approximate representation has the same form as the classical partition function for a cyclic system of linked identical harmonic oscillators with an elastic constant determined by the mass of the particle, temperature, the constant $\hbar$, and the number of subdivisions of the cyclic 'trajectory'.¶ The 'trajectory' characterises the quantum dispersion of the H atom and is specific to each H atom.

Thus, in order to find the quantum dispersion and the average value of f, one may carry out the classical MD modelling of the motion of a cyclic chain of linked oscillators for each atom. The centre of gravity of both chains is then retained by force on the chosen hypersurface. The classical limit of the modelling corresponds to the contraction of the chains into a point on the trajectory s. In addition to hydrogen atoms, such modelling has been carried out for the eight copper atoms closest to the H_2 molecule. The chains consisted of 50 units.

The results of the calculations showed that the quantum effects begin to exert an influence at a temperature below 600 K, where the delocalisation of the hydrogen atoms is manifested, leading to a decrease in the effective activation energy $E_a = \partial(\beta\Delta F)/\partial\beta$ from 0.70 to 0.45 eV. However, the absolute value of $\beta\Delta F$ proved to be somewhat too high. This yielded an unduly low sticking coefficient ($\alpha = 1 \times 10^{-7}$) compared with the measured value ($\alpha = 4 \times 10^{-6}$) at 600 K. The authors[109] attributed the difference to the inaccurate choice of the H_2–Cu model potential surface.

Calculations with frozen vibrational and rotational degrees of freedom showed that the excitation of these degrees of freedom does not play a notable role. The principal quantum effect is delocalisation; the authors[109] attribute the 30% decrease in the energy of activation in the quantum region to tunnelling by the hydrogen atoms.

New numerical approaches to the solution of the nonstationary Schrödinger equation have been considered by Pollard and Friessner.[110]

Trajectory approaches. It is seen from the preceding sections that new molecular modelling methods are continuously being sought for nonstationary quantum problems. Frequently these methods are supplemented by the MMD.

At the same time attempts have been made to devise methods for the numerical solution of the time quantum problem, which are related to the classical MD and are based on the trajectory interpretation of quantum mechanics. The approach, proposed by Podlipchuk[112,113] in studies where a stochastic ordinary differential equation in a complex space was obtained instead of the nonstationary Schrödinger equation for the description of the quantum assembly, is promising. Here it is in fact numerically much simpler to carry out the nonstationary process than to seek stationary states.

A new variant of quantum molecular modelling of time quantum processes, in which the Wigner formulation of quantum mechanics is employed, has been proposed.[114] A combination of the classical MMD and the Monte Carlo method, analogous to the Monte Carlo method developed in statistical dynamics, was used for the solution of the Wigner–Liouville equation.[12] Systematic calculations were performed for the motion of the electron in a one-, two-, and three-dimensional potential well with and without a barrier. The time dependences of the quantum-mechanical average values of the coordinate and momentum, their dispersions, and energy were calculated. Test calculations for a low-energy particle on the bottom of the well yielded results in good agreement with the analytical solution in terms of the harmonic approximation. The rate of tunnelling through the barrier was found by calculating the trace of the operator of the autocorrelation function of the momentum.

VIII. Transition from dynamic to probability modelling

The dynamic methods examined in the previous section proved to be a powerful and flexible instrument for the investigation of a wide variety of elementary processes on the surface. However, a number of difficulties arise in the application of these methods to chemical modification problems. The most evident are the limitations as regards the speed and memory of the computers.

Material limitations of the dynamic methods. The technologically important scales of the surface modification processes are $\tau \sim 1$ μs in time and $l \sim 1-10$ μm in length. Modern computers permit classical MD modelling for times $\tau < 1$ ns and in terms of the length scale $l < 100$ Å. For quantum dynamic modelling, these quantities are even smaller. The limiting possibilities of the existing computers are then employed. Clearly the possibilities of modelling lag by orders of magnitude behind the requirements.

We may note that the current attempts to model, for example, the deposition process employ unrealistically short time intervals between the steps involving the incidence of particles on the surface.[4] On the one hand, this makes the rate of growth of the surface be of the order of magnitude of the speed of sound. On the other hand, the shortening of the time interval between elementary steps distorts the state of the surface which participates in the next elementary step.

Optimists may assume that these are temporary difficulties at the present stage of the development of the computer techniques. Whatever is the truth, there nevertheless are serious limitations which make the task of expanding the scale of the purely dynamic modelling of the chemical modification of surfaces pointless.

Fundamental limitations of the dynamic methods. Chemical reactions with electronic transitions play an important if not the principal role in the chemical modification of the surface. As shown in the previous sections, such processes cannot be modelled with the aid of the classical and adiabatic quantum MD.

Quantum-mechanical approaches based on the solution of the nonstationary Schrödinger equation have been developing for the study of such problems (electronic transitions, tunnelling, etc. — see Sections VI and VII). These methods impose even more severe requirements on the computer resources, particularly in the study of surfaces.† However, this is not the most important factor. The main feature is the appearance of a new qualitative element in such modelling. In the course of the computation, it becomes necessary in fact to make a choice between mutually exclusive possibilities ("splitting" of the trajectory). In the case of a surface, these are, for example, variants of the behaviour of the

¶ The 'trajectory' lies on the five-dimensional surface already discussed above and should not be confused with the trajectory s. For this reason, we place it in quotation marks.

† Apart from the microscopic quantum interactions involving several particles, 'macroscopic' interactions, not localised in space, are significant in this case. The reconstruction of a large section of the surface induced by the incidence and adsorption of a single atom may serve as an example.

particle (adsorbed atom) after its physical adsorption. The adsorbed atom can change its location whilst remaining a physically adsorbed particle, chemical bonds may be formed between the adsorbed atom and the surface atoms, which is accompanied by electronic transitions, and, finally, there is a possibility of quantum diffusion, thermal desorption, etc.

Thus in molecular modelling which uses the nonstationary Schrödinger equation, the extent to which the process is determined is inevitably weakened because at the branching points the choice of the variant is probabilistic in character. This is not associated with the numerical schemes for the solution but is due to the physical significance of the quantum mechanics itself. Indeed, the determination of the state of a quantum system makes it necessary to make a measurement (reduction of the wave packet), i.e. to pass from the probability amplitude (wave function) to the probability density (square of the modulus of the wave function). In a series of measurements, the results will be distributed in accordance with this probability. Such a series of 'measurements' is in fact performed in quantum modelling.

We may note that the classical MMD is also not in fact purely dynamic.[7-9] As a consequence of the instability of the equations of motion for a system of many particles and the errors in the numerical integration, which play the role of perturbations, the MMD trajectory deviates exponentially from the Newtonian trajectory for the same initial conditions, remaining close to the latter only for relatively short times. For long computational times, the MD trajectory moves under these conditions from one set of sections of the Newtonian trajectory to others, which are 'dynamically remote'. These transitions are probabilistic in character because many-particle systems are of the mixing type.

In nature, the phase trajectories of molecular systems, which can be regarded as classical, are also continually perturbed (for example, because any such system is open). For this reason, the motion of such systems is also stochastic in character.[10,11]

It is clear from the foregoing that the need to resort to probability methods in molecular modelling is predetermined by the very physics of the problem. On the other hand, the attempts to remain within the framework of 'pure' dynamics particularly in calculations for large time scales, are not simply unproductive but are in essence pointless.

Probability methods. Since probability modelling is inevitable in the key stages of the solution of the problem, it is useful to exclude altogether from consideration the long sections of the dynamic phase trajectories without an information content. This is possible when the time intervals between successive incidences of the particles on the surface are much longer than the time required for the transition of the system to a new stationary state (the overall time of the chemical reactions, reconstruction, dissipation of excess kinetic energy, etc.). The dynamic methods are retained for the calculation of the probabilities of elementary processes (sticking, chemical reactions, reconstruction shifts, etc.). Knowing the possible states of the system as well as the probabilities of the transitions between them, the kinetic calculations for these transitions can be performed by the Monte Carlo method.

Such an approach makes it possible, in principle, to shorten the computation time by several orders of magnitude, firstly by accelerating the 'selection' of the elementary steps and, secondly, as a result of the fact that the required probabilities should be ideally determined 'once and for all'. However, the multiplicity of the individual surface geometries (steps, groups of adsorbed atoms, vacancies, etc.) is extremely large. It is virtually impossible to guess all the states of the system during its evolution and to calculate beforehand the probabilities of the transitions for these states. It is therefore necessary to have in addition a simple and at the same time an acceptably accurate method for the determination of the electronic structures of the current states of the system and hence the transition probabilities. The method must be applicable in the probability modelling process itself. The principles governing the development of this method on the basis of quantum-chemical ideas are described in the preceding sections.

The loss of information about the dynamics of certain transitions is insignificant for the description of the evolution of the chemical modification of the surface, provided that the rate of modification is determined by the rate of arrival of the reagent on the surface. The knowledge of the times of individual transitions is important in order to be able to discover in which cases this is really so.

Thus it is possible to devise an algorithmic scheme modelling the real shape formation for fairly large crystal specimens. This algorithm must contain the following elements: (1) fragments of the dynamic description; (2) the determination of the stationary states and the probabilities of the transitions between them; (3) the modelling of the probability processes for these transitions (the Monte Carlo method). This modelling procedure constitutes a combination of the MD, quantum-chemical, and Monte Carlo methods.

The dynamic and probability methods were previously compared in attempts to discover which of them is more effective.[4] In fact, they are complementary and their joint employment intensifies the strong aspects and eliminates certain weak aspects of each method.

IX. The simplest probability models. Cellular automata

1. Discrete modelling. Morphology of the surface

The crystal is specified within the framework of the lattice model, a proportion of the crystal lattice sites located on the boundaries of the crystal being assumed vacant. In the simplest models, the crystal lattices are considered in an extremely simplified form (frequently with a smaller dimensionality).

The set of the possible outcomes of the elementary process is determined. The location of the elementary step on the surface is selected at random. The process reaches its conclusion at this point, with the aid of a priori specified probabilities, the crystal is then prepared for the next step, etc. Whatever its form, this procedure is applied in all the simplest models of the chemical modification of the crystal surface considered in this section. Sometimes a model procedure of this type is referred to as cellular (lattice) automata.[115,116]

This aspect may be called morphological because the study of the modification is limited to the 'geometrical' modelling of the morphology and only phenomenological ideas concerning the process on the surface are used. However, the principal concepts and ideas — the language in which one may speak of the form of the surface of the crystal — were formulated in this connection.

Among the studies concerned with this aspect, we may name the simplest models of random deposition.[117-119] The surface is characterised by concepts such as 'coarseness' (roughness, thickness). It has been found that the dispersion of the height of the surface formed (a measure of its roughness) is proportional to the square root of the height of the deposited layer.

The ballistic deposition models,[120-122] describing the appearance of projections, holes, and shadows, may be mentioned as more complex ones. A power dependence of the thickness of the surface not only on the height of the deposited layer but also on the linear dimensions of the support appears. The statistical modelling of various formations with dimensionalities equal to unity or 2 — strings, terraces, etc. — becomes possible.[121-123]

The development of discrete models is virtually completed by the studies described in Refs 124-126 — the transition to the consideration of specific chemical properties begins with the appearance of new information about the surface. The study[127] in which the kinetics of the growth were modelled on the basis of the local properties of the surface being modified is typical. Such properties, in particular the differences between the energies of the surface and bulk-phase atoms, have been calculated[128] in the

form of the stress tensor. Further development should follow the path involving the modelling of chemical bonds.

The simplest models make it possible to represent the way in which the form of the crystal changes and to specify which characteristics describe it sufficiently completely and at the same time are susceptible to investigation. However, the possibilities of such modelling are extremely limited. Firstly, no account is taken of the dependence of the probabilities of the elementary processes at any point on its local environment. Secondly, the set of elementary processes specified a priori does not exhaust the true diversity of the real processes.

2. Continuous modelling

In this approach, the form of the surface is considered as a continuous function $H(r, t)$ of the spatial coordinates and time. The processes involved in the establishment of equilibrium have proved extremely important. There are two limiting cases. In the thermodynamic limit, the surface modification process is infinitely slow so that there is sufficient time for the attainment of thermodynamic equilibrium after each modification step. In this limit, $H(r, t)$ represents either a flat surface or a system of projections and hollows along thermodynamically stable crystallographic faces. The other limit is kinetic. In this case, the modifying particles land so frequently that there is insufficient time for the occurrence of the material transfer processes along the surface between successive collisions.

The real process is always of an intermediate type, i.e. the rate of landing of the modifying particles is finite and the tendency of the form of the surface to attain the thermodynamic equilibrium form is distorted by kinetic processes.

The equation of the surface $H(r, t)$ assumes the following simplest form:

$$\frac{\partial H(r,t)}{\partial t} = \eta(r,t) + \hat{A}\{H(r,t)\}, \tag{18}$$

where $\eta(r, t)$ is a random source describing the variation of the roughness of the surface during the deposition process or during etching as a result of the discreteness of the elementary steps. The operator $\hat{A}$ describes the influence of the smoothing or other shape-forming factors of the type of three-dimensional or surface diffusion. The competition between the processes involving the formation of the locally rough surface and the formation of a gentler relief is the main cause of the diversity of the forms of surfaces.[129-130]

On the most general hypotheses concerning the type of the second term of Eqn (18), one may investigate the degree of roughness of the surface being modified by determining $w_L^2(t) = \overline{(H - \bar{H})^2}$. This quantity exhibits different scaling behaviour depending on the lengths L with respect to which averaging is carried out.[130-132] For small values of L, this quantity is almost independent of time and is determined solely by the value of L, while for large L it ceases to depend on the averaging length and depends solely on the observation time:

$$w_L(t) \sim \begin{cases} L^{\alpha}, & L \ll L_c \\ t^{\beta}, & L \gg L_c \end{cases} \tag{19}$$

The boundary L_c between the regimes depends on time: $L_c \sim t^{\beta/\alpha}$.[130] In the thermodynamic and kinetic limits, the exponent α should become zero (the quantity w_L in the limiting cases should be independent of the averaging length). On attainment of thermodynamic equilibrium, the exponent β should also become zero (the causes giving rise to a time dependence are absent in this case). In the kinetic limit, the function $\bar{H}(t)$ should obey the standard Poisson distribution and hence $\beta = \frac{1}{2}$.

One may expect that, for specific models of the surface modification, the exponent α varies nonmonotonically on transition from the thermodynamic to the kinetic case and reaches a nonnegative maximum at some point. On the other hand, the quantity β apparently varies monotonically — in the kinetic limit the time variation is a maximum, so that the real value of β is in the range $0 < \beta < \frac{1}{2}$.

The constants α and β may be determined for different continuous models with a different specific form of the operator $\hat{A}$. They can be obtained also in computer modelling for different discrete models and in experiments on the deposition and etching of crystal surfaces. The scaling exponents yield information about the extent to which the real modification regimes are close to the thermodynamic or kinetic limit. They make it possible to compare the continuous and discrete models of the modification of the surface and also to discover how well particular models describe the real experiments on deposition and etching.

X. Quantum description of the chemical bond on the surface

Elementary ideas. We may recall the simplest chemical system — two hydrogen-like atoms. In terms of the basis set of atomic wave functions, the diagonal elements of the Hamiltonian coincide with the energies of the electronic states in the individual atoms E_1 and E_2, while the nondiagonal elements represent the amplitude of the probability of the transition of the electron from one atom to another (v). The stationary states of a two-atom system are found to be the bonding and antibonding states with the energies

$$E_{a,b} = \varepsilon \pm (\delta^2 + v^2)^{1/2}, \qquad \varepsilon = \frac{E_1 + E_2}{2}, \qquad \delta = \frac{E_1 - E_2}{2}. \tag{20}$$

For the ground states of identical atoms, $E_1 = E_2$ and $E_{a,b} = \varepsilon \pm v$.

When the chemical interaction of a solid with an atom (molecule) is considered, the state of the atom (molecule) remains as one of the electronic states in Eqn (20), while the set of the electronic states of the solid is chosen as the other. The highest occupied electronic states (the states near the Fermi level) play the main role. Eqn (20) reflects the simplified situation where each chemical reactant has one electronic state ready for coupling. In the general case, there are several (valence) states of this kind and Eqn (20) is accordingly also generalised‡.

The atoms which can modify the surface come into contact only with the surface of the crystal, so that the surface electronic states and not the bulk-phase states should be considered as the electronic states in Eqn (20).

The surface of the crystal is reconstructed, i.e. acquires a lower symmetry compared with the case when the atoms on the surface remain at lattice sites. The spontaneous decrease in the symmetry of the crystal surface is a transition of the Jahn–Teller type, in which the coordinates of the surface atoms and the positions of the surface electronic states change. The energies of the occupied and unoccupied surface states as a rule move apart under these conditions.

Examples involving the consideration of chemical bonds. Tomasek et al.[128] deduced the surface states of adsorbed atoms in a very simple way — from the number of ruptured bonds, i.e. without taking into account reconstruction. They suggest that the differences between the interactions of the surface atoms and the atoms in the bulk phase be described phenomenologically with the aid of the stresses tensor. Chadi[133] surveyed the electronic and atomic structures of semiconductor surfaces with low indices — [100], [111], and [110]. The conclusion that the recon-struction of the covalent surfaces is induced mainly by the tendency towards an increase in the bond orders of the surface atoms agrees well with the possibility of describing the

‡ Henceforth, in referring to Eqn (20) this generalised form will be understood.

differences between the surface and bulk phase with the aid of the stress tensor.[128]

Significantly more detailed methods for the description of chemisorption on semiconductor surfaces have also been adopted.[134,135] The molecular orbital method made it possible to calculate the positions of the oxygen atom on the surface of silicon. A quantitative agreement has been achieved between the calculated and experimental vibration frequencies of the oxygen atoms.[134] Zheng and Cao[135] described three stages in the oxidation of silicon: the chemisorption of oxygen molecules, the dissociation of molecular oxygen, and the diffusion of atomic oxygen from the bridging adsorption layer into the bulk of the crystal with formation of an SiO_2 film. However, progress in the understanding of the process has been achieved at the expense of the loss of flexibility and universality of the description. The three-step representation of the chemical reaction hinders the inclusion of this stage of the computation in the algorithm for the modelling of the chemical modification of the cellular automaton type. Indeed, each of the stages of the process requires the processing of a large amount of information and depends significantly on the composition and state of the vicinity of the section being modified.

The energies of the surface states have been calculated[136] for the reconstructed Si(111)-(2 × 1) surface. The dependences of the energies on the magnitude of the reconstruction shifts were obtained. The study of Yamaduchi and Fujima[137] may serve as an example of the calculation of the surface states localised on a step. Their structure is related to the configuration of the atoms on the edge of the step, which consists of a zig-zag chain of dimers.

This approach proved productive in the study of the interaction of ion beams with the surface of a solid,[139-141] where it was assumed that the structure of the electronic states corresponds to the bulk-phase state. The scattering singularities are manifested in cases where the energies of the electronic states of the incoming ion and the crystal are identical. Electron exchange is of the resonance type. Even if chemical reactions do not occur under these conditions, the scattering singularities constitute high-energy echoes of such reactions.

We may note that the scheme of the bulk-phase electronic states of the crystals employed in the studies of Balidchik and coworkers[139-141] is appropriate only when interactions with high-energy particles (hundreds of eV) are considered. In this case, the interaction energy is so high that the details of the electronic structure of the crystal are unimportant — the position of the Fermi level is the most significant feature. For lower energies, the singularities will arise when the levels of the atomic particle coincide with the unoccupied and occupied surface states closest to the Fermi level. When a sufficiently selective diagnostic procedure is available which permitts the resolution of these singularities, their analysis might prove a promising instrument for the study of the electronic states of a reconstructed surface.

The approach to the description of the chemical properties of solids based on the consideration of surface states, reconstruction, etc. has been used in qualitative studies.[138] Unanimity has been achieved in the understanding of many chemical processes on the surfaces of solids.

The studies under discussion§ have led to progress in the description of individual chemical bonds in the bulk phase and on the surface of a solid, but they cannot serve as a basis for universal modelling. For such modelling, it is necessary to find a standard approach to the calculation of the energies of the surface states and the matrix elements in Eqn (20).[142,143]

§We may also indicate the following reviews: G M Zhidomirov, A A Bagatur'yants, I A Abronin. *Prikladnaya Kvantovya Khimiya* (Applied Quantum Chemistry). Khimiya, Moscow, 1979; N P Gambaryan, I V Stankevich. *Usp. Khim.* **58** 1945 (1989) [Russ. Chem. Rev. 1103]; I D Mikheikin, I A Abronin, I K Vorontsova. In *Materialy VI Mezhdunarodnogo Shkoly-Simpoziuma po Khimicheskoi Fizike* (Proceedings of the VIth International School-Symposium on Chemical Physics). MATI, Moscow, 1994, p. 174.

XI. The method based on the generalised periodic system of the elements

1. Massive crystals

A method was proposed by Harrison[14] in a general form for definite groups of elements in the Periodic System. For this reason, the method (or more precisely the set of parameters used in it) is referred to as the generalised Periodic System of the elements (GPSE). For elements forming covalent tetrahedral crystals, such parameters are the lattice constant d, the energies ε_s and ε_p of the s and p electrons in the ground configuration of the atom, and the Fermi momentum k_F. The radius r_c of the non-coulombic component of the interaction is also used for the construction of the pseudo-potential describing the interaction of the valence electrons with the core electrons.

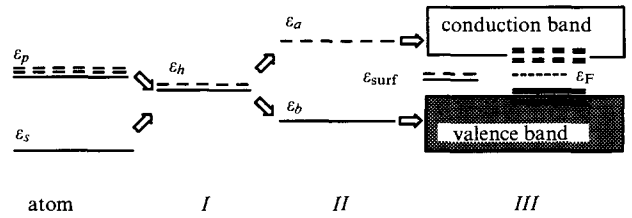


Figure 13. Stages in the construction of the electronic states of a silicon crystal with the aid of the GPSE. Continuous lines — occupied states; dashed lines — unoccupied states. The surface states ε_{surf} are indicated in order to explain Fig. 14.

Fig. 13 explains the essential features of the method. To make the treatment specific, the values of the parameters of the electronic states correspond to silicon. In the first stage, the s and p valence states are hybridised, i.e. a transition to new orthonormalised functions is carried out. They are not eigenfunctions of the Hamiltonian but they do have a symmetry convenient for the description of diamond-like crystals. These states have the same average energy

$$\varepsilon_h = \frac{\varepsilon_s + 3\varepsilon_p}{4}.$$

In the second approximation, account is taken of the overlap of the sp^3-hybridised orbitals in the direction of nearest neighbours only (these are in fact the ones participating in the formation of the chemical bond). The GPSE method involves convenient universal formulae for the overlap integrals. For example, the following expression is used for the overlap integral V_c^h (the energy of the covalent bond involving hybridised orbitals):[14]

$$V_c^h = \frac{-V_{ss\sigma} + 2\sqrt{3}V_{sp\sigma} + 3V_{pp\sigma}}{4},$$

where the subscripts $ij\alpha$ define the atomic (Roman letters) and molecular (Greek letters) quantum numbers. The dependence of the overlap integrals on the distance d is given by the estimate

$$V_{ij\alpha} \approx \eta_{ij\alpha}\frac{\hbar^2}{md^2}, \qquad (21)$$

where m is the mass of the particle. The coefficients $\eta_{ij\alpha}$, where $i, j = s, p, d$ and $\alpha = \sigma, \pi$, have been published.[14] We obtain for the energy of the bonding and antibonding orbitals

$$\varepsilon_{a,b} = \varepsilon^h \pm V_c^h. \qquad (22)$$

For covalent crystals formed by different atoms, for example GaAs or ZnS, a second interatomic matrix element V_i^h (the energy of the ionic bond involving hybridised orbitals) is introduced. It is defined as half the difference between the energies of the hybridised states of different atoms:

$$V_i^h = \frac{\varepsilon_h^A - \varepsilon_h^B}{2}.$$

The energies of the bonding and antibonding states are given by the expression

$$\varepsilon_{a,b} = \frac{\varepsilon_h^A - \varepsilon_h^B}{2} \pm \alpha(d, \varepsilon_s, \varepsilon_p) \ , \qquad (23)$$

where

$$\alpha(d, \varepsilon_s, \varepsilon_p) = [(V_c^h)^2 + (V_i^h)^2]^{1/2}.$$

In the third approximation (Fig. 13), account is taken of the overlap of the orbitals obtained in the direction of the translational vectors.[14] This makes it possible to find the splitting of these levels into valence and conduction bands, to determine the structure of the subbands, and to obtain the dependence of the energies on the quasimomenta k.

The fourth approximation is not fully unambiguous. In the most successful version, the main correction is the matrix element describing the interaction of the valence electrons with the core electrons. For simple metals, such a correction is given by a pseudo-potential, which is regarded as a perturbation. In the case of covalent crystals, the interaction of the valence electrons with the core electrons cannot be regarded as small. Here the wave functions are determined by the maximum Fourier component of such a pseudo-potential with the wave vector along the [111] direction. The additional dependence on k_F and r_c appears only in the fourth approximation.

Somewhat different sets of parameters and other procedures for the construction of the electronic states and for the description of chemical properties have been proposed for other groups of elements — the halogens, simple metals, and metals with an unfilled d or f shell.[14] Thus the GPSE makes it possible to isolate the common features in the description of different groups of substances and to formulate for each of them a procedure analogous to that described above for covalent crystals. Many computational procedures for different groups of elements proved to be similar — LCAO for the construction of valence bands, the approximation of almost free electrons for conduction bands, and the description of the interaction of valence electrons with core electrons with the aid of a pseudo-potential.

2. The surface

a. Surface electronic states

Fig. 14 illustrates the region corresponding to the forbidden band gap *III* in Fig. 13. The surface energy levels are formed in this region. The initial idea concerning the surface state may be the concept of a broken bond arising when some of the atoms are removed from the crystal; the wave functions adopted are those of the sp^3-hybridised state. Neglecting the amplitude of the translational transitions, the energy of such a state may be regarded as identical with ε_h (Fig. 14*a*). Further consideration (allowance for the amplitudes leading to the appearance of bands at the level of the third or fourth approximation) leads to different results depending on the geometry of the interface.

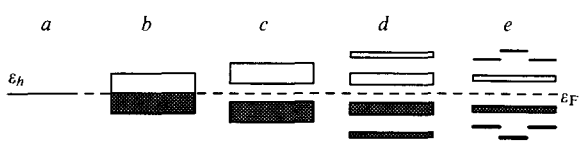


Figure 14. The energy diagrams for surface states: (*a*) crystals with ruptured bonds; (*b*) flat smooth surface; (*c*) reconstructed surface; (*d*) reconstructed surface with regular structures; (*e*) surface with an arbitrary geometry. The occupied bands are shown shaded.

Ideally flat surface. The positions of the atoms in the surface layers coincide with the positions of the crystal lattice sites of the bulk phase crystal and the Miller indices for the surface do not exceed unity. The amplitudes of the transition in the direction of two minimal translational surface vectors can be determined with the aid of the standard GPSE procedure.[14] The solution of the problem of the eigenvalues leads to the appearance of a half-filled band of surface states (14*b*). The energy of these states $\mathscr{E}_0(\mathscr{K})$ depends on the two-dimensional quasi-momentum $\mathscr{K}$, which ranges over the values in the Brillouin surface band determined by the symmetry of the interface.

Reconstruction. Linear structures. The set of reconstruction and relaxation shifts is described by the vector $\vec{\Delta}$. In the simplest case, where the reconstructed surface has two-dimensional translational symmetry, the dimensionality of $\vec{\Delta}$ is $3 \times m$, where n is the number of atoms in the surface unit cell for the nonreconstructed surface and m is the number of nonreconstructed cells in the reconstructed surface (we restrict the treatment to the approximation where the displacement of surface atoms may be regarded as sufficient for the description of the reconstruction). For example, for the 2×1 reconstruction the number of cells $m = 2$, whilst for the 2×4 reconstruction the corresponding number is $m = 8$.

As a result of the reconstruction, the bands of surface states are changed. As a rule, an unoccupied band tends to be 'repelled' from an occupied one (Fig. 14*c*) and their positions on the energy scale are altered (sometimes they move outside the limits of the forbidden band gap). Even greater changes are observed as a function of the energy of the quasi-momentum $\mathscr{E}_{\Delta,i}(\mathscr{K})$ in different bands (the subscript i indicates that the surface states belong to a particular band). As a rule, the region where this function is defined diminishes on reconstruction (for example, the Brillouin surface band decreases by a factor of 2 for the 2×1 reconstruction); there is a corresponding increase in the number of bands of surface states (Fig. 14*d*).

Under certain conditions, structures possessing only linear translational symmetry arise on the interface. the simplest examples may be the bands of the reconstruction dimers, the symmetry of which is disturbed in the direction perpendicular to the band or the polyatomic steps arising on the interface when the latter is a plane perpendicular to one of the crystallographic axes and is inclined at a low angle relative to the integral crystallographic plane. In this case, additional bands of surface states arise, for which the range of values of the quasi-momentum degenerates to a one-dimensional segment.

For the construction of a system of linear equations defining the energies of the surface states, the overlap integrals, found with the aid of the GPSE, are sufficient.

A surface with a complex shape. When partial symmetry is retained (reconstruction with a large cell, repeating corners, steps, etc.), the number of components of the vector $\vec{\Delta}$ and the range of values of i increase. The nature of the band structure remains the same as in Fig. 14*d* and the only difference is that new bands of surface states arise and hence the region where the functions $\mathscr{E}_{\Delta,i}(\mathscr{K})$ are defined becomes depleted (for certain values of i, the range of values of $\mathscr{K}$ may degenerate to a segment).

Further specification of the shape of the surface in an individual form leads to loss of symmetry. Together with bands of surface states, individual states appear (Fig. 14*e*), in which the range of values of $\mathscr{K}$ is zero-dimensional. These surface states are

localised in one or several cells; they are formed as a rule on individual (nonrepeating) pits, irregular hillocks, or even atoms. The decrease in symmetry is accompanied by an increase in the dimensionality of the vector $\vec{\Delta}$. When the surface has fully lost the two-dimensional translational symmetry, the dimensionality of $\vec{\Delta}$ is equal to three times the number of surface atoms.

In order to determine the electronic spectrum and the electronic surface states, it is necessary to solve a system comprising a larger number of equations than in solid state problems having three- or two-dimensional translational symmetry. The lack of symmetry in a surface with an individual shape makes it necessary to calculate a set of different overlap integrals and to solve systems of equations of an enormous dimensionality—this is in fact the main difficulty. In reality, only the GPSE in the form of Eqn (21) permits numerous valid solutions of this problem for a wide variety of configurations.[142,143] In addition, it is necessary to investigate the dependence of the reconstruction shifts on the nature of the assumptions made.

b. The model of the chemical modification of the surface

Fig. 15 illustrates schematically a block-diagram for the modelling of the chemical modification of the surface.[97,143]

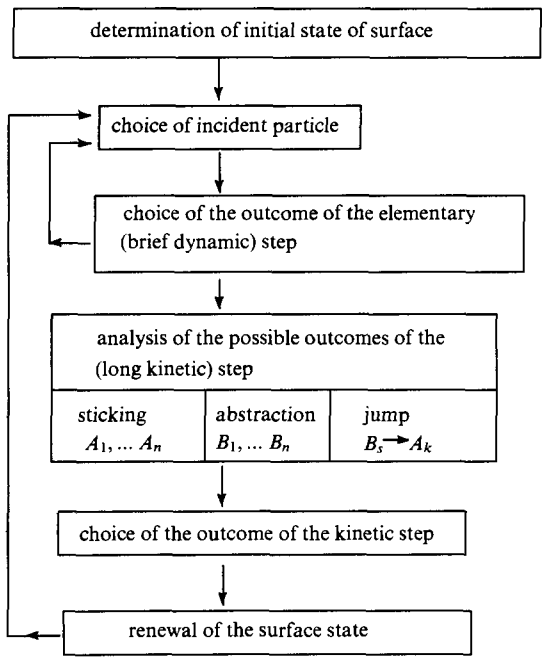


Figure 15. Block diagram of the modelling algorithm.

1. Initial state of the surface. The geometry of the near-surface atoms is specified by a three-dimensional Boolean matrix. Each lattice site is characterised by the numerals 1 or 0 depending on whether the site is occupied by an atom or not. The reconstruction and relaxation shifts of the atoms (the vector $\vec{\Delta}$) are calculated or those known beforehand are employed. The atoms are assumed to be stationary and their positions are averaged with respect to thermal motion. The spectrum and wave functions of the electronic surface states are calculated.

2. The choice of the incident particle. The number of the projection of the unit cell entered by the particle is selected. If the stream of particles has a nonuniform composition, then the kind of incident particle is selected.

3. The outcome of the elementary dynamic step. With the aid of the probabilities of elementary processes selected beforehand and averaged in one way or another, the specific outcome of a dynamic event is determined: sticking, dissociative sticking, etc. In the case of reflection the calculation has to be restarted again from block 2.

4. Analysis of the possible outcomes of the kinetic process. The sticking particle does not immediately occupy a stationary state. This process is fairly prolonged and its result (at least at nonzero temperatures) may not be unambiguous. The particle passes from one metastable state to another (if the activation energy is comparable to the temperature) in the search for the most stable state. We shall regard this process as kinetic and shall describe it statistically.

In the case of the deposition of particles, for example those of silicon, on the surface of a silicon crystal, all the vacancies A_i which the given adsorbed atom can fill are considered. The bond energy is calculated for each of them. This is done with the aid of the standard expression (20) for the surface + adsorbed atom system, the spectrum and wave functions of the surface states determined in the first stage of the algorithm being used for the surface, while the nondiagonal elements are adopted in the form of overlap integrals, which are estimated in accordance with the general GPSE rules.

In the vicinity of the incidence of the modifying particle, the possibility of the extraction of each surface atom B_i is considered in succession. The energies of such extraction are calculated (the procedure is in a certain sense the opposite of that mentioned above for the calculation of the bond energy). A procedure is specified for the removal from the surface of clusters of definite composition (for example, SiF_2 in the etching of silicon by fluorine-containing substances)

Furthermore, the possibility of the extraction of any of the surface atoms at the point B_s with its subsequent deposition at the point A_k, which describes surface diffusion, is considered. With the aid of the combination of the procedures classified previously, the activation energies for each of the possibilities and the extent to which they are energetically favourable are determined.

5. Selection of the outcome of the kinetic step. The result of the kinetic step arises statistically depending on the temperature of the surface and the energy changes in each of the alternative transitions.

6. The renewal of the state of the surface. In conformity with the results obtained in block 5, the Boolean matrix of the state is corrected, the construction shifts $\vec{\Delta}$ are redetermined, and the spectrum of the electronic surface states is found. The computation returns to block 2, after which a new particle is incident on the surface.

Measured quantities. Despite its apparent self-evident nature, the determination of the local surface level is not entirely unambiguous. Its position has been determined[97,143] on the basis of the condition that the number of atoms above the surface level is equal to the number of vacancies under it in the same column of atoms (a column of the Boolean matrix).

The average characteristics, the simplest of which is the average surface level and the rate of its change v, as well as the fractal dimensionality of the surface d and the dynamics of its change $d(t)$, are of principal interest. The quantities v, d, and $d(t)$ are found to depend only slightly on the method used to find the local surface level, which indicates that their determination is correct.

Furthermore, it is possible to determine the statistical properties of the surface—the scaling exponents α and β. A necessary condition for this is the possibility of modelling sections of the surface, the linear dimensions of which exceed L_c significantly.

The geometrical properties of the surface were considered above. Together with these, it is possible to determine the parameters characterising the chemical properties of the individual surface obtained in the computation. The algorithm makes it possible to calculate the energies of the unoccupied and occupied electronic surface states relative to the Fermi level and to model the possible overlap integrals of these states with the wave functions of the additional adsorbed atoms.

3. The surfaces of polymers

The differences between the structures and the electronic states of polyethylene molecules on the surface and in the bulk phase are not quite so great as, say, in silicon. In the modelling of the chemical modification of the surface by reactive incident particles, this makes it possible to disregard the surface state of the polymer and to employ the states of the molecules. Thus we do not differentiate between the modification of the units on the surface and the units in the succeeding layers to which the reactive particle can permeate by diffusion.

Extremely sophisticated computational methods have been developed in the theory of polymers. The GPSE method cannot compete with them as regards the accuracy of the determination of the structure and properties of specific molecules. However, this method permits estimates in fairly complex cases, in particular for large organic molecules, which can be regarded as a set of fragments the centres of which are tetravalent carbon atoms. In the consideration of covalent bonds between the atoms of Group IV elements, the simplicity and universality of the GPSE method have been manifested particularly clearly. We shall demonstrate this approach to the qualitative description of the chemical modification of polymers[142] in relation to polyethylene as an example.

a. The molecule

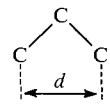
Polyethylene consists of macromolecules the structural unit of which is the $-CH_2-$ fragment. Since the pitch of the helix is significantly greater than the distance between these fragments, we shall consider it as a chain based on a zig-zag arrangement of carbon atoms. By virtue of the similarity of the energy of the *s* state of hydrogen and the average energy of the sp^3-hybridised state of carbon, a tetrahedral symmetry of the chemical bond is obtained for each carbon atom. In this approximation, the angles between the bonds in the $-CH_2-$ fragment of the polyethylene molecule are the same as in the CH_4 molecules or in the diamond crystal.

In considering the C–C bond (Fig. 16a), we can employ the same procedure as in the consideration of the chemical bonds in crystallised silicon (Fig. 13). The overlap integral between the orbitals of the nearest carbon atoms, calculated with the aid of the GPSE procedure, determine the bonding and antibonding states of the C–C bond [Eqn (22)], while the overlap integrals between the bonding and antibonding states of neighbouring units determine the width of the one-dimensional quasi-band.

The C–H bond can be considered similarly (Fig. 16*b*), but in this case the bonding and antibonding states in Eqn (23) are made up of the *s* orbital of hydrogen and the sp^3-orbital of carbon (approximation *IIa*). The smallness of the overlap integral between the two bonding (as well as antibonding) states adjoining a single carbon atom gives rise to some scatter of the latter as a function of the type of symmetry in relation to the transposition of the hydrogen atoms (approximation *IIb*). The width of the one-dimensional quasi-bands may be neglected for C–H bonds.

The complete scheme of the electronic states is presented in Fig. 16*c*.

For a rough test of our model, one can compare the form of the zig-zag with the real, experimental shape of the polyethylene molecule. The angle between two C–C bonds is tetrahedral and the length of the C–C bond obtained by the GPSE procedure is 1.54 Å; accordingly, the linear period of the molecule *d* is found to be 2.50 Å. The measured bond angle in the polyethylene molecule is 112° and the measured period is 2.55 Å, which are close to the calculated values (109° and 2.50 Å). This shows that the model which we have proposed describes the real molecule quite well.



b. Modification of the surface

In order that the metal atoms (M) should be able to modify polyethylene, it is necessary that the energies of the vacant states of the metal should be significantly higher than the energy of the antibonding orbital of the C–H bond. In this case, the valence electrons of the metal pass to the antibonding C–H orbitals (Fig. 16*c*). The presence of an electron in this orbital weakens the C–H bond, the hydrogen atom is split off, and the electron given up by the metal occupies an even more favourable position at the bonding level of the C–M bond formed.

The appearance of the metal on the surface of polyethylene decreases its permeability to gases. Firstly, the metal atoms are positively charged owing to the displacement of electrons towards carbon, which leads to their interaction with the induced dipole moments of the molecules of the permeating gases. Secondly, the residual partially unpaired valence electrons of the metal lead in some cases (for example on permeation of oxygen) to the formation of oxides which decrease the unoccupied gaps between the molecules. Thirdly, the metal atoms may cross-link the neighbouring polyethylene molecules.

We may note that the deposition of the metal on polyethylene presents certain difficulties. This problem has been studied experimentally, for example for magnesium.[144] It was noted that sticking becomes possible if polyethylene is first treated with a plasma or by ion bombardment. Novak et al.[144] did not explain this effect. The application of the GPSE method makes it possible to understand that in this type of treatment an electron is transferred from the bonding C–H state to the antibonding state and the mechanism under discussion ceases to operate immediately from the second stage, which does not require any additional assistance.

Thus, by virtue of its relative simplicity, the GPSE method makes it possible to model fairly complex processes which have not been investigated by other methods. We emphasise that the GPSE method can be applied in two stages of the investigation. With its aid, one models, firstly, the interaction of the incident particle with the surface and, secondly, the surface itself.

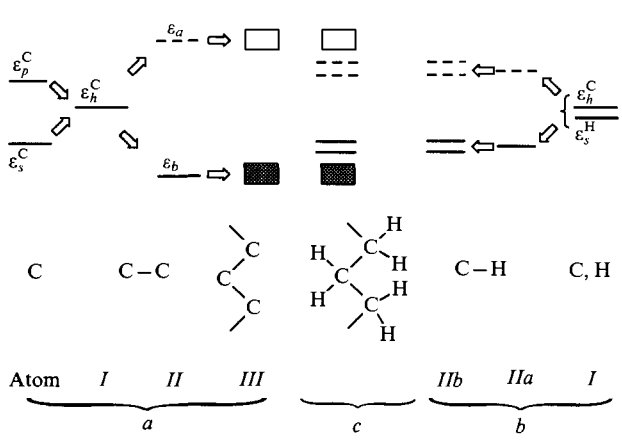


Figure 16. Construction of the energy diagram for the electronic states of a polymer molecule: (*a*) C–C bond; (*b*) C–H bond; (*c*) macromolecule.

XII. Results of the modelling of the modification of the surface

1. Continuous models

Apart from the competition between random deposition or etching (increase in the roughness of the surface) and diffusion (smoothing), which are common to the majority of such models, Karkar et al.[145] took into account also the competition within the $\hat{A}\{H(r,t)\}$ term between processes with different spatial locations.[129]

$$\frac{\partial H(r,t)}{\partial t} = \gamma\nabla^2 H(r,t) + \frac{\lambda}{2}[\nabla H(r,t)]^2 + \eta(r,t) \ .$$

The first term takes into account the revaporisation-condensation of the substance and hence the decrease in the surface area owing to the decrease in the height of hills and the filling of valleys. The second describes the growth of the surface in the direction of the local normal (which happens in the isotropic deposition of the modifying particles, i.e. at high pressures). The scaling exponents α and β proved to be independent of the numerical values of γ and λ: $\alpha = 0.38$ and $\beta = 0.24$.

Another smoothing mechanism—diffusion along the surface—has been considered by Wolf and Villain.[146] This process is characterised by a smaller scale than that considered by Kardar et al.[145] The equation for $H(r,t)$ was proposed in the following form:

$$\frac{\partial H(r,t)}{\partial t} = -\nu\nabla^4 H(r,t) + \eta(r,t) \ .$$

The values $\alpha = 1$ and $\beta = 1/4$ were found. A deficiency of the proposed operator $\hat{A}$ in this form is the failure to retain the surface diffusion flux. A nonlinear term was introduced to retain this flux.[147,148] In this case

$$\frac{\partial H(r,t)}{\partial t} = -\nu\nabla^4 H(r,t) + \lambda\nabla^2[\nabla H(r,t)]^2 + \eta(r,t) \ .$$

It has been shown[147] that for short times the first term predominates and the scaling exponents are close to those obtained by Wolf and Villain.[146] In the course of time, the second term becomes dominant and the scaling exponents approach $\alpha = 2/3$ and $\beta = 1/5$. It has been shown that allowance for nonlinearity in any form should decrease the scaling exponents.

Experimental values of the scaling exponents. A study has been made[149] of the deposition of copper chloride on the (111) surface of calcium fluoride by the method of molecular-beam epitaxy. The measured local static roughness index α proved to be 0.84 ± 0.05, which permitted the conclusion that the smoothing processes which accompanied the nonuniform deposition are much closer to surface diffusion[146] than to revaporisation.[145] The value of α found is somewhat lower than that determined by Kardar et al.,[145] which is evidence in support of the view that nonlinearity in the equation for $H(r,t)$ exerts an influence, but α is greater than in studies[147,148] involving a specific form of the nonlinear term ensuring the retention of the surface diffusion flux.

Iwamoto et al.[150] investigated the kinetics of the surface roughness in the electrodeposition of copper. The local roughness index, measured over small sections, proved to be identical, within the limits of the accuracy of measurement, with the index found by Tong et al.:[149] $\alpha = 0.87 \pm 0.05$. This confirms the conclusion[149] that surface diffusion predominates over revaporisation.

The results of averaging over large distances proved to be more unexpected. The measured dynamic exponent β proved to be 0.45 ± 0.05, which does not fit the concept that nonlinear terms exert an influence.[149] This has been attributed[150] to the effect of the electric field, which increases the vertical component of the growth of the surface, suppressing the lateral component.

2. Corrosion

A method has been proposed[151] for modelling corrosion within the framework of a two-dimensional cell model, only two parameters being employed: the passivation rate constant k_p and the depassivation rate constant k_d. The initial state is a two-dimensional rectangular grid (periodic boundary conditions are imposed along one of the coordinates) divided in such a way that the metal atoms are located at the nodes of one half-plane (capable of corroding) while particles inducing corrosion are at the nodes of the other half-plane. The interface is represented by passivating particles (oxide molecules adsorbed on the metal). Particles of a fourth kind can arise during corrosion: an inactive particle (a nonadsorbed molecule of the corrosion product, a neutral molecule, or an unoccupied node).

The process begins with spontaneous breakdown of the integrity of the interface. After a certain time δt, the probabilities of passivation (P_p) and depassivation (P_d) are established.

$$P_p = \delta t\, N_s k_p, \qquad P_d = \delta t\, N_p k_d \, .$$

In these expressions, N_s and N_p are the number of unprotected metal atoms (capable of coming into contact with the corroding particles) and the number of protected metal atoms (on which oxides are adsorbed) respectively. During corrosion, each lattice site can be occupied by a particle of one of the four kinds indicated above.

The cases of small scales and times (specimen length equivalent to 128 particles) and large scales and times (specimen length equivalent to 8192 particles) were considered. The first case (to some extent arbitrary owing to its two-dimensionality) corresponds to the condition $L_c \ll L$, whilst the second corresponds to $L_c \gg L$ in Eqn (19). The methods used to represent the results are also different.

In the first case, virtually nothing happens for large values of k_p—the cavity formed passivates itself. For low values of both k_p and k_d, the cavities grow in a stable manner and have an approximately hemispherical shape and relatively smooth edges. For large values of k_d, the structure of the interface becomes increasingly irregular. The fractal dimensionality of the interface increases with increase in the ratio k_d/k_p.

In the second case, the time variations of the corrosion current yields more information. Such variations have as a rule a typical pulsed form with a characteristic sharp initial rise corresponding to the onset of the formation of the cavity. The rises on the curve indicate the onset of the formation of new corrosion centres in the cavity. It has been noted that minor corrosion current pulses and shorter intervals between the pulses correspond to large values of k_p and k_d respectively. A universal empirical time dependence of the average corrosion current has been proposed:

$$I(t) \sim \frac{f(t/t^*)}{\ln t} \ ,$$

where the function $f(x)$ is constant for small values of x, decreasing rapidly for high values of x. The parameter t^* is related to the passivation rate constant by the expression

$$k_p^2 t^* \ln t^* \sim \text{const.}$$

Despite its approximate nature, this model describes correctly many aspects of the phenomenon and the principal process. Agreement has been found with the results of the continuous modelling of the morphology of the surface. The parameters k_d and k_p apparently characterise the universal corrosion mechanisms for different solid and liquid metals under the influence of various corrosion factors. Depending on their magnitude, the model describes both stable and unstable growth of the corrosion cavities.

3. Deposition and etching

The modelling of the chemical modification of the surface carried out [97, 143] with the aid of the algorithm described in Section X may be regarded as a demonstration. Many processes determined by surface states have not so far been modelled. At the same time modelling even at this level makes it possible to describe the selective filling of vacancies with the largest number of possible bonds (or the elimination of the least bound atoms) and to discover the characteristic features of the crystal lattice shape formation. It permits the description of different modification regimes: deposition, polishing, and etching, and permits a comparison of the qualitative aspects of the morphology with certain models by using literature data.

The chemical modification of the crystal surface of silicon with the base perpendicular to the [001] direction has been modelled. The initial surface (Fig. 17) was specified in a form such that the evolution of both smooth and sharp changes in relief could be observed. Streams of particles characterised by a conventional chemical energy E were considered for the modelling of the possible regime. Numerical experiments with various values of this quantity revealed three characteristic regimes: the changes in the form of the surface in all these regimes after the deposition of 20 000, 80 000, and 200 000 particles on the support are illustrated in Figs. 18*a*, 18*b*, and 18*c*.

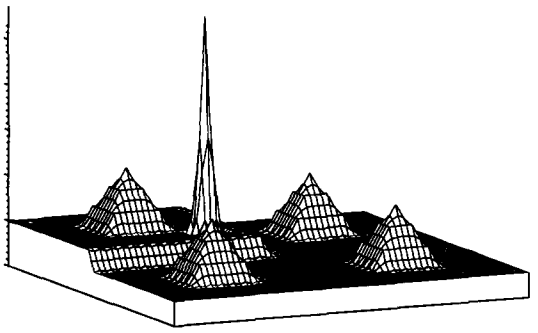


Figure 17. Initial relief of the modelled surface. The size of the section is 123 × 123 Å.

Deposition. In the first regime, particles with a low value of E fall on the support. There is then a certain number of particles capable of rupturing one and two bonds and very few particles capable of rupturing three bonds; there are virtually no particles which can rupture four bonds. If surface atoms with free bonds fall within the range of the influence of the valence electrons of the incident particles, new bonds may be formed. The effect of particles with such energy leads to a gradual growth of the crystalline layer, whereupon the form of the surface is approximately retained, being distorted mainly as a result of nonuniform sticking. Particles are eliminated rarely, such elimination being most notably manifested in the smoothing of sharp variations of the relief, in which the particles have the smallest number of bonds.

In the initial stage, the modification of the surface is close to that described by the simplest random deposition model.[117] It may be assumed that in the given instance the quantity L_c is fairly small and the roughness of the film is approximately proportional to the square root of the change in the height of the support. In the course of time (with increase in the number of incident particles), features characteristic of the ballistic deposition model appear [120–122] and projections and holes arise. The quantity $L_c \sim t^{\beta/\alpha}$ also increases and exceeds the size of the modelled crystal specimen. The dependence of the thickness of the film not only on the height of the support but also on its linear dimensions also begins to correspond to a power function. The fractal dimensionality of the surface formed increases. It may be expected that it tends to a definite limit with increase in the number of deposited particles.

Polishing. When particles with higher values of E are deposited, the situation changes radically. In this regime, almost all the deposited particles are capable of breaking one bond, quite a few particles are capable of breaking two and three bonds, and there are also particles able to break four bonds. The quantity E is

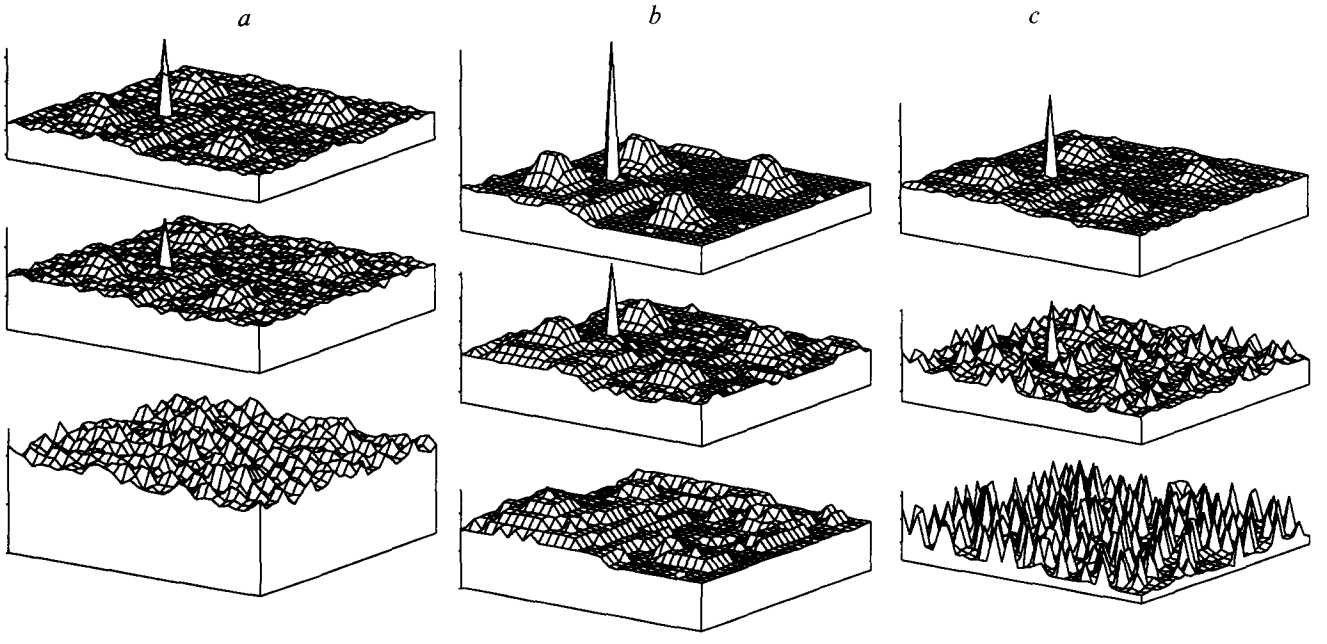


Figure 18. Modification of the surface in different regimes: (*a*) deposition; (*b*) polishing; (*c*) etching. The successive diagrams (from top to bottom) correspond to the deposition of 20 000, 80 000, and 200 000 particles.

selected so that the probability of rupture of the existing bonds corresponds to the probability of the formation of new ones. In the course of time, the surface relief becomes increasingly even. Projections are disrupted (the disruption of sharp ones is particularly rapid), but the average height of the support does not increase. The description of the surface modification processes under the influence of particles with such energy no longer corresponds to the models.[117,120] These processes are closer to those which may be described in terms of the statistical terraces model[121,122] and other models[123] describing the dynamics of the variation of formations with dimensionalities 1 or 2.

Etching. The situation again changes for a stream of particles with even higher values of E. In this regime, the majority of the particles have a chemical energy sufficient for the dissociation of three bonds and an appreciable number of particles are capable of rupturing all four bonds. The probability of the sticking of such particles to the surface is low and that of the dislodgment of crystal atoms is high, so that the thickness of the film diminishes. The initial form of the surface is gradually forgotten and is transformed into a very random landscape in the course of time. The fractal dimensionality of the modified surface increases as in the case of particles with low values of E (by analogy with this case, one may expect that the dimensionality tends to a limit with increase in the number of deposited particles). In a certain sense, the random and ballistic etching models, and not deposition models as described in the above investigations,[117,120–122] operate.

Within the framework of the calculations carried out, particles with low values of E play the role of silicon atoms in the absence of oxidising particles, while those with large values of E play the role of atoms (or molecules) of fluorine or other oxidising substances. This analogy, like that with cold or very hot particles, is extremely arbitrary. Effects such as etching after the formation of a monolayer cannot be modelled either.

Thus, within the framework of one model,[97,143] it has been possible to obtain different regimes in the modification of the surface and in the alteration of its morphology (Fig. 19), which had previously been described by means of various approaches.

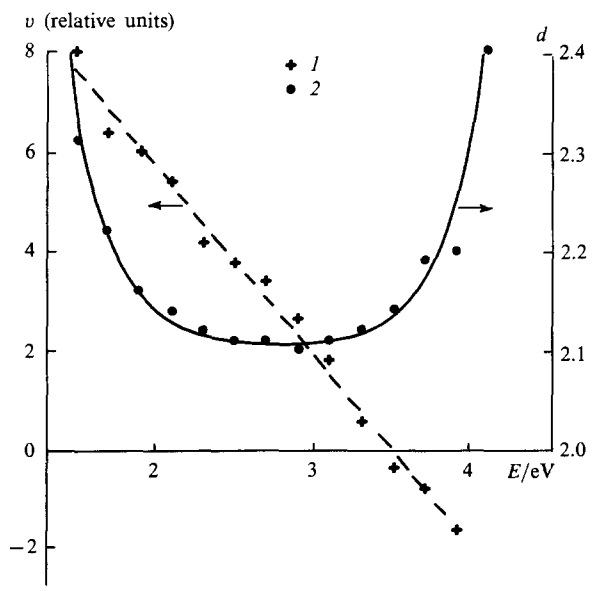


Figure 19. Rate of modification of the surface υ and the fractal dimensionality d as functions of the conventional chemical energy E of the incident atoms. The dashed line was obtained by fitting $\upsilon \sim (3.5 - E)$ and the continuous line was obtained by fitting $-d(E) = 2.1 + 0.1(E - 2.8)^4$.

The rate of change of the average level of the modified surface depends linearly on the quantity E, whereas the fractal dimensionality of the final surface is satisfactorily represented by a fourth degree parabola.

The existence of these relations throws light on the significance of the quantity E, which has hitherto played the role of a model parameter. Its linear relation with the rate of change of the average level of the surface makes it possible to employ E as a unique quantitative parameter (instead of a whole set of concentrations of various particles, their temperatures, etc.) characterising the effectiveness of the chemical action of a gas-plasma stream on the surface.

The minimum in the fractal dimensionality of the final surface is correlated with the passage of the rate of change of the level through zero. We may note that in a real situation the conclusion that the minimum in the fractal dimensionality of the final surface is related to the constancy of the thickness of the support may prove not to be universal. Thus an important factor in the description of surface modification processes may prove to be the presence of several kinds of incident particles with different values of E—some particles may etch the surface, whilst others are deposited. In different situations, the smoothness, the purity of the composition and the rate of change of the thickness of the support may be ensured by different groups of particles.

4. Problems with several time and length scales

As mentioned in Section VIII, the dynamic and probability methods have different applications, which supplement one another. This makes it useful to achieve their joint employment. Both these and other methods have extremely different versions and for this reason the procedures for combining them are also quite diverse.

Thermal desorption. The approaches combining the MMD and the transition state theory (the probability approach) make it possible to investigate rare events. Thus a study has been made[151] of the thermal desorption of a Xe atom from a Pt(111) surface. With the aid of the transition state theory,[152] the process probability being sought is represented by 'equilibrium' and 'dynamic' cofactors. The latter is expressed in terms of the sticking coefficient of the atom incident on the surface and is calculated by the MD method. The equilibrium factor can be determined by various methods, both statistical and dynamic. In both cases the application of special procedures is needed to improve the statistics in the 'bottleneck' within the phase space, the crossing of which by the phase trajectory is unlikely, but this 'bottleneck' determines the thermal desorption section. Several such procedures (stochastic dynamics and the 'boxes' and compensating potential methods) have been described[151] for the dynamic version of the calculation of the equilibrium cofactor.

A similar approach has been used[153] to calculate the rate of evaporation of a 14-atom cluster at low temperatures.

Diffusion of adsorbed atoms. Among the most recent studies, those[154,155] in which the diffusion of adsorbed Si atoms on the Si(100)–(2 × 1) surface and of Ge atoms on the Ge(100)–(2 × 1) surface as well as the dynamics of the adsorbed Si atom and the mechanism of the epitaxial growth of the Si(100)–(2 × 1) surface with a terrace are the most characteristic.

Such processes are characterised by two time scales: for short times, the atom captured by the surface seeks a stable adsorption site, while for long times the atom diffuses by jumps from one adsorption site to another and the scale is determined by the residence time of the atom at the sites. The calculation is therefore carried out in two stages, in each of which different methods are applied.

In the first stage, the adsorption energy profile was determined by the MD method along the surface modelled by several layers of mobile particles. The Tersoff potential was used.[23] The Si

atom was projected onto the Si surface and was allowed to select a sticking point (long arrest at a particular site). The surface was then gradually brought to zero temperature and its energy was calculated. The energy difference between the equilibrium surface and the surface with an adsorbed atom at the given point was assumed to be the adsorption energy. Such depositions were repeated many times at different points on the surface, which made it possible to construct a detailed adsorption energy profile.

The activation energies for the jump to a neighbouring adsorption site and the vibration frequencies of the adsorbed atoms at different sites were determined from the calculated profile and were subsequently used in the second stage of the calculation, where a probability method was employed. The Si atom was placed at random at a certain point on the calculated surface $E_a(x, y)$, where E_a is the adsorption energy and x and y are the coordinates along the surface. The probability P_{ij} of a jump from the adsorption site i to a nieghbouring site j was then selected stochastically. According to the transition state theory, $P_{ij} = \upsilon_{ij} \exp(E_{ij}/kT)$, where υ_{ij} is the vibration frequency of the adsorbed atom at i in the direction of the transition to j and E_{ij} is the activation energy for the transition.

The results[154] showed that the adsorbed atoms diffuse predominantly in the direction along rows of dimers, which has in fact been observed experimentally.

In epitaxy on a stepped surface,[155] the procedure is similar. The diffusion of the given adsorbed atom is terminated artificially at the instant when the next adsorbed atom appears on the surface (in accordance with the rate of deposition).

Condensation of supersaturated vapour. A model of the initial stage in the formation of clusters in supersaturated vapour has been considered.[156,157] The problem involves processes differing in both time and length scales: elementary steps involving sticking and evaporation and the kinetics of the growth of the size and number of drop nuclei. Processes of the first type are dynamic, while those of the second are statistical. The system of kinetic equations for the variation of the concentrations of the atoms in the clusters in a rarefied gas is used as the initial system. These equations include the rate of formation of dimers, the rate of sticking of atoms to the clusters and of the clusters to one another, and the rate of evaporation of atoms from the clusters and of the break up of the clusters. The problem is divided into two stages. In the first stage, the rates of elementary processes are calculated by the MD method, whilst in the second the kinetic equations are integrated numerically. This approach has been used in a calculation for the condensation of metals behind the shock wave front propagated in an inert gas in the presence of different amounts of an added volatile compound of the metal[156] and for the condensation of argon in a hypersonic stream.[157]

Deposition. As an example of the possible application of the ideas outlined in Section XI, we shall consider the deposition of gold on a silver support at room temperature. This problem has been modelled[158] by the MD method. Two assumptions were made. Firstly, the rate of deposition (one gold atom during a period $\lesssim 1$ ns on an area comprising 6×8 silver atoms) was assumed to be greater by many orders of magnitude than in the real deposition. Secondly, in order to compensate for such a high rate, an annealing procedure was introduced: each Au atom fell on a surface heated to 810 K, which was cooled after relaxation. This simulated the conditions where after each elementary step the surface returned to the equilibrium state. In particular, the gold atoms diffused into the first and second layers of silver atoms and the silver atoms were displaced to the state of adsorbed atoms.

In a real process, there are two markedly different time scales. With the aid of the above procedures, the authors[158] shortened the deposition time to values close to the time of an elementary step. The problem can be solved also by a different procedure after dividing it into two stages. In the first stage, the elementary steps modelled by the MD method are differentiated: the incidence of a gold atom on a clean silver surface and on sections of the silver surface with one, two, three, and more gold atoms in characteristic positions. Together with sticking processes, the subsequent diffusion is modelled and the energies of the potential barriers and the temperature variations of the pre-exponential factors are determined and extrapolated to low temperatures.

In the second stage, the deposition process at the required temperature is modelled with the aid of probability approaches using the information already obtained about the elementary steps. This approach would make it possible to expand significantly the temporal and spatial framework of the problem compared with those considered in the study of Haftel et al.[158] and also to turn attention to cases where there is insufficient time for the attainment of equilibrium between successive incidences of the atoms. In order to determine the extent to which the state of equilibrium is attained in the given processes, it is necessary to include in the consideration surface phonons and other types of surface excitation arising during the incidence of the particles.

5. Certain future tasks

Without claiming to quote a complete list, we shall present certain examples from the physics and chemistry of surfaces which may become the field of the active application of molecular modelling methods.

Elementary chemical processes. Scanning tunnel microscopy and certain other methods have made it possible to proceed to the study of the structure of the surface and the processes occurring on it at the level of individual molecules or atoms, for example the dynamics of the dissociative chemisorption of $Cl_2/Si(111)-(2 \times 1)$,[159] the dynamics of the deposition of an individual atom (iridium) on the iridium surface (steps and clusters),[160] the diffusion of $Si(001)-(2 \times 1)$ vacancies,[161] etc. Such studies naturally stimulate the development of molecular modelling methods.

Heterogeneous catalysis. The phenomena in heterogeneous catalysis are based on the change of the chemical properties of the atoms and molecules which have formed chemical bonds with the surface. For example,[143] data on the decrease in the dissociation energy of the O_2^- molecular ion on the surfaces of transition metals by an order of magnitude (under certain conditions by two orders of magnitude)[162] and on the increase in the interatomic distance[163] have been quoted to illustrate the enhancement of the oxidative properties of an adsorbed oxygen molecule. Quali-tatively, this phenomenon can be understood within the framework of the idea concerning the chemical properties of a surface described in Section X. This refers also to the results of a study[164] where an increase in the Fermi level as a result of the additional filling of the surface states by the valence electrons of the adsorbed sodium atoms and its decrease as a result of the reverse process in the adsorption of sulfur atoms were described. For a quantitative description and development of methods for controlling catalytic properties, molecular modelling is required.

Reconstruction dynamics. The calculation of the surface reconstruction time is an interesting and hitherto unsolved problem. Here there are no differentiated atoms and it is not always evident how many atoms should be considered in the modelling of a nonstationary quantum process. There remain many problems even for the stationary case of a thoroughly investigated surface such as $Si(001)-(2 \times 1)$.[165]

Nonequilibrium materials. The study of the structure of a surface with different ratios for the rate of reconstruction and the rate of deposition may lead to the explanation of the difference between the lattice constants of the ultradisperse powders obtained by the plasmochemical method[166] and its value for a massive specimen.

Multilevel molecular modelling makes it possible to understand the properties of nonequilibrium crystals and facilitates the search for ways of synthesising them.

Modification of the surface. The structure of the surface and the dynamics of its variation have become the object of experimental studies at the molecular level, in particular by means of tunnel microscopes.[167–169] The effect involving the appearance of instability in the form of the surface in molecular-beam epitaxy as a function of changes in the deposition regime has been observed.[167,168] Modelling demonstrated its usefulness even in the simplest geometric version.

Multilevel modelling. The problem is formulated so that: all the levels into which the problem is divided (elementary steps, collective processes, macroscopic description, etc.) are discovered; descriptive procedures for each level are selected; the channels for the transmission of information between the levels (initial data, parameters, initial and boundary conditions etc.) are established; the required level of accuracy of the final result is specified in the scheme, establishing thereby the required accuracy at each level or, conversely, the attainable accuracy of the final result is determined on the basis of the worst current accuracy for one of the levels.

In Dodson's review,[4] it is concluded that, because of the abundance of unelucidated questions, the molecular modelling methods still remain the objects of study and not a means of carrying out studies. The authors of the present review attempted to show how, by combining the dynamic and probability modelling procedures, it is possible to convert them into a means whereby research can be carried out. The choice of modelling problems is determined by physical effects, applied purposes, and the possibility of comparison with experiment.

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Rearrangements of cationic organic σ- and π-complexes

G I Borodkin, V G Shubin

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Abstract. The structure-kinetic and stereochemical aspects of rearrangements of cationic σ- and π-complexes of unsaturated organic compounds with electrophilic reagents containing no metal atoms and the effects of the medium and phase state on these rearrangements are considered. The bibliography includes 299 references.

I. Introduction

In recent decades the structures and reactivities of cationic organic σ- and π-complexes† generated under 'long lifetime' conditions have been intensively studied.[1–33] 'Long-lived' σ- and π-complexes attract the steady attention of researchers, because they are close structural analogues of the intermediates of some organic reactions of great theoretical and practical importance. These reactions include electrophilic aromatic substitution,[20,36–38] acid-catalysed transformations of organic compounds,[39–41] electrophilic addition,[42] and solvolysis with anchimeric assistance.[43]

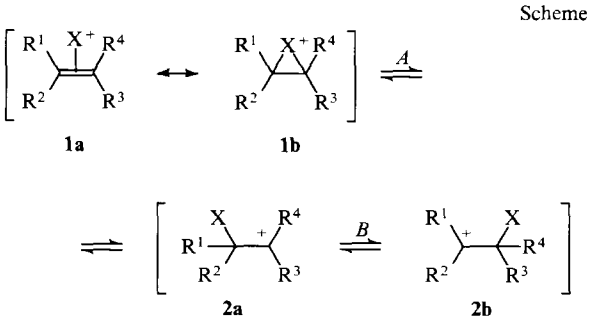
The wide use of modern physical methods has produced extensive information on the structures and reactivities of cationic σ-complexes.[1–33] However, studies of the structures and reactivities of cationic π-complexes are few, and their results are often ambiguous (see, for example, Refs 2, 23, 25, 29). Experimental data on the interconversion of cationic σ- and π-complexes (Scheme 1, path *A*) are even more scarce, despite the fact that in many cases this interconversion is the key step and determines the composition of the reaction products.[20,42,43]

† We use the term 'σ-complex' in its traditional sense [20] to denote a species that is formed by one-centred σ-bonding of an electrophilic agent to an unsaturated system via two electrons of the π-system. The term π-complex corresponds to an adduct formed by *n*-centred bonding ($n > 1$) of an electrophilic agent to the π-system of an unsaturated compound.[34,35]

G I Borodkin, V G Shubin Novosibirsk Institute of Organic Chemistry, Siberian Branch of the Russian Academy of Sciences, 9 prosp. Acad. Lavrent'eva, 630090 Novosibirsk, Russian Federation.
Fax (7-383) 235 47 52; Tel. (7-383) 235 16 51;
E-mail: vshubin@orchem.nsk.su

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Scheme 1



In principle, data on the energy of interconversion of cationic and anionic σ- and π-complexes can be obtained from quantum-chemical calculations (see Refs 44–47). However, this approach has essential limitations caused, in particular, by the unreliability of the calculation techniques.[46,48] This is clearly demonstrated by the results of quantum-chemical calculations on the simplest σ- and π-complexes, the ethyl cation and its π-analogue, for which the of relative energy varied over very wide limits (from 23.5 to −33.2 kcal mol^{-1}), depending on the chosen method of calculation.

The purpose of the present review is to consider the state of investigations, first of all, of the experimental ones, on rearrangements of cationic σ- and π-complexes. This is necessary for the development of approaches to the control of numerous organic reactions involving these complexes as intermediates. We shall confine the discussion to complexes formed by compounds and electrophilic reagents containing no metal ions. Considerable attention is paid to degenerate rearrangements of σ- and π-complexes in which the initial and the final species have identical energies. In conformity with the Marcus concept [49,50] and other similar approaches,[51] the kinetic characteristics of the degenerate processes are fundamental in the structural kinetic theory.

II. Types of rearrangements of σ- and π-complexes

Three main types of rearrangements of σ- and π-complexes can be distinguished, namely, σ,σ-, σ,π-, and π,π-rearrangements (see Fig. 1). One-step rearrangements of σ-complexes (*a*) as well as two-step rearrangements involving the formation of π-complexes as unstable intermediates (*b*) belong to the first type. The rearrangements characterised by similar stabilities of σ and π-complexes may be assigned to the σ,π-type (*c*). Finally, one-step

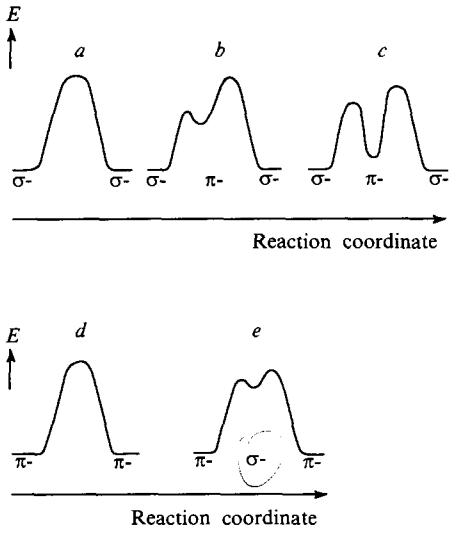


Figure 1. Dependence of the energy on the reaction coordinate for some types of rearrangements of σ- and π-complexes.

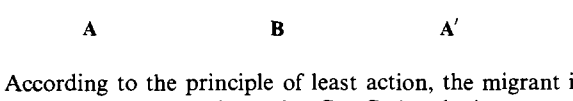
rearrangements of π-complexes (*d*) or two-step rearrangements involving the formation of unstable σ-complexes (*e*) may be referred to as π,π-rearrangements.

A more detailed classification of σ,σ-rearrangements includes allowance for the number of cleaved (*n*) and of formed (*m*) σ-bonds (an *n*σ,*m*σ-rearrangement). If one takes into account the possibility of coordination of the apical group (migrant) with different numbers of atoms of the complex core, then interconversions of π-complexes may be defined as π(*n*η),π(*m*η)-rearrangements. In conformity with this the interconversion of σ- and π-complexes may be referred to as a *n*σ,π(*m*η)-rearrangement.

III. σ,σ-Rearrangements

The most significant and extensively studied of σ,σ-rearrangements of cationic σ-complexes are those occurring through the 1,2-shift of a migrant (R_m) to the electron-deficient carbon atom, viz. the carbocationic centre (C_t) (Scheme 2).

Scheme 2



According to the principle of least action, the migrant in a 1,2-shift should move along the C_0-C_t bond via a state of π-bonding (an intermediate or transition state **B**),[20,22] and, with certain assumptions, the kinetic parameters of these rearrangements can characterise the relative stabilities of σ- and π-complexes. The main tool for the investigation of these rearrangements which occur at high rates is dynamic NMR,[15,16,20,21,52] while slow transformations are mostly studied by the radioactive tracer method.[15-17,20,53] Degenerate rearrangements of 'long-lived' cationic σ-complexes with a variety of migrants of σ-, π-, or *n*-type have been studied. The kinetic characteristics of the 1,2-shifts of these migrants are presented in Tables 1-4.

An important point is that the published data[15,17,20,21] indicate that the nature of the counter-ion or the solvent does not significantly affect the rates of intramolecular rearrangements of 'long-lived' cationic σ-complexes. Therefore, we shall consider initially the structure-kinetic regularities of these rearrangements. An approach consisting in separating a σ-complex into two structural fragments, the migrant (R_m) and the core (the rest of the ion), and in establishing the relationships between the structures of these fragments and the rate of the rearrangement was successful in identifying these regularities.[3,15,20,21]

1. The structural effects of the core

It is apparent that, in the absence of complicating factors, the rate of rearrangement for a given migrant should increase with the electrophilicity of the carbocationic centre C_t (see Ref. 76). In fact, for 1,2-shifts of migrants of σ-(H,Me), π-(Ph), and *n*-(Cl) types in arenonium ions (see Tables 1-4), the following linear correlations have been identified:

$$y = a_i + b_i\zeta\,, \qquad (1)$$

where y is $\lg k$ (k is the rate constant), free energy of activation ($\Delta G^{\neq}$), or activation energy (E_a); ζ, the chemical shift of the C_t atom (δC_t^+), reflecting the degree of electron deficiency,[138] or q_i^+ the total or π-charge.[78-81,97,102,111,125,129,134]

Borodkin et al.[102] reported a simplified interpretation of dependences of this sort in terms of the method of vacant molecular orbitals.[139] A more rigorous quantum-chemical analysis of the variation of the coefficients a_i and b_i with variation of the migrants R_m was later carried out.[140-143] The a_i and b_i coefficients in the relationship (1) behave so that the relative abilities of R_m of different types (H, Me, Ph, Cl, NO_2) to migrate do not form a universal sequence.[21,78,129]

It is noteworthy that $\Delta G^{\neq} = 0$ for the extrapolation curves is achieved at various values of δC_t^+. This apparently indicates the possibility of inversion of the relative arrangement of energy levels of the σ-complexes (**A**, **A'**) and the π-complex (**B**) (or the corresponding transition state **B**) (see Scheme 2) with increase in the charge on the carbonium centre; the tendency of the migrants R_m to form π-complexes increases in the sequence $H < Me < Ph < NO_2 < Cl$.[78,129]

The degree of electron deficiency on the C_t atom in a series of related σ-complexes can be characterised, as well as by δC^+ and q_i^+, by the σ^+-constants of the substituents[78,102,125] or by the ν(CO) stretching frequencies of the ketones resulting from the replacement of the C_t^+-Me fragment in the σ-complex by a C = O fragment.[78,125,144] The validity of linear correlation dependences of this type has been confirmed using the 1,2-shifts of hydrogen atoms,[78] Me[144] and Ph[125] groups in arenium ions as examples.

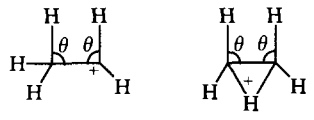
The relationships of type (1) ($\zeta = \delta C_t^+$ or q_π^+) do not hold for rearrangements of 1-R_m-1,2-dimethyl-3,4,5,6-tetrafluorobenzenium ions (R_m = H, Cl)[80,135] or 1-R_m-1,2,3,4-tetramethylbiphenylenium ions (R_m = H, Me).[82,98] In the former case the quality of the correlation can be substantially improved by using the difference between the chemical shifts of the C_t atom of the arenium ion and its precursor, the corresponding arene, instead of δC_t^+ (see Ref. 135). Morozov et al.[145] have shown that by taking into account the logarithms of the basicity constants of arenes ($\lg K$), obtained by the imaginary abstraction of the migrant R_m^+ from the cation, as well as the q_π^+ parameter, one can quantitatively describe rearrangements of arenium ions of both the benzoid and nonbenzoid types in the framework of the two-parameter correlation

$$\Delta G^{\neq} = a + bq_i + c\lg K\,. \qquad (2)$$

This approach was later extended to the rearrangements of aliphatic carbocations.[146]

More serious limitations arise when one attempts to use type (1) relationships for quantitative descriptions of the rearrangements of σ-complexes with different types of cores. For example, in the case of 1-R_m-1,2-dimethylacenaphthylenium ions (R_m = H, Me,[85] Cl[134]), the differences between experimentally determined $\Delta G^{\neq}$ values and those calculated from type (1) relationships can reach 5-7 kcal mol^{-1}. An increase in the

activation barrier with decrease in the size of the ring against which the migration occurs has also been found for the isomeric σ-complexes **24a** and **25** (see Table 1). A similar increase in ΔG is observed on going from the 2-butyl cation ($\Delta G^{\neq}_{-140\,°C} < 1.9$ kcal mol^{-1})‡ (see Refs 15, 54) to the cyclobutyl ion (**5a**) (see Table 1).[57] Using MINDO/3 and ab initio calculations, Chandrasekhar and Schleyer[149] have determined the dependence of the difference between the energies of the σ-complex (**C**) and the π-complex (**D**) on the magnitude of the angle θ and have shown that the activation barrier to the 1,2-shift of a hydrogen atom increases as this angle decreases.

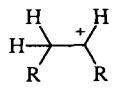


C **D**

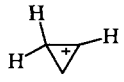


c **d**

One of the reasons for the increase in the activation barrier to the 1,2-shift is the increase in the antibonding interaction between the atomic orbitals in the occupied MO (**c** and **d**) corresponding to structures **C** and **D**, which is due to the shortening of the C_0-C_t bond (1.49 and 1.40 Å, respectively). MINDO/3 and ab initio calculations of the barriers to the 1,2-shifts of hydrogen in acyclic and in cyclic σ-complexes **5a**, **6a**, **9a**, **77 – 79** confirm the conclusions suggested by the above-mentioned model.



R = H (**77**), Me (**78**)



79

Apart from the 'ring effect' against whose background the migration occurs, the influence of other factors (in particular, orbital orientation) also can lead to deviations from type (1) dependences.[17, 21, 22, 103, 150 – 153] An unfavourable mutual orientation of the C_0-R_m bond and the vacant atomic *p*-orbital makes the transition state more strained[153] (see Ref. 71) and the rate of the rearrangement decreases. The allowance for the aromatic or antiaromatic character of the transition state can be important[21] (see Ref. 71). The latter is probably responsible to a substantial degree for the increase in the activation barriers to the 1,2-shifts of hydrogen and methyl groups in the ions **24a, b** and **37** compared with those expected from calculations using dependences of type (1).[82, 83, 98] This retarding factor is even more pronounced in the case of 1-R_m-1,2,3,4-tetramethylcyclobutenyl cations for which no rearrangements occurring via 1,2-shifts of migrants (R_m = H, Me, Ph) can be detected even under quite rigorous conditions (see Tables 1 – 3), although other rearrangements associated with the reconstruction of the system of bonds in these ions occur quite readily.[15, 88, 89] (see Ref. 71).

The aggregate of the charge factor and other factors can be taken into account (at least, for identical migrants) by choosing a 'chemical' parameter, the free energy of activation (or lg *k*, E_a) of the 1,2-shift of the standard migrant as a generalised parameter.§ The legitimacy of using this approach to the quantitative description of rearrangements of different cationic σ-complexes has been shown for the first time for the 1,2-shifts of hydrogen atom and methyl group chosen as the standard group.[155] It turned out that for a wide range of rearranging ions, 1-R_m-1,2,3,4,5,6 hexamethylbenzenium, 2,7- and 3,6-substituted 9-R_m-9,10-dimethylphenanthrenium, 1-R_m-1,2-dimethyl-acenaphthylenium, and 1,4-di-X-2-R_m-2,3-dimethylnorbornyl ions the following correlation relationships hold:[78]

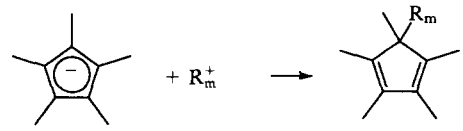
$$\Delta G^{\neq}(R_m) = a_1 + b_1 \Delta G^{\neq}(Me), \quad (3)$$

$$\lg k(R_m) = a_2 + b_2 \lg k(Me), \quad (4)$$

$$E_a(R_m) = a_3 + b_3 E_a(Me). \quad (5)$$

Later the range of rearranging σ-complexes covered by analogous dependences has been extended by including the data for rearrangements of 2-R_m-2,3-dimethylbutyl, 2-R_m-1,2,3,4-tetramethylnaphthalenium, and 2-R_m-1,2,3,4-tetramethylbiphenylenium ions and neutral structures, i.e. 5-R_m-1,2,3,4,5-pentamethyl-1,3-cyclopentadienes (**80**),[156] which can be regarded as neutral σ-complexes formed by linking a 1,2,3,4,5-pentamethylcyclopentadienyl anion to an R_m^+ cation (Scheme 3).[98]

Scheme 3



80a – d

R_m = H (**a**),[156, 157] Me (**b**),[158] Ph (**c**),[159] NO_2 (**d**).[160]

It should be noted that when the whole set of data is processed, the above-presented correlation relationships can describe a very wide range of rearrangement rates $\Delta\Delta G^{\neq}(Me) \approx 40$ kcal mol^{-1} including structures with formal charges between 0 and 1.

Analogous dependences have also been found for other migrants (Ph[159] and NO_2[160]) using the methyl group as the standard migrant. The fact that dependences of types (3) – (5) are valid for both cationic and uncharged σ-complexes indicates a fundamental inherent alliance between rearrangements of carbocations and those of neutral compounds. An analysis of the behaviour of type (3) dependences for the H, Me, Ph, and NO_2 migrants has shown[159] that as the activity grows [the $\Delta G^{\neq}(Me)$ value decreases], the selectivity [$\Delta G^{\neq}(R_m^1) - \Delta G^{\neq}(R_m^2)$] diminishes until the isoselectivity points located in the region of low $\Delta G^{\neq}(Me)$ values are reached, which is in conformity with the 'activity – selectivity'¶ principle (see Refs 161 – 164).

2. Influence of the nature of the migrant

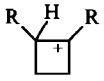
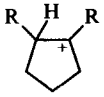
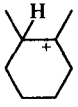
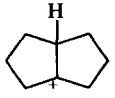
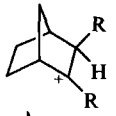
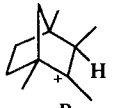
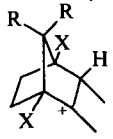
Predicting the rates of rearrangements of carbocations that occur via 1,2-shifts of various atoms or groups is one of the fundamental problems in the theory of molecular rearrangements,[15, 20, 21, 166, 167] and, it is also one of the most complex problems, since both the structure of the core of the carbocation (electrophilic agent) and the nature of the migrant atom subjected to the attack vary over wide limits. As was noted above, quantum-chemical calculations do not allow the rates of carbocation rearrangements to be predicted reliably enough (see Refs 168 – 180). We believe that the approach based on the use of correlation relationships and experimentally determined parameters characterising the nature of the migrant is a more promising approach to the quantitative description of the rearrangements of cationic σ-complexes. In this connection, illustrative data have been obtained for the 1,2-shifts of isosteric migrants, *meta*- and *para*-substituted phenyl groups. The rearrangements of 9-(X-phenyl)-9,10-dimethylphenanthrenium

‡ The value of $\Delta G^{\neq}$ probably refers to the interconversion of the 2-butyl cation and the corresponding π-complex of type **B** (see Scheme 2 and Refs 25, 147, 148).

§ The fruitfulness of using 'chemical' parameters in organic chemistry is well known. Typical examples are Hammet and Brønsted equations, etc.[154]

¶ Note that the behaviour of the migrants C_6F_5S or C_6F_5Se in similar rearrangements does not obey the 'activity-selectivity' principle.[165]

Table 1. Kinetic characteristics of the 1,2-shift of hydrogen atom for degenerate rearrangements of σ-complexes.

Structural formula	σ-Complex	R (X or Y)	Acid, solvent	E_a/kcal mol^{-1}	lg $A_{1,2}$	$\Delta G^{\neq}$/kcal mol^{-1} [a]	Ref.
	**3a**	Me	$SO_2ClF-SO_2F_2$ [b]			3.1±0.1 (−138 °C)	54
	3b	CD_3	$SO_2ClF-SO_2F_2$ [b]			3.0±0.1 (−138 °C)	54
	3c	Et	$SO_2ClF-SO_2F_2$ [b]			4.4±0.2 (−116 °C)	54
	3d	Ph	HSO_3F-SO_2ClF			> 10.2 (−80 °C)	55
	**4a**	Ph	HSO_3F-SO_2ClF			> 16.8 (37 °C)	55
	4b	*p*-MeC_6H_4	$CF_3SO_3H-SO_2ClF$			> 14.7 (0 °C)	56
	**5a**	H	$SbF_5-SO_2ClF-SO_2F_2$			> 10 (−61 °C)	57
	5b	Me	SbF_5-SO_2ClF			⩽ 6.6±0.5 (−95 °C)	58
	**6a**	H	$HSO_3F-SbF_5-SO_2ClF$ or $HF-SbF_5-SO_2ClF$			> 5.5 (−130 °C)	59, 60
			$SbF_5-SO_2ClF-SO_2F_2$			⩽ 4.7 (−150 °C)	61
	6b	Me	$SO_2ClF-SO_2F_2$ [b]			3.1±0.1 (−139°C)	54
	**7**		$SO_2ClF-SO_2F_2$ [b]			3.7±0.1 (−137 °C)	54
	**8**		$HSO_3F-SbF_5-SO_2ClF$			4.0 [d]	62
	**9a**	H	$SbF_5-SO_2-SO_2F_2$	10.8 ± 0.6 [e]	12.3 [e]	11.5 (25 °C)	64
	9b	Me	HSO_3F-SO_2ClF			⩾ 12.0 [d]	65
	**10**		HSO_3F-SO_2ClF			> 14.1 (−10 °C)	66
	**11a**	R = H, X = H	HSO_3F-SO_2ClF			7.2 (25 °C)	65
	11b	R = H, X = Me	HSO_3F-SO_2ClF			7.3 (−115 °C)	66, cf. 65, 67

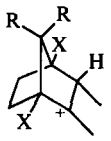
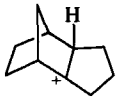
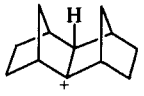
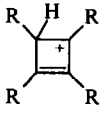
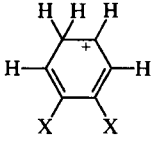
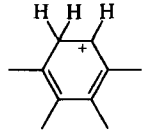
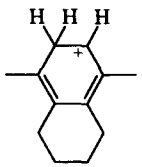
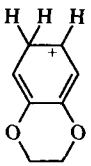
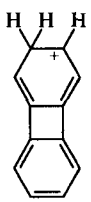
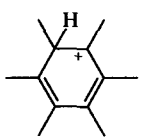
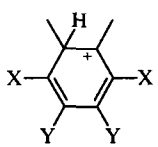
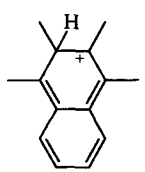
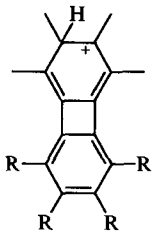
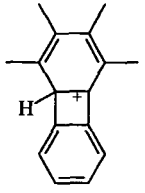
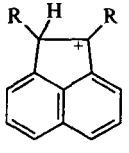
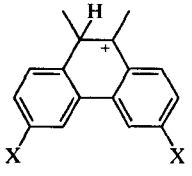
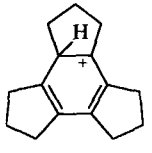
	**11c**	R = Me, X = Me	HSO_3F-SO_2ClF			7.4 (−110 °C)	67
	**12**		SbF_5-SO_2ClF			7.2±0.5 (−110 °C)	68
	**13**		HSO_3F-SO_2ClF			7.0[d]	62, 69
	**14**		SbF_5-SO_2ClF			⩾15 (0 °C)	62
	**15a**	H	$HSO_3F-SbF_5-SO_2ClF$ (SO_2)			> 15.8 (20 °C)[c]	70
	15b	Me	CH_2Cl_2 (AlC_4^- anion)			> 19.2 (80 °C)[c]	71
	**16a**	H	$HF-SbF_5-SO_2ClF-SO_2F_2$	10.0±1	15.3±1.6	6.6 (25 °C)	72, 73
	16b	Me	$HF-SbF_5-SO_2ClF$	5.3±0.8	8.5±0.6	11.2 (25 °C)	74
	16c	F	$HF-SbF_5-SO_2ClF$	5.7±0.8	8.6±0.7	11.4 (25 °C)	74
	16d	OH	$HSO_3F-SbF_5-SO_2ClF$			> 13.6 (−20 °C)[c]	75
	16e	OMe	$HF-BF_3$			> 14.7 (20 °C)	76
	**17**		$HF-BF_3$	11.6	13.0	11.3 (25 °C)	76

Table 1 (continued)

Structural formula	σ-Complex	R (X or Y)	Acid, solvent	E_a/kcal mol^{-1}	lg $A_{1,2}$	$\Delta G^{\neq}$/kcal mol^{-1} [a]	Ref.
	**18**		$HF-BF_3$	11.2	13.0	10.9 (25 °C)	76
	**19**		$HF-BF_3$			> 16.3 (0 °C)	76
	**20**		$HSO_3F-SbF_5-SO_2ClF$			~12.4 (−32 °C)	77
	**21**		$HF-BF_3$ or $HF-SbF_5$ $HSO_3F-SbF_5-SO_2ClF$	11.3 11.8±0.2	13.3 13.5±0.2	10.6 (25 °C) 10.8 (25 °C)	76 78
	**22a**	X = Cl, Y = Me	$HF-SbF_5-SO_2ClF$			~10.9 (−60 °C)	79
	22b	X = Cl, Y = Cl	$HF-SbF_5-SO_2ClF$	8.5±0.2	11.1±0.2	10.8 (25 °C)	80
	22c	X = F, Y = F	$HF-SbF_5-SO_2ClF$	10.2±0.2	12.6±0.2	10.5 (25 °C)	80
	**23**		$CF_3SO_3H-SbF_5$			12.8 (62 °C)	81

	**24a**	H	$CF_3SO_3H-SO_2ClF$	12.6±0.1	12.6±0.1	12.8 (25 °C)	82
	24b	Me	$HCl-Al_2Cl_6-CH_2Cl_2$			~15 (3 °C)	83
	**25**		$CF_3SO_3H-SO_2ClF$			> 14.6 (−2 °C)	82
	**26a**	H	$HSO_3F-SbF_5-SO_2ClF$			> 16.9 (40 °C)[c]	84
	26b	Me	$HSO_3F-SbF_5-SO_2ClF$	13.8±0.3	13.3±0.3	13.1 (25 °C)	85 (cf 84)
	**27a**	H	$HSO_3F-SbF_5-SO_2ClF-SO_2F_2$	8.7±0.3	12.8±0.3	8.7 (25 °C)	78
	27b	Br	$HSO_3F-SbF_5-SO_2ClF-SO_2F_2$	8.8±0.2	12.8±0.2	8.8 (25 °C)	78
	27c	Me	$HSO_3F-SO_2ClF-SO_2F_2$	9.8±0.3	12.8±0.4	9.8 (25 °C)	78
	27d	CF_3	$HSO_3F-SbF_5-SO_2ClF-SO_2F_2$	7.5±0.3	13.5±0.5	6.5 (25 °C)	78
	**28**		$HSO_3F-SbF_5-SO_2ClF$			8.2 (−30 °C)	86

Note. From this point on, free valence lines in structural formulae denote methyl groups. For the sake of simplicity, π-,σ-delocalisation is not shown in the structural formulae.

[a] The values of $\Delta G^{\neq}$ have been calculated from the equation: $\Delta G^{\neq} = 2.3RT[\lg(kT/h) - \lg k_{1,2}]$ (the corresponding temperatures are given in parentheses), $\lg A_{1,2} = \lg A - \lg f$, where f is the statistical factor taken as $f=4$ for the ion **16a**, $f=2$ for the cations **16b,c**, **17**, **18**, **20**, **21**.

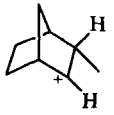
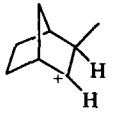
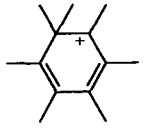
[b] The acid is not specified, it is probably SbF_5.

[c] Based on the data, it was assumed that $k < 10\,s^{-1}$.

[d] The temperature is not given.

[e] According to the published data,[61,63] the values of the kinetic parameters given in the Table refer to the 1,2-shift of the *exo*-H atom; the value of $\Delta G^{\neq}$ for the 1,2-shift of the *endo*-H atom exceeds 20 kcal mol^{-1}.

Table 2. Kinetic characteristics of the 1,2-shifts of alkyl groups in degenerate rearrangements of σ-complexes.

Structural formula	σ-Complex	R or X	Acid, solvent	E_a/kcal mol^{-1}	lg $A_{1,2}$	$\Delta G^{\neq}$/kcal mol^{-1} [a]	Ref.
	**29**		$SO_2ClF-SO_2F_2$ [b]			3.8±0.1 (−136 °C)	54
	**30**					>20 [c]	4
	**31**					14.5 [c]	4
	**32a**	H	HSO_3F-SO_2ClF			8.3(25 °C) [d]	87
	32b	Me	HSO_3F-SO_2ClF			9.4 (−94 °C)	67
	**33a**	H	HSO_3F-SO_2ClF			9.4 (−67 °C) [e]	67
	33b	Me	HSO_3F-SO_2ClF			~12.9 (−50 °C) [f]	67
	**34a**	Me	CH_2Cl_2 ($AlCl_4^-$ anion)			>16.1 (25 °C) [g]	71
			94% H_2SO_4			>19.2 (80 °C)	88, 89
			HSO_3F			>27.5 (70 °C)	88, 89
	**35**		HSO_3Cl	18.2±0.6	12.9±0.4	18.1 (25 °C)	90
			9.4 M H_2SO_4	15.2 18.3±1.8 [h]	11.7 13.0±1.2 [h]	18.0 (25 °C)	91
			CF_3COOH ($AlCl_4^-$ anion)	18.4±0.8	13.1±0.6	17.9 (25 °C)	92
				16.5±0.1	11.5±0.1	18.3 (25 °C)	93

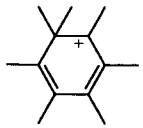
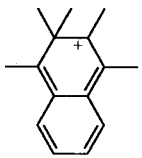
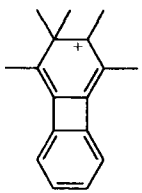
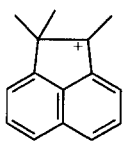
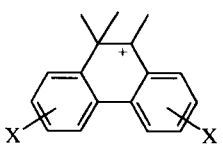
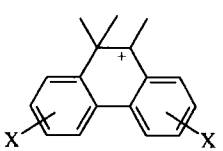
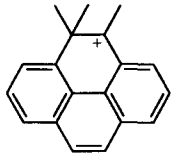
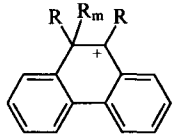
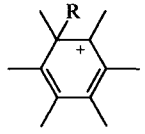
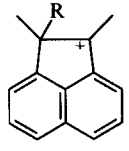
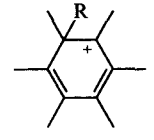
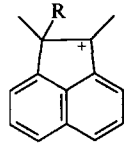
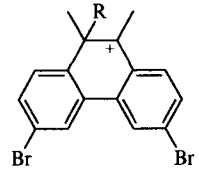
	**35**		CH_2Cl_2 ($SbCl_6^-$ anion)	17.4±0.2	12.4±0.1	17.9 (25 °C)	94,95
			$SOCl_2$ ($AlCl_4^-$ anion)	10.5±0.2	4.8±0.2	21.4 (25 °C)	93,95
			Crystal (BF_4^- anion)	16.4±0.5	10.2±0.5	19.9 (25 °C)	95
			Crystal (BPh_4^- anion)	15.1±0.5	9.2±0.5	20.0 (25 °C)	95
			Crystal ($SbCl_6^-$ anion)	18.3±0.2	13.5±0.2	17.3 (25 °C)	94,95
			Crystal ($AlCl_4^-$ anion), on Al_2O_3	15.0±0.2	10.3±0.2	18.4 (25 °C)	96
	**36**		CF_3SO_3H, $HSO_3F-SO_2ClF-SO_2F_2$			22.7 (−125 °C)	97
	**37**		CF_3SO_3H	19.4±0.4	13.5±0.2	18.5 (25 °C)	98
	**38**		CF_3SO_3H	18.5±0.3	12.9±0.2	18.4 (25 °C)	85
			Crystal ($AlCl_4^-$ anion)	22.5±0.5	13.7±0.4	21.3 (25 °C)	99,100
	**39a**	H	$HCl-Al_2Cl_6-CH_2Cl_2$	12.1±0.2	13.2±0.2	11.5 (25 °C)	101
			HSO_3F-SO_2ClF	12.2±0.1	13.3±0.1	11.5 (25 °C)	102
	39b	3,6-Br_2	HSO_3F-SO_2ClF	11.2±0.2	12.5±0.1	11.6 (25 °C)	102
	39c	3,6-Me_2	HSO_3F-SO_2ClF	13.4±0.3	12.8±0.2	13.4 (25 °C)	102
	**39d**	3,6-$(CF_3)_2$	HSO_3F-SO_2ClF	7.9±0.1	11.5±0.1	9.7 (25 °C)	102
	39e	2,7-Br_2	HSO_3F-SO_2ClF	10.2±0.2	12.3±0.2	10.9 (25 °C)	102
	39f	4,5-Me_2	CF_3SO_3H, HSO_3F-SO_2ClF	14.1±0.2	12.8±0.2	14.1 (25 °C)	103

Table 2 (continued)

Structural formula	σ-Complex	R or X	Acid, solvent	E_a/kcal mol^{-1}	lg $A_{1,2}$	$\Delta G^{\neq}$/kcal mol^{-1} [a]	Ref.
	**40**		HSO_3F-SO_2ClF	11.7±0.1	12.8±0.1	11.7 (25 °C)	102
	**41a**	R_m = Me, R = Et	$HCl-Al_2Cl_6-CH_2Cl_2$			~12 (25 °C)	104
	41b	R_m = Et, R = Me	$HCl-Al_2Cl_6-CH_2Cl_2$			10.1 (25 °C)	104
	41c	R_m = Et, R = Et	$HCl-Al_2Cl_6-CH_2Cl_2$	10.1	12.4	10.6 (25 °C)	104, 105
	**42**	Et	CF_3COOH			16.0 (25 °C)	105, 106
	**43**	Et	CF_3SO_3H	16.3±0.3	12.3±0.2	17.0 (25 °C)	107
	**44**	$CH_2-CH=CH_2$	HSO_3F			> 12.8 (−50 °C)	108
	**45**	$CH_2-CH=CH_2$	HSO_3F			> 15.9 (0 °C)	108
	**46**	$CH_2-CH=CH_2$	HSO_3F-SO_2ClF			8.1 (−90 °C)	108

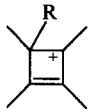
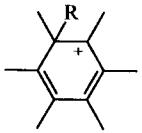
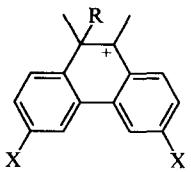
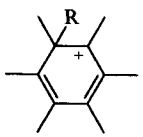
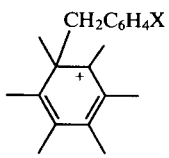
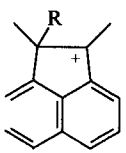
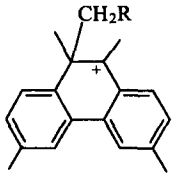
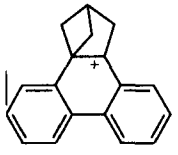
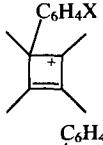
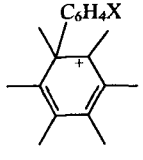
	**34b**	$CH_2-CH=CH_2$	HSO_3F-SO_2ClF			> 12.9 (−90 °C)	109
	**47**	CH_2Cl	HSO_3F or CF_3COOH			> 19.5 (60 °C)	106, 110
	**48a**	Me	CF_3SO_3H	17.7±0.5	12.7±0.4	17.8 (25 °C)	111
	48b	CF_3	HSO_3F	13.8±0.3	13.0±0.2	13.5 (25 °C)	111
	48c	Br	HSO_3F	16.2±0.4	13.0±0.3	15.9 (25 °C)	111
	**49**	$CHCl_2$	$CHCl_3$ ($Al_2Cl_7^-$ anion)			> 18.3 (40 °C)	105, 106
	50	CH_2CHO	HSO_3F			> 11.7 (−70 °C)	105, 106
	**51a**	H	HSO_3F-SO_2ClF	12.4±0.3	13.9±0.3	10.9 (25 °C)	112
	51b	*p*-Me	$HSO_3F-SO_2ClF-SO_2F_2$	10.4±0.3	13.4±0.3	9.6 (25 °C)	113
	51c	*p*-CF_3	HSO_3F-SO_2ClF	14.5±0.3	13.4±0.2	13.7 (25 °C)	113
	51d	*p*-Cl	HSO_3F-SO_2ClF	12.6±0.4	13.7±0.4	11.4 (25 °C)	113
	51e	*m*-F	HSO_3F-SO_2ClF	13.4±0.2	13.2±0.2	12.8 (25 °C)	113
	**52**	$CH_2C_6H_4Cl$-*p*	HSO_3F			14.7 (0 °C)	107, 114

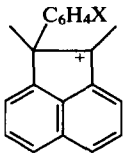
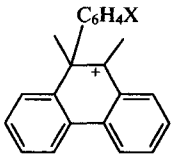
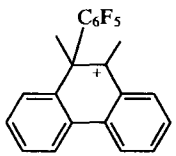
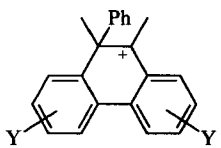
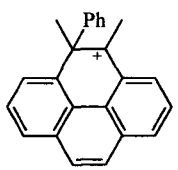
Table 2 (continued)

Structural formula	σ-Complex	R or X	Acid, solvent	E_a/kcal mol^{-1}	lg $A_{1,2}$	$\Delta G^{\neq}$/kcal mol^{-1} [a]	Ref.
	**53a**	Ph	HSO_3F-SO_2ClF	7.9±0.2	11.6±0.2	9.5 (25 °C)	115
	53b	$C_6H_4CF_3$-*m*	HSO_3F-SO_2ClF	9.2±0.1	12.2±0.1	10.0 (25 °C)	115
	53c	C_6H_4Cl-*p*	HSO_3F-SO_2ClF	8.8±0.1	12.3±0.1	9.5 (25 °C)	115
	53d	C_6H_4Cl-*m*	HSO_3F-SO_2ClF	8.2±0.2	11.5±0.2	10.0 (25 °C)	115
	53e	3,5-$Cl_2C_6H_3$	HSO_3F-SO_2ClF	9.8±0.1	12.6±0.1	10.1 (25 °C)	115, 116
	**54**		HSO_3F-SO_2ClF			≤6.6 (−105 °C)	117

[a] See footnote 'a' to Table 1; the values were taken as $f = 4$ for ion **35**, $f = 3$ for ion **29**, $f = 2$ for cations **36–40**, **41c**.
[b] The acid is not given, it is probably SbF_5.
[c] The value has been evaluated (the temperature was not given). [d] For the shift of the *exo*-methyl group; for the shift of the *endo*-methyl group, $\Delta G^{\neq}_{-64\,°C} > 10.7$ kcal mol^{-1} (see Refs 4, 87).
[e] For the shift of the *exo*-methyl group; for the shift of the *endo*-methyl group, $\Delta G^{\neq}_{-64\,°C} = 19.5$ kcal mol^{-1} (see Ref 63).
[f] Apparently, for the shift of the *exo*-methyl group.
[g] Based on the published data, it was assumed that $k < 10\,s^{-1}$.
[h] The values were calculated by Koptyug and Shubin[15] based on the kinetic data reported in the literature.[91]

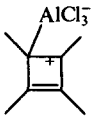
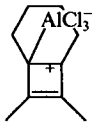
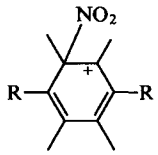
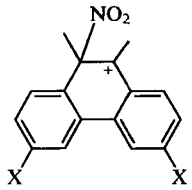
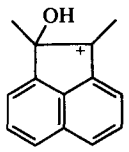
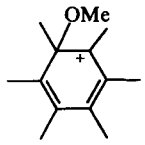
Table 3. Kinetic characteristics of 1,2-shifts of aryl groups for degenerate rearrangements of σ-complexes

Structural formula	σ-Complex	R or X	Acid, solvent	E_a/kcal mol^{-1}	lg $A_{1,2}$	$\Delta G^{\neq}$/kcal mol^{-1} [a]	Ref.
	**55a**	H	94% H_2SO_4			>17.5 (50 °C) [b]	15, 89
			PhCl ($Al_2Cl_7^-$ anion)			>20.3 (100 °C) [b]	15, 89
	55b	*p*-FSO_2	HSO_3F			>18.6 (70 °C) [b]	15, 89
	**56a**	H	$CF_3SO_3H-SO_2ClF$	16.8±0.2	12.5±0.2	17.2	118
			Crystal ($AlCl_4^-$ anion)	13.6±0.1	5.9±0.1	23.0	119
	56b	*p*-Me	$CF_3SO_3H-SO_2ClF$	16.0±0.8	12.6±0.9	16.3	120, cf 121
	56c	*p*-Cl	$CF_3SO_3H-SO_2ClF$	17.9±0.3	12.8±0.3	17.9	120, cf 121
	56d	*m*-CF_3	$CF_3SO_3H-SO_2ClF$	20.0±0.3	12.8±0.3	20.0	120, cf 121

	**57a**	H	CF_3SO_3H	11.4±0.2	11.7±0.2	12.8	122, cf 123
	57b	*p*-Me	$CF_3SO_3H-SO_2ClF$	9.4±0.1	11.6±0.1	11.1	122, cf 123
	57c	*p*-Cl	CF_3SO_3H	12.2±0.3	11.8±0.2	13.6	122, cf 123
	57d	*m*-Cl	CF_3SO_3H	14.4±0.2	12.0±0.1	15.5	122, cf 123
	57e	*p*-CF_3	CF_3SO_3H	17.1±0.1	13.1±0.1	16.7	122, cf 123
	57f	*m*-CF_3	CF_3SO_3H	16.4±0.2	12.9±0.1	16.3	122, cf 123
	**58a**	H	$HCl-Al_2Cl_6-CH_2Cl_2$	8.9±0.1	12.1±0.1	9.7	124
			HSO_3F-SO_2ClF	9.0±0.2	12.2±0.2	9.8	124
			HSO_3F-SO_2ClF	9.4±0.1	12.5±0.1	9.8	125
	58b	*p*-Me	HSO_3F-SO_2ClF	6.5±0.2	11.0±0.2	8.9	124
	58c	*p*-MeO	HSO_3F-SO_2ClF			6.5	106
	58d	*p*-Cl	HSO_3F-SO_2ClF	9.8±0.1	12.4±0.1	10.3	124
	58e	*p*-F	HSO_3F-SO_2ClF	9.3±0.1	12.5±0.1	9.7	124
	58f	*m*-F	HSO_3F-SO_2ClF	11.5±0.1	12.6±0.1	11.8	124
	58g	*p*-CF_3	HSO_3F-SO_2ClF	11.7±0.2	12.0±0.1	12.8	124
	**59**		HSO_3F			> 19.1 (60°C)	106, 124
	**60a**	3,6-Br_2	HSO_3F-SO_2ClF	8.2±0.2	11.6±0.2	9.8	125
	60b	3,6-Me_2	HSO_3F-SO_2ClF	10.7±0.1	11.9±0.1	11.9	125
	60c	3,6-$(CF_3)_2$	$HSO_3F-SO_2ClF-SO_2F_2$	6.4±0.2	12.7±0.3	6.5	125
	60d	2,7-Br_2	$HSO_3F-SO_2ClF-SO_2F_2$	7.3±0.1	11.8±0.2	8.7	125
	**61**		HSO_3F-SO_2ClF	9.4±0.2	12.4±0.2	9.9	125

[a] See footnote 'a' to Table 1; $f = 2$ for the ions **56a–d**. [b] Based on the published data,[89] it was assumed that $k < 10\,s^{-1}$.

Table 4. Kinetic characteristics of 1,2-shifts of the migrants $AlCl_3^-$, NO_2, OR, SO_3H, and Hal for degenerate rearrangements of σ-complexes

Structural formula	σ-Complex	R or X	Acid, solvent	E_a/kcal mol^{-1}	$\lg A_{1,2}$	$\Delta G^{\neq}$/kcal mol^{-1} [a]	Ref.
	**62**		$Cl_2CHCHCl_2$	20.3	16.1	15.8 (25 °C)	126
	**63**		$Cl_2CHCHCl_2$			19.8 (92 °C)	126
	**64a**	Me	HSO_3F-SO_2	16.8±1.5			127,
				13.3±1.3 [b]	13.1±1.2 [b]	12.9 (25 °C)[b]	cf 128
			HSO_3F-SO_2ClF	13.2±0.3	13.5±0.2	12.2 (25 °C)	129
			$HSO_3F-SbF_5-SO_2ClF$	12.6±0.4	12.9±0.4	12.4 (25 °C)	129
	64b	Cl	HSO_3F-SO_2ClF or $CF_3SO_3H-SO_2ClF$			9.0 (−100 °C)	79
			HSO_3F-SO_2ClF			8.9 (−90 °C)	79
	**65a**	H	$CF_3SO_3H-SO_2ClF-SO_2F_2$			7 (−105 °C)	129
	65b	Me	HSO_3F-SO_2ClF			9.9 (−89 °C)	129
			$CF_3SO_3H-SO_2ClF$			9.8 (−85 °C)	129
	**66**		HSO_3F-SO_2ClF	15.4±0.3	16.4±0.3	10.5 (25 °C)	130
	**67**		HSO_3F			>11.7 (−75 °C)	106, 131

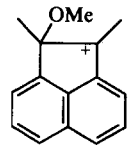
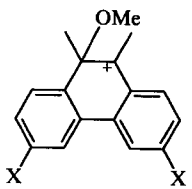
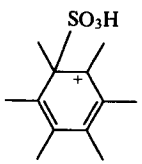
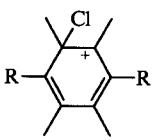
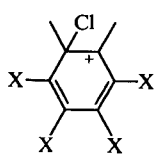
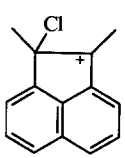
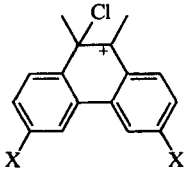
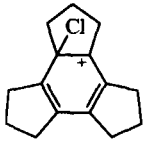
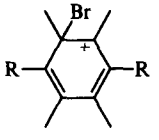
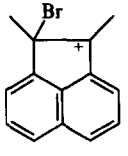
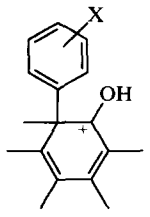
	**68**		HSO_3F-SO_2ClF (1:1)	13.0±0.5	14.8±0.5	10.3 (25 °C)	132
			HSO_3F-SO_2ClF (1:3)	12.2±0.4	14.5±0.4	9.9 (25 °C)	132
			HSO_3F-SO_2ClF (1:6)	9.4±0.3	12.3±0.3	10.1 (25 °C)	132
			HSO_3F-SO_2ClF (1:8)			9.1 (−110 °C)	132
			HSO_3F-SO_2 (1:4)			10.4 (−55 °C)	132
			HF			10.1 (−57 °C)	132
			$CF_3SO_3H-SO_2ClF$ (1:4)			9.0 (−102 °C)	132
			$HSO_3F-n SbF_5-SO_2ClF$ [c]	13.5±0.9	13.6±0.3	12.4 (25 °C)	132
				15.2±0.3	16.0±0.3	10.8 (25 °C)	132
				15.2±0.3	16.4±0.3	10.3 (25 °C)	132
				14.8±0.2	16.2±0.2	10.2 (25 °C)	132
				14.4±0.2	16.2±0.2	9.8 (25 °C)	132
			$(HSO_3F-SbF_5)/SO_2ClF$ (1:2)			14.3 (0 °C)	132
	69a	H	HSO_3F-SO_2ClF			<9.2 (−100 °C)[d]	133
	69b	Br	HSO_3F-SO_2ClF			<9.2 (−100 °C)[d]	133
	69c	Me	HSO_3F-SO_2ClF			<10.3 (−80 °C)[d]	133
	**70**		HSO_3F	19.2±0.4	15.4±0.3	15.6 (25 °C)	128
	**71a**	Me	HSO_3F	15.7±0.3	13.5±0.2	14.7 (25 °C)	134
			$HCl-Al_2Cl_6-CH_2Cl_2$	14.9±0.9	13.0±0.7	14.6 (25 °C)	134
	71b	Cl	HSO_3F			13.2 (−15 °C)	79
	**72a**	Cl	$HF-SbF_5-SO_2ClF$	10.7±0.2	12.0±0.1	11.8 (25 °C)	135
	72b	F	$HF-SbF_5-SO_2ClF$			12.3 (−42 °C)	135
	**73**		HSO_3F-SO_2ClF	10.5±0.2	13.5±0.2	9.5 (25°C)	134

Table 4 (continued)

Structural formula	σ-Complex	R or X	Acid, solvent	E_a/kcal mol^{-1}	lg $A_{1,2}$	$\Delta G^{\neq}$/kcal mol^{-1} [a]	Ref.
	**74a**	H	$CF_3SO_3H-SO_2ClF-SO_2F_2$	~5.6		~6.3 (−110 °C)	134
	74b	Me	$CF_3SO_3H-SO_2ClF$	6.6±0.1	11.5±0.1	8.3 (25 °C)	134
	**75**		$HSO_3F-SbF_5-SO_2ClF$			11.6 (−40 °C)	86
	**75a**	Me	HSO_3F-SO_2ClF	10.3±0.3	13.6±0.4	9.2 (25 °C)	136
	75b	Cl	HSO_3F-SO_2ClF			~7.4 (−110 °C)	79
	**76**		HSO_3F-SO_2ClF	5.1±0.2	12.3±0.2	5.8 (25 °C)	137
			$AlBr_3-CH_2Cl_2$	3.9±0.2	11.1±0.2	6.2 (25 °C)	137

[a] See footnote 'a' to Table 1; f = 2 for the ions **62**, **64a**, **70**, **71a**, **75a**.
[b] Calculated by Koptyug and Shubin[15] based on the kinetic data reported in the literature[127], see Ref 106.
[c] In these experiments, $0 < n < 1$, the value of n increases from bottom to top. The acid : diluent ratio is 1 : 2.
[d] Based on the published data,[133] it was assumed that $k < 10$ s^{-1}.

(**58a–g**),[124] 1-(X-phenyl)-1,2,3,4,5,6-hexamethylbenzenium (**56a–d**),[120,121] and 1-(X-phenyl)-1,2-dimethylacenaphthylenium (**57a–f**)[122,123] ions have been used to demonstrate the validity of the relationships $\lg(k_X/k_H) = \rho\sigma_X^+$. Judging by the absolute values of $\rho^+_{-50\,°C}$ (−4.5, −4.47, and −6.64, respectively), the series of the relative migration ability are not universal even in the case of structurally similar migrants, i.e. substituted phenyl groups. Analogous dependences hold for the nondegenerate rearrangements of 1-(X-phenyl)-2-hydroxy-1,3,4,5,6-pentamethylbenzenium ions (**81a–f**) ($\rho^+_{-50\,°C} = -3.37$)[181] and also for the 1,2-shifts of $XC_6H_4CH_2$ groups in 1-(X-benzyl)-1,2,3,4,5,6-hexamethylbenzenium cations ($\rho^+_{-50\,°C} = -4.42$)[113] and 9-(X-benzyl)-9,10-dimethylphenanthrenium cations ($\rho^+_{-50\,°C} = -1.08$).[115] Borodkin et al.[115,120] have analysed the behaviour of the sensitivity constants ρ^+ for the 1,2-shifts of XC_6H_4 and $XC_6H_4CH_2$ groups as a function of the structure of the core in terms of the O'Ferrall–Jencks model.

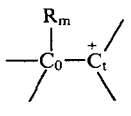


81a–f

X = H (**a**), *p*-Me (**b**), *p*-MeO (**c**), *p*-CF_3 (**d**), *m*-CF_3 (**e**), *p*-Cl (**f**).

A comparison of the selectivity (ρ^+) and activity [$\lg k$(Ph)] parameters for the rearrangements of ions **56a–d**, **57a–f**, **58a–g**, and **81a–f** shows that the 'activity-selectivity' principle (cf Refs 161–164) is not obeyed even for the isosteric XC_6H_4 migrants.[113] One may expect an antiparallel relationship between the activity and the selectivity when only one of the factors influencing the reaction rate is varied (for example, the inductive or the resonance effect)[22] (cf Ref 164). Comparing the activation free energies of the 1,2-shifts of the CH_2R groups (R = H, Me, Cl) in arenium ions with the chemical shifts of the carbocationic centre indicates that the 'activity-selectivity' principle is obeyed in the case of σ-migrants whose migration ability for ions with a fixed core is mainly determined by the inductive effect of the substituent R.[111] The $XC_6H_4CH_2$ groups behave anomalously in the series of migrants of the CH_2R type. This is shown by the intersection of the lines corresponding to the *p*-$ClC_6H_4CH_2$, $C_6H_5CH_2$, and CH_3CH_2 groups which intersect in the region of experimentally accessible values of δC^+ and $\Delta G^{\neq}$ (see Ref. 115). The violation of the 'activity-selectivity' principle in this case, as also for XC_6H_4 groups, may be associated with the simultaneous influence of the inductive and resonance effects of the substituents R (or X), the ratio between whose contributions probably varies with the activity parameter.[113,115]

A substantially more complicated problem arises in developing approaches to the quantitative description of the migration ability of different types of migrant (see Refs 140–143). Borodkin et al.[182] took the first step in this direction. They assumed that the activation free energy of the 1,2-shifts of different migrants in the cationic σ-complexes can be expressed as the sum of two constituents one of which (E_1) reflects the consumption of energy for elongation of the C_0-R_m bond and for deformation of the $C_t-C_0-R_m$ bond angle when the transition state is achieved, and the other (E_2) is the gain in energy resulting from the interaction of the migrant with the carbocationic centre.



$$\Delta G^{\neq} = a + b_1E_1 + c_1E_2. \quad (6)$$

The energy required to cleave the $C-R_m$ bond in the compounds CH_3R_m [$E_b(CH_3R_m)$] [or the force constant of the deformation vibration of the $C_t-C_0-R_m$ fragment (K_{def})] and the proton affinity of compounds CH_3R_m (PA) have been suggested as characteristic parameters of the E_1 and E_2 energies. It would be more reasonable to use the affinity of CH_3R_m to the CH_3^+ cation, but these data are quite limited. In terms of this simplified model, allowing for the limited relationship of the charge on the carbocationic centre (q^+) to the value of chemical shift of the C_t atom,[138] we obtain:

$$\Delta G^{\neq}(R_m) = a + bD + cq_t^+[d + e(PA)(CH_3R_m)], \quad (7)$$

where $D = E_b(CH_3R_m)$ or K_{def}; $q_t^+ = f + g\delta C^+$.

A comparison of the free energies of activation of the 1,2-shifts of the migrants in 1-R_m-1,2,3,4,5,6-hexamethylbenzenium, 9-R_m-9,10-dimethylphenanthrenium, 9-R_m-9,10-dimethylpyrenium, and 2-R_m-1,2,3,4-tetramethylnaphthalenium ions (R_m = Me, Et, XC_6H_4, Cl, Br) (see Tables 2–4) with the corresponding values of $E_b(CH_3R_m)$, $(PA)(CH_3R_m)$, and $\delta C^+(CH_3)$ produces the following correlation:†

$$\Delta G^{\neq}_{25\,°C} = 0.9 + 0.329E_b - 0.00129(PA)(\delta C^+ - 130), \quad (8)$$

$$r = 0.987,\ s = 0.7,\ n = 29.$$

The activation free energies of the 1,2-shifts of hydrogen atoms do not obey the correlation (8). This may be due to the fact that the deformation of the C_t-C_0-H fragment occurs more easily than that of other fragments, which results in an increase in the migration ability of hydrogen and probably reflects the well known tendency of hydrogen to form bridged structures (see Refs 183–187). However, when the parameter E_1 is characterised by the force constant of the deformation vibration of the $C_t-C_0-R_m$ fragment, the correlation is more general:

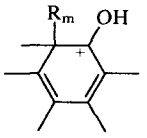
$$\Delta G^{\neq}_{25°C} = 17.1 + 14.5K_{def} - 0.00127(PA)(\delta C^+ - 130), \quad (9)$$

$$r = 0.963,\ s = 0.7,\ n = 33.$$

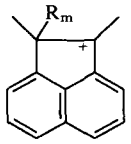
For a series of cationic σ-complexes with a fixed core ($q_t^+ \approx$ const, $\delta C^+ \approx$ const), the relationships (8) and (9) are transformed into simpler dependences:

$$\Delta G^{\neq} = a + bD + d(PA). \quad (10)$$

This makes it possible to verify the applicability of these dependences to the quantitative description of nondegenerate rearrangements of arenonium ions and of rearrangements of carbocations that differ from arenium ions in the type of core. A comparison of the activation free energies of the 1,2-shifts of migrants in 1-R_m-2-hydroxy-1,3,4,5,6-pentamethylbenzenium ions (**81, 82**)[181,188,189] and 1-R_m-1,2-dimethylacenaphthylenium ions (**83**) with the corresponding $E(CH_3R_m)$, K_{def}, and (PA) parameters produces correlation relationships whose characteristics are presented in Table 5.[100,190] The values of the free energies of activation of degenerate and nondegenerate 1,2-shifts of the migrants R_m in arenium ions and in 1-R_m-1,2-dimethylacenaphthylenium cations calculated from type (7) and (10) relationships are in good agreement with experimental data: the discrepancy between $\Delta G^{\neq}$ values normally does not exceed 1 kcal mol^{-1}, the range of their variation being ~ 20 kcal mol^{-1}.[100]



82a–c



83a–c

† The chemical shifts of the corresponding ions with the standard migrant, the Me group, were taken as the values of δC^+.

Table 5. The parameters of correlations of type (10) for 1,2-shifts of the R_m migrants in 1-R_m-2-hydroxy-1,3,4,5,6-pentamethylbenzenium and 1-R_m-1,2-dimethylacenaphthylenium ions at 25 °C.

Ions	Parameter					
	D	*a*	*b*	*d*	*r*	*s*
81a–f, 82a–c	E_b	14.5	0.312	−0.121	0.98	0.3
81a–f, 82a–c	K_{def}	31.0	16.6	−0.142	0.96	0.5
38, 43, 57a–f, 73, 76	E_b	20.7	0.406	−0.268	0.97	1.1
26b, 38, 43, 57a–f, 73	K_{def}	43.4	30.4	−0.358	0.92	1.3

3. Influence of the medium on the rates of degenerate σ,σ-rearrangements

When the data on the rearrangements of cationic σ-complexes are compared in terms of structure-kinetics relationships the question of how the medium influences the rate of an 1,2-shift is of importance. The influence of the liquid medium (solvent and counter-ion) has been most extensively studied for the 1,2-shift of a methyl group in the heptamethylbenzenium ion (**35**). The rate constants of the rearrangement of this ion turned out to be virtually identical in the following media: HSO_3F,[191] HSO_3Cl,[90,191] H_2SO_4,[91,191,192] CF_3COOH,[92] HCOOH,[191] HSO_3F-SbF_5 (9:1),[191] a 20% solution of SO_3 in HSO_3F,[192] CH_2Cl_2 (with $AlCl_4^-$ as the anion),[93,191] $HC(SO_2F)_3$,[193] $SOCl_2$ (with $SbCl_6^-$ as the anion),[94,95] $PhNO_2$ (with the $AlCl_4^-$ anion),[191] C_6F_6 (with the $Al_2Cl_7^-$ anion),[21] $PhNO_2$ (with the Ph_4B^- anion).[21] The same conclusion applies to the rearrangements of 9,9,10-trimethylphenanthrenium (**39a**),[101,102,104,194,195] 3,6,9,9,10-pentamethylphenanthrenium (**39c**),[102,193] and 1,1,2-trimethylacenaphthylenium (**38**)[85] ions. No appreciable influence of the medium on the rates of 1,2-shifts of hydrogen has been detected for 1-*H*-1,2,3,4,5,6-hexamethylbenzenium (**21**),[21,76,78] 9*H*-3,6,9,10-tetramethylphenanthrenium (**27c**),[78] 2-*H*-1,2,3,4-tetramethylbiphenylenium (**24a**),[82] 1-*H*-1,2-dimethylacenaphthylenium (**26b**),[84,85] 2,3-dimethyl-2-norbornyl (**11a**),[65] 1-*H*-1,2-dimethyl-3,4,5,6-tetra-X-benzenium (X=Cl, F (**22b**),[80] 1,2,3,4-tetramethylnaphthalenium (**23**),[81] 2-methyl-2-butyl,[21,152,196–198] or 4-R-1,2,3,4,5-pentamethylcyclopentenyl (R = H, Me)[21,199] ions. Likewise, very low sensitivities of the rearrangement rates to variation of the medium have been found for the 1,2-shifts of XC_6H_4 groups in 1-phenyl-1,2,3,4,5,6-hexamethylbenzenium (**56a**),[118] 9-phenyl-9,10-dimethylphenanthrenium (**58a**),[124,125] and 9,9,10-tri-(*p*-X-phenyl)phenanthrenium[200] ions as well as for the 1,2-shifts of halogen atoms in 1-chloro-1,2,3,4,5,6-hexamethylbenzenium (**71a**)[134] and 1-bromo-1,2-dimethylacenaphthylenium (**76**)[137] cations (see Table 4). The rate of the 1,2-shift of the $AlCl_3^-$ group in the ion **62** is also virtually unchanged on going from CH_2Cl_2 to $CHCl_2CHCl_2$.[126]

The lack of influence of the medium on the rates of the 1,2-shifts in the π-delocalised carbocations considered above is probably due to the fact that the location of the 'centre of gravity' of the positive charge on the cation varies only slightly on going from the ground state to the transition state.[21]

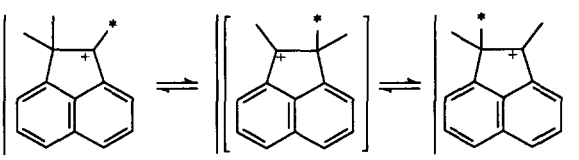
As would be expected, in the case of migrants susceptible to specific solvation the influence of the medium on the rates of rearrangements becomes dominant. For example, the rate of the degenerate rearrangement of the 1-nitro-1,2,3,4,5,6-hexamethylbenzenium ion (**64a**) in the $HSO_3F-SbF_5-SO_2ClF$ system, which occurs via the 1,2-shift of the nitro group, decreases as the concentration of SbF_5 increases.[129] Similar effects have been observed for OH,[130] OMe,[132] and Alk–OCO [201] groups (see Ref. 202). It is likely that in these cases, owing to specific solvation of the migrant by the medium, the magnitude of the positive charge on the migrant increases and this leads to a diminution of the rate of rearrangement.

In view of the data considered above, the problem of controlling the rates of 1,2-shifts of migrants by using ordered media is of great interest. The first attempts along these lines were undertaken by Borodkin et al.,[203] who studied the rearrangement of the 1,1-dimethyl-2-ethyl-acenaphthylenium ion to the 1-ethyl-1,2-dimethylacenaphthylenium cation (**43**). However, it was found that the rate of this rearrangement virtually does not change on going from liquid to frozen CF_3SO_3H as the solvent. Later it was shown[204] by CPMAS ^{13}C NMR that the rates of hydride shifts in norbornyl and 2-butyl cations are also almost insensitive to the change in the phase state of solutions in SbF_5 (see Ref. 205).

Data on the strong influence of an ordered medium on the rates of 1,2-shifts in cationic σ-complexes were obtained for the first time for the crystalline tetrachloroaluminate of the hexamethylbenzenium ion.[93] The values of the kinetic parameters (E_a, lg*A*) of the 1,2-shift of the methyl group in this cation in the crystalline state were found to be appreciably lower than those in solution (see Table 2). At −77 °C an isokinetic point was observed and at higher temperatures the rate constants of the rearrangement were larger in the case of the liquid phase. Variation of the counter-ions in crystalline heptamethylbenzenium salts ($AlCl_4^-$, BF_4^-, BPh_4^-, $SbCl_6^-$) results in strong changes in both the kinetic parameters (see Table 2) and the rate of the 1,2-shift of the methyl group.[95] Unexpectedly, the intramolecular rearrangement of the $SbCl_6^-$ salt of this ion accelerates on going from solution to the crystalline state (see Table 2).[94,95] This fact and also the decrease in the activation energy found in some other cases are probably due to the Coulomb interaction of the neighbouring counter-ions with the rearranging ion, in particular, the stabilising interaction of the neighbouring anion with the methyl group which carries a partial positive charge in the transition state.[93,95] This is confirmed by the existence of linear correlations of the logarithms of the ratios between the rate constants of the 1,2-shifts of Me and Ph migrants in the ions **35** and **56a** in the crystalline phase and in solution with the values of the difference between the energies of Coulomb interaction of the rearranging ion with their environment in the ground and the transition states.[95] Considerable retardation of the carbocation rearrangements on going from solution to the crystalline state has been found for the tetrachloroaluminate of 1-phenyl-1,2,3,4,5,6-hexamethylbenzenium ion[119] (**56a**, see Table 2).

In the crystalline state the rearrangements of 1-R_m-1,2,3,4,5,6-hexamethylbenzenium ions (R_m = Me, Ph) are degenerate rearrangements as regards both the structure of the ion and the environment, i.e. the rearranging ion preserves its topochemical properties after each act of migration of the R_m group.[206] These rearrangements may be referred to as 'topodegenerate'. Another type of solid-state carbocationic rearrangement, which is degenerate as regards the structure of the ion but nondegenerate as regards the environment ('topo-nondegenerate' rearrangement), has been found in a study of the crystalline tetrachloroaluminate of the 1,1,2-trimethylacenaphthylenium ion (**38**)[99] by the radioactive tracer method. The 1,2-shift of methyl in this ion leads to a structure that is formally identical to the original one (Scheme 4),‡ but has a distorted unit cell. The rate of the rearrangement of ion **38** in the crystalline state is appreciably lower than in solution (see Table 2), which is obviously due to the fact that the structure of ion **38′** does not correspond to the unit cell.

Scheme 4

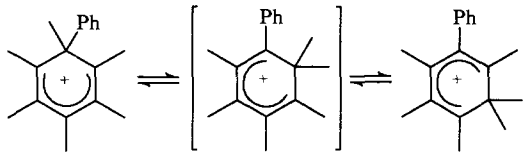


38 **38′**

‡ The vertical line in Scheme 4 conventionally denotes the dissimilar environments of ions **38** and **38′** in the crystal.

One might expect that similar retardation effects would be seen in the case of carbocationic rearrangements that are non-degenerate with respect to both the ion structure and the environment. In fact, the nondegenerate rearrangement of ion **56a** occurring in solution via a 1,2-shift of the methyl group (Scheme 5),[118] does not proceed in the crystalline state to any noticeable degree even under very rigorous conditions (70 °C, 2 h).[119]

Scheme 5



56a

Thus, the selectivity of the process (the k^{Ph}/k^{Me} ratio) increases on passing from solution to the crystalline state.

Surprisingly, the Arrhenius parameters of the rearrangement of heptamethylbenzenium tetrachloroaluminate deposited on Al_2O_3 are intermediate between those found for the reactions in solution and in the crystalline phase (see Table 2).[96] The fact that lg$A$ is larger than in the crystalline state may indicate that this cation possesses a relatively high mobility on the Al_2O_3 surface. By analogy with the crystal-degenerate rearrangement of this ion, the decrease in the activation energy compared with the E_a value for the solution may be caused by the electrostatic interaction of the partial positive charge of the migrant with the nucleophilic centres of alumina and $AlCl_4^-$.

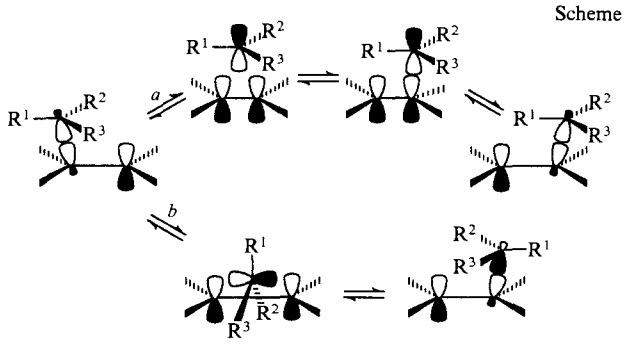
These results show that the transition to ordered or 'partially ordered' media is an effective means of controlling rearrangements in cationic σ-complexes.

4. Stereochemical aspects of cationic σ,σ-rearrangements

The stereochemistry of a migrant is one of the most important aspects of the theory of sigmatropic rearrangements occurring via 1,2-shifts of alkyl or other similar groups. For suprafacial 1,2-shifts of $CR^1R^2R^3$ groups,§ (see Refs 207, 208) the configuration of the C atom bound to R^1, R^2, and R^3 groups can be either retained (Scheme 6, path *a*) or inverted (path *b*).

The stereochemistry of tetragonal migrants involved in 1,2-shifts in 'long-lived' carbocations has been studied for the first time for 1-CH_2R-1,2-dimethylacenaphthylenium ions (R = Me, *p*-ClC_6H_4)[107,114] by an approach based on the fact that the methylene protons are diastereotopic and by using dynamic NMR.[52] A comparison of the rate constants of the rearrangement determined from the variation of the forms of signals of the CH_3 and CH_2R groups showed that they are almost identical. This implies that the 1,2-shifts of C_2H_5 and *p*-$ClC_6H_4CH_2$ groups in ions **43** and **52** occur with retention of the configuration of the methylene C atom, which is consistent with the theory of pericyclic reactions.[207,208]

Scheme 6



§ Antarafacial 1,2-shifts seem to be very unlikely, especially in cyclic systems.[153,207] In a study of degenerate rearrangement of 4,5,9,9,10-pentamethylphenanthrenium ion, it has been found that the 1,2-shift of methyl occurs as a suprafacial process.[103]

Later similar results were obtained for an ion of a different structural type, i.e. the 9-(3′,5′-dichlorobenzyl)-3,6,9,10-tetramethylphenanthrenium cation (**53e**).[116] Assuming that 1,2-shifts in these ions are one-step processes, one can treat these results as experimental evidence for the Miller[209] postulate concerning the stereospecificity of the elementary step of a chemical reaction.[107]

As in the data obtained for 'long-lived' cations, retention of the configuration at the migrating centre has also been observed in the pinacol–pinacolone[210] and other cationoid rearrangements[211–213] whose key step is the 1,2-shift of a migrant to a carbonium centre.

It is noteworthy that the 1,2-shift of the methyl group in the 1,1,2,3,4-pentamethylcyclobutenyl cation (**34a**) does not occur even under very rigorous conditions ($\Delta G^{\neq} > 27.5$ kcal mol^{-1}),[88,89] though according to the theory of pericyclic reactions, this shift is allowed as a suprafacial process with inversion of the configuration of the migrant.

IV. σ,π-Rearrangements

The tendency of cationic σ-complexes to rearrange caused by their 'inherent instability' is closely related to their tendency to form in some cases multicentre migrant—core bonds. Owing to the large deviations of the bond angles from their normal values, the resulting π-complexes are rather strained systems, and the peculiarities of their electronic structures are not adequately characterised by the classical views of the nature of the chemical bond[214] (cf Ref. 35).



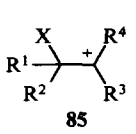
84a **84b**

These structures were described for the first time by Dewar[34] in the framework of the method of molecular orbitals. Dewar et al.[35,139] considered the evolution of concepts in the field of the theory of π-complexes. According to the modern views, strong and weak π-complexes are distinguished depending on the ratio between the forward ($\pi-p$) and back (π^*-p) donation.[35] In the case of strong π-complexes (**84a**), the contribution of the forward donation predominates, whereas for weak π-complexes (**84b**), these contributions are comparable.[35] As the electronegativity of the X fragment increases, the role of back donation should diminish.[35,214] The foregoing should be taken into account while considering the relative stabilities of σ- and π-complexes.

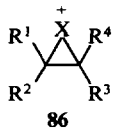
According to Dewar and Dougherty,[139] the change in energy on going from a σ- to a π-complex is determined by the following relationship:

$$\Delta E = (E_{C-X} - E_{\pi}) + (E_{C-C} - E_{C=C}),$$

where E_{C-X}, E_{C-C}, and $E_{C=C}$ are the energies of the corresponding bonds and E_{π} is the energy of the bond between the apical group and the core in the π-complex. Despite the fact that the strengths of the C–X bonds in σ- and π-complexes should vary in parallel, the C–X bond in a σ-complex is the stronger and the variation of the E_{C-X} value should be greater than that of E_{π}. Therefore, the stronger the C–X bond, the more stable is the σ-complex. In addition, one might expect that the transition from a σ-complex to a π-complex would lead to an increase in the positive charge on the X fragment.[139] Therefore this transition should be hampered for electronegative groups or atoms X (see Ref. 35). Finally, when X has unshared *p* or *d* electrons, back coordination is possible in the π-complex. The interaction between the occupied AO of the X fragment and the antibonding π-MO will be more effective, the closer their energies. Most of these views are qualitatively confirmed by calculated and experimental data on the relative stabilities of σ- and π-complexes and **85** and **86** (Table 6).



85



86

As shown in Table 6, those X groups whose central atoms are elements of the third or higher periods and have lower electronegativities and relatively less strong C–X bonds tend to stabilise a π-complex.[215] Depending on the chosen quantum-chemical approximation, the ΔE values are in some cases substantially different. The order of relative stabilities of σ- and π-complexes is indicated somewhat better.

It should be emphasised that experimental data on the relative stabilities of the cationic σ- and π-complexes are scarce and mostly refer to the gaseous phase. The construction of a 'chemical scale' of relative stabilities of σ- and π-complexes based on the data on rearrangements of long-lived carbocations occurring via 1,2-shifts is of great interest. During a 1,2-shift the migrant passes through a π-bonded state, and if the distinctions between the transition state and the π-complex are small (see Refs 44, 218), the $\Delta G^{\neq}_{1,2}$ values should reflect the relative stabilities of σ- and π-complexes. To construct this 'chemical scale', which is essentially a kinetic scale, relationship (8) (obtained for degenerate rearrangements of arenium ions by extrapolating the δC^+ values to the region of carbocations of the aliphatic series) has been used. The $\Delta E_{\sigma,\pi}$ values thus found are in agreement with the experimental and quantum-chemical data on the relative stabilities of σ- and π-complexes (see Table 6). The negative values of $\Delta E_{\sigma,\pi}$ indicate that, for aliphatic systems, π-complexes are more stable than σ-complexes. In fact, stable cyclic cations **86** ($R^1 = R^2 = R^3 = R^4 = H$) with $X^+ = RS^+$,[222] RO^+,[223] Ph^+,[224] I^+, Br^+, Cl^{+2} have been detected experimentally.

Borodkin et al.[225] suggested a similar scale based on 1-R-1,2-dimethylacenaphthylenium ions as model systems and a relationship of type (10).

The relative stabilities of the σ- and π-complexes **85** and **86** are substantially affected by the substituents $R^1 - R^4$ at basal C(1), C(2) atoms. As can be seen from the data of Table 6, the relative stabilities of σ-complexes **85** increase as the number of methyl groups at these atoms increases. Previously it has been noted that the 2,3-dimethyl-2-butyl cation **3a** is an open ion that undergoes a very rapid degenerate rearrangement (see Table 1). As estimates for the gaseous phase have shown, in the of case the ethyl cation the equilibrium *A* (see Scheme 1) is shifted toward the π-complex ($\Delta G^\circ = 0.8 \pm 0.1$ kcal mol^{-1}).[226] This is consistent with the results of high-level ab initio calculations.[170] A similar situation might also be expected for 2-butyl cation (**87**). In fact, the ^{13}C NMR spectrum of ion **87** shows a signal at δ 173.4 ppm (see Ref. 25) corresponding to the C(2) and C(3) atoms; no exchange broadening of this signal has been detected up to −140°C.[54] This gives the upper limit of 2.4 kcal mol^{-1} for the free energy of activation of a hypothetical rearrangement occurring via the 1,2-hydride shift (see Ref. 54).

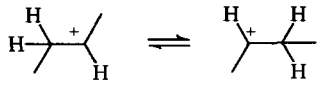
The application of the CPMAS ^{13}C NMR method yielded the spectrum of the 2-butyl cation in the solid state; no static structure was detected down to −190 °C.[227] Since the rates of intramolecular sigmatropic processes in carbocations normally diminish on going from the liquid to the solid state (cf Ref. 205), the $\Delta G^{\neq}$ value of this rearrangement in solution should apparently be lower than 2.4 kcal mol^{-1}. The chemical shift due to equilibrium **87** ⇄ **87′** averaged, and Et evaluated using the data for 2-propyl- and 2-methyl-2-butyl cations is equal to (320 + 57.5)/2 = 189 ppm, which differs from the observed value (173.4 ppm).[25] This may be accounted for by assuming that bridged structures **88a,b** are involved in the equilibrium, apart from σ-complexes **87**, **87′** (a σ,π-rearrangement). The relatively small value of the isotopic perturbation on replacement of one hydrogen atom in the methyl group by deuterium ($\delta_{-111\,°C}$ = 11 ppm) compared with the corresponding value (22.5 ppm) for the equilibrium of 2,3-dimethyl-2-butyl cations[228] is consistent with this assumption. Nevertheless,

Table 6. Relative energies of isomeric σ- and π-complexes **85**, **86**.

X	R^1, R^3	R^2, R^4	ΔE/kcal mol^{-1}					$\Delta E_{\sigma,\pi}$ (25 °C)[e]
			MINDO/3[a]	MNDO[b]	ab initio[c] (basis set)	CEPA[d]	Experimental[47]	
H	H	H	−8.00	15.0	7.3 (4-31G)	−7.33		
Me	H	H	−5.91	15.8	0.4 (4-31G)	−11.03 (~−7.9)	~−8	−2.3
Ph	H	H			−35.4			−7.2
p-MeC_6H_4	H	H						−9.6
p-ClC_6H_4	H	H						−7.4
p-$CF_3C_6H_4$	H	H						−4.9
F	H	H	−31.14	18.7	11.4 (4-31G)	−1.41		2.8
Cl	H	H	−29.28	−5.6	−9.2 (4-31G)	−30.00		−8.6
					−14.6 (6-31G**)			
					−27.2 (MP2/6-31G**)			
Br	H	H			−30.1 (STO-3G)			−13.8
I	H	H			−37.0 (STO-3G)			−20.0
OH	H	H	−24.1	−5.0	−9.1 (4-31G)	−22.1	−20	−11.1
SH	H	H	−40.1	−16.7	−20.1 (4-31G)	−48.3	(< −5.3)	−17.5
NH_2	H	H		−31.9	−42.6 (4-31G)		−43	−21.5
PH_2	H	H		−12.1				−9.4
CN	H	H			−1.0 (STO-3G)			
					9.4 (4-31G)			
					9.6 (DZP)			
SiH_3	H	H		5.8	−9			
H	Me	H	−5.1					
H	Me	Me	1.2					

[a] See Refs 17, 171, 217. [b] See Refs 35, 217, 218. [c] See Refs 6, 35, 174, 219–221. [d] See Refs 171, 217.

[e] Calculated from Eqn (8) with the value δC^+ = 309.2, obtained from the data for Pr^{i+} cation with allowance for the increment that reflects the replacement of the methyl group by the hydrogen atom.[138] The value for X = H is not presented, since in this case Eqn (8) does not hold. The E_b and (*PA*) values were taken from the literature.[182, 215, 216]

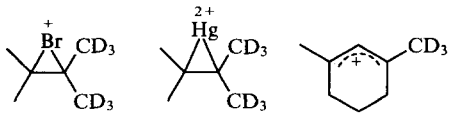


87 87'



88a 88b

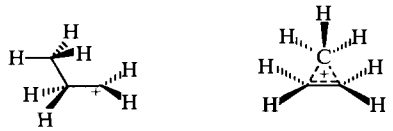
the observed δ value for 2-butyl cations is appreciably greater than those detected in the case of the 'isotopic perturbation of resonance' [17,147,229] in structures **89**, **90**,[230] and **91**[185] (1.81, 3.08, and 0.3 ppm, respectively), which contain more 'perturbing' deuterium atoms. According to the evaluation made by Edward,[148] based on the data on isotopic perturbation, the energy of the π-complex **88** is lower by 0.29 – 0.77 kcal mol^{-1} than that of the σ-complex **87**.



89 90 91

The introduction of more effective electron-donating groups in the core of type **85** carbocations favours an increase in the stability of σ-complexes compared with π-complexes **86**. This is illustrated by the data in Tables 1 and 2.

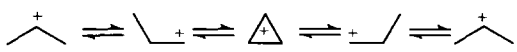
In conformity with the kinetic scale of relative stabilities of σ- and π-complexes, the methyl group shows a moderate tendency to form bridged structures (see Table 6), therefore one might expect that systems with poor delocalisation of the positive charge in the core would contain appreciable quantities of π-complexes in equilibrium with σ-complexes. Cations of the general formula $C_3H_7^+$ are one of these systems. According to detailed ab initio calculations in the STO-3G basis set with refinements in the STO-4-31G basis set, the difference between the energy of the 1-propyl cation (**92**) and that of the corresponding bridged structure **93** is small (<1 kcal mol^{-1}) and the open structure has a distorted geometry with an unusual C – C – C angle (83.4°). This geometry is favourable to the transition to the bridged ion[231] (see Ref. 232).



92 93

More recent and rigorous ab initio calculations with allowance for electron correlation (the CTHF method) as well as experimental data for the gaseous phase indicate that the π-complex **93** is more stable than the σ-complex **92** (see Table 6). Experimental data on the relative stability of the σ- and π-complexes under consideration are lacking. However, the results of a study of the isotope distribution of the label in (1,1,1-D_3), (2-D), and (2-^{13}C) enriched isopropyl cations [233,234] suggest easy interconversion of these complexes in accordance with Scheme 7.

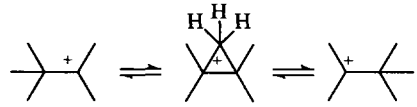
Scheme 7



As has been noted above, the 2,3,3-trimethyl-2-butyl cation undergoes a very rapid degenerate rearrangement ($\Delta G^{\neq}_{-136\,°C}$ = 3.8 kcal mol^{-1}),[54] and, according to the data on isotopic perturbation, the proportion of the π-complex existing in equilibrium with it (Scheme 8) is small.[24]

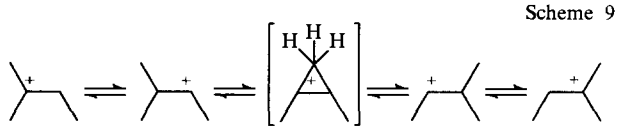
In the case of the 2-methyl-2-butyl cation (**94**), one might expect a situation intermediate between those considered above

Scheme 8



for the 1-propyl and 2,3,3-trimethyl-2-butyl cations. In fact, the ion **94** undergoes degenerate rearrangement via 1,2-H and 1,2-methyl shifts, as shown in Scheme 9, and the activation energy of the rearrangement is 15.3 ± 0.2 kcal mol^{-1}.[196]

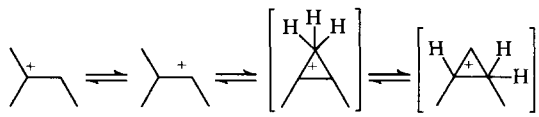
Scheme 9



94 95 96

Taking into account the difference in energy between the tertiary (**94**) and secondary (**95**) ions (10 – 11 kcal mol^{-1}),[27,235] one can infer that the 1,2-shift of the methyl group should occur with an activation energy of less than 5 kcal mol^{-1}, which may be regarded as the upper limit of the relative stability of the σ- and π-complexes **95** and **96**. The assumption that the π-complex **96** is an intermediate rather than a transition state is supported by the following data. At temperatures of >100 °C, 'confusion' of the protons of the CH_3 and CH_2 groups occurs in ion **94**, apart from the above-mentioned rearrangement (E_a = 18.8 ± 1 kcal mol^{-1}).[236] Since the mechanism involving the formation of primary ions is characterised by a higher energy barrier (~ 30 kcal mol^{-1}, see Ref. 24), this rearrangement involves the intermediates **96** and **97**: (Scheme 10).[236]

Scheme 10



94 95 96 97

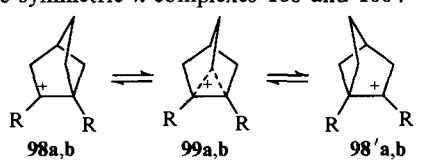
In the case of polycyclic carbocations the specific spatial arrangement of their fragments may result in an increase in the stabilities of π-complexes with respect to σ-complexes even in the presence of apical groups with a low tendency to form multi-centre electron-deficient bonds. Systems of the norbornane series, in particular, 2-norbornyl cation, which has been the object of investigation in the series of nonclassical cations for more than 30 years, can serve as examples.[1,7,23,27] As investigations have shown, the 2-norbornyl cation is thermodynamically more stable in the gaseous phase than the secondary aliphatic ions[237] (see Refs 238, 239). Although the numerous quantum-chemical calculations produce contradictory results for this cation (see citations in Ref 240), the most rigorous of these (ab initio 4-21P* with allowance for electron correlation)[240] support the π-complex. The assemblage of data on the ^{1}H and ^{13}C NMR spectra, heats of formation, and effects of the increase in the electron demand and isotopic perturbation obtained for this ion generated in condensed media under 'long lifetime' conditions show its π-complex (nonclassical) nature.[23]

This point of view has been confirmed by the CPMAS ^{13}C NMR data obtained for a frozen solution of 2-norbornyl cation at 5 K.[241] An attempt to interpret these data by invoking the concept of double-well potential and heavy atom tunneling[242] (see Ref. 243) was unsuccessful,[244] since the ^{13}C NMR spectrum of the norbornyl ion did not show the expected splitting of the corresponding signals even at 5 K, and on raising the temperature no broadening of the signals was observed.¶

¶ Recently Kramer and Scouten criticised the concept of a 2-norbornyl cation as a nonclassical ion.[28]

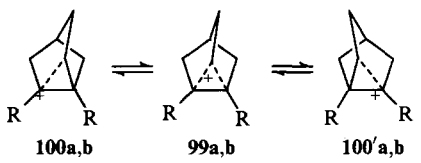
The introduction to the C(1) and C(2) atoms of methyl groups should apparently lead to an increase in the proportion of the σ-complex in equilibrium with the π-complex. The data on the isotopic perturbation for ions **98b** and **99b** ($R = CD_3$) are consistent with this assumption.[147] Taking into account the data from ^1H and ^{13}C NMR spectroscopy (see Ref. 245), one may infer that interconversion of the ions **98**, **98′** proceeds according to either Scheme 11 or Scheme 12 involving interconversions of the symmetric π-complexes **100** and **100′**.

Scheme 11



98a,b **99a,b** **98′a,b**

Scheme 12



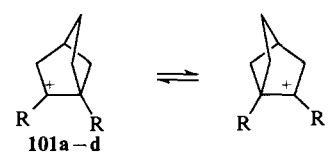
100a,b **99a,b** **100′a,b**

R = Me (**a**), CD_3 (**b**).

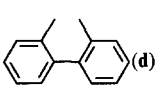
The latter scheme is supported by the results of an X-ray structural study[246] in which the 1,2,4,7-tetramethyl-2-norbornyl cation was shown to be an asymmetric bridged ion with C(1)–C(6) and C(2)–C(6) bond lengths of 1.74 Å and 2.09 Å, respectively. In view of the fact that the mechanisms under consideration differ from one another only in some details of the structures of the interconverting initial cations **98** and **100**, it is difficult at present to choose between these mechanisms.

The addition to the C(1), C(2) atoms of groups more electron-donating than methyl increases the stability of σ-complexes compared with π-complexes. For example, Nickon and Lin[247] have found that the 1,2-dimethoxy-2-norbonyl cation **101a** is classical and undergoes a rapid degenerate rearrangement, in conformity with Scheme 13.

Scheme 13



101a–d

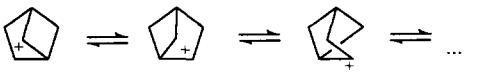
R = MeO (**a**), Ph (**b**), *p*-$MeOC_6H_4$ (**c**), R + R =  (**d**)

A similar situation has been observed for the ions **101b–d** with π-electron delocalisation in the core.[248–251]

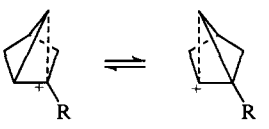
It is of interest to compare the properties of 1,2-R-2-norbornyl ions with those of their closest lower homologues, i.e. 1,2-R-2-bicyclo[2.1.1]hexyl cations. The shortening of the apical group by one unit may lead to a change in the relative proportions of σ- and π-complexes in the equilibrium mixture. The views on the structure of the parent ion of this series, the 2-bicyclo[2.1.1]hexyl cation, have varied and have not yet settled. For example, Seybold et al.[252] who studied the structure of this ion under 'long lifetime' conditions by ^1H NMR, rationalised the results obtained by assuming 'extra fast' equilibrium of nonclassical ions (π-complexes).



MINDO/3 calculations confirmed the bridged structure of the ion.[253] At the same time, analysis of the ^{13}C NMR spectra of 2-bicyclo[2.1.1]hexyl cations[254] and of 2-aryl-2-bicyclo-[2.1.1]hexyl ions[255] (the method of increase in the electron demand) suggested the presence of an equilibrium in which interconverting σ-complexes make the greatest contribution to the averaging of the corresponding NMR signals.



Sorensen and Schmitz[256] attempted to clarify the situation by solving the structure of the 2-bicyclo[2.1.1]hexyl ion. In their opinion, this ion exhibits properties intermediate between those of classical (σ-complexes) and nonclassical (π-complexes) ions, i.e. it is an asymmetric nonclassical ion (asymmetric π-complex) that undergoes degenerate rearrangement:



102a,b **102′a,b**

R = H (**a**), D (**b**).

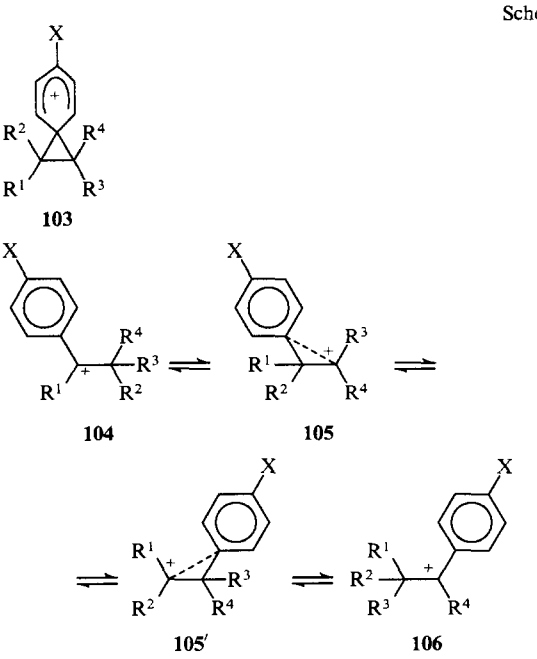
The small magnitude of the isotopic perturbation in the D-analogue of the **102b** ion ($\delta_{-115\,^\circ C}$ = 1.18 ppm)[147] is consistent with this inference.

The introduction of methyl groups in positions 1 and 2 dramatically lowers the π-complex character of the ion, which is shown by the large isotopic perturbation δ on replacing one of these groups by a CD_3 group ($\delta_{-100\,^\circ C}$ = 36.5 ppm).[256] This value is intermediate between those observed for 1,2-dimethyl-2-norbornyl[257] and 1,2-dimethylcyclopentyl cations.[25,257] Thus, the 1,2-dimethyl-2-bicyclo-[2.1.1]hexyl cation is a σ-complex that undergoes very rapid degenerate rearrangement ($\Delta G^{\neq} < 2.8$ kcal mol^{-1}), the relative proportion of the isomeric π-complex in the equilibrium being probably small.

In conformity with the kinetic scale of the relative stabilities of σ- and π-complexes (see Table 6), the phenyl group exhibits a greater tendency to form bridged structures than alkyl groups. The experimental data obtained so far are not inconsistent with this inference. In fact, the ionisation of 2-chloroethylbenzene in superacids affords a π-complex (**103**, X = R^1 = R^2 = R^3 = R^4 = H).[224,258] Ab initio calculations (STO-3G) confirm the greater stability of this complex compared with the β-phenylethyl cation[172] (see Refs 259, 260).

The evaluation of the relative proportions of σ- and π-complexes for the model structures **103** and **104** (Scheme 14) is complicated by the presence of isomeric ions of the benzyl type (**106**). In fact, the ionisation of 2-chloro-3-

Scheme 14



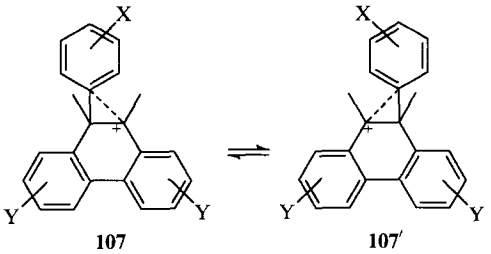
103 **104** **105** **105′** **106**

(*p*-methoxyphenyl)butane in the $HF-SbF_5-SO_2FCl$ system at −78°C affords exclusively 2-(*p*-methoxyphenyl)-2-butyl cations.[261] A similar picture has been observed for 2-chloro-3-phenylbutane.[261] According to the interpretation of Olah et al.,[261] during ionisation of 2-chloro-3-phenyl-2,3-dimethylbutane under these conditions, an equilibrium mixture is formed consisting of an ion of the benzyl type (**104**) and asymmetric π-bridged cations **105** and **105′** that undergo very rapid degenerate rearrangement (see Scheme 14) ($\Delta G^{\neq} < 5$ kcal mol^{-1}). Similarly, ions with substituents X = CF_3, Me, ($R^1 = R^2 = R^3 = R^4$ = Me) are considered to be asymmetric π-bridged structures (**105** and **105′**) existing in a rapid equilibrium with the isomers **104**,[261] (see Ref. 262). The presence of more effective electron-donating substituents X in the phenyl ring (X = MeO) produces the ion **104** of the benzyl type in the SbF_5-SO_2ClF acid system (X = MeO, $R^1 = R^2 = R^3 = R^4$ = Me).[261]

Among the transformations of ions of type **103–106** considered above, the 'extra fast' interconversion of ions **105** ⇄ **105′** is of special interest. The possibility of interaction of the aromatic ring with a carbocationic centre has been shown in a study of the donor-acceptor interaction in 9-(*p*-X-phenyl)-9,10-dimethylphenanthrenium ions (**58**)[263] as well as in 2,7- and 3,6-substituted 9-phenyl-9,10-dimethylphenanthrenium[264] ions. However, the energy of this interaction in the ground state is small, as shown by the low sensitivity of the chemical shift of the C atom carbocationic centre to the effects of substituents X in the XC_6H_4 group[265] and also by the fact that the activation free energies of the rotation barriers of XC_6H_4 groups for substituents with different types of electronic affect (X = Me, Cl, CF_3; $\Delta G^{\neq}_{-100\,°C} = 8.5 \pm 0.1$ kcal mol^{-1}) coincide.[263] The facts that the chemical shifts of the C atoms — carbocationic centres — in 2,7- and 3,6-di-Y-9-R-9,10-dimethylphenanthrenium ions (R = Ph, Me) are close to each other and the difference between them is approximately constant (3–4 ppm) are in agreement with this assumption[102,264] (see Ref. 266).

Although the donor-acceptor interaction in the ground state is weak, the degenerate rearrangements of type **107** ions mentioned above (Scheme 15) can also be considered to be interconversions of asymmetric π-complexes.

Scheme 15



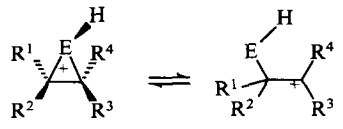
107 **107′**

It is reasonable to assume that owing to the increase in the positive charge on the carbocationic centre on going from ions **107** of the phenanthrene series to cations **105** of the β-arylethyl type, the extent of the donor-acceptor interaction in the ground state increases. This has been confirmed by ab initio calculations, according to which the 3-phenyl-2,3-dimethyl-2-butyl cation has a very distorted geometric structure with an unusually small C(2)–C_{ipso} distance (1.925 Å).[178]

In conformity with the kinetic scale of the relative stabilities of σ- and π-complexes (see Table 6), the migrants EH incorporating Group VI elements E (Scheme 16) show a pronounced tendency to form bridged structures. In the gaseous phase, π-complexes **108a,b** are more stable than isomeric σ-complexes **109a,b**, which is consistent with the data of quantum-chemical calculations (see Table 6).

A number of π-complexes (**108b–e**) have been generated in superacid systems at low temperatures. The oxygen-containing complexes **108c,e** were shown to be converted into the corresponding protonated aldehydes on raising the temperature, apparently via the isomeric σ-complexes **109c,e**.[267] The

Scheme 16



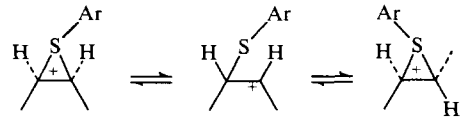
108a–k **109a–k**

	E	R^1	R^2	R^3	R^4
a	O	H	H	H	H
b	S	H	H	H	H
c	O	H	H	H	Me
d	S	H	H	H	Me
e	O	H	H	Me	Me
f	O	H	Me	Me	H
g	O	Me	Me	Me	Me
h	S	Me	Me	Me	Me
i	S	H	Bu^t	H	Bu^t
j	S	Bu^t	H	H	Bu^t
k	S	H	Bu^t	Bu^t	H

authors cited were not able to isolate the π-complexes **108f,g** with a symmetrical arrangement of R^1-R^4 substituents in the individual state under the conditions studied, since these complexes were rapidly converted into the corresponding protonated ketones.[267] This indirectly indicates that the interconversion of σ- and π-complexes **108f,g** ⇄ **109f,g** occurs readily. The analogous sulfur-centred π-complexes **108** are probably more stable than the corresponding isomeric σ-complexes (see Refs 267, 268). This is shown, in particular, by the fact that the ^1H NMR spectra of solutions of salts of π-complexes **108h,j,k** and **108i** are invariably in the temperature ranges from −50 to −80 °C and from 20 to −110 °C, respectively.[268]

There is little information concerning the interconversion of episulfonium ions and of the σ-complexes isomeric to them (see Refs 269, 270). For example, Vorob'eva et al.[271] discovered interconversion of π-complexes **110a** or **112a** kept in CH_2Cl_2 solutions at ambient temperature for ~1 h, which obviously proceeds via opening of the bridge and formation of the σ-complex **111a** as an intermediate (π,σ-rearrangement) (Scheme 17).

Scheme 17



110a,b **111a,b** **112a,b**

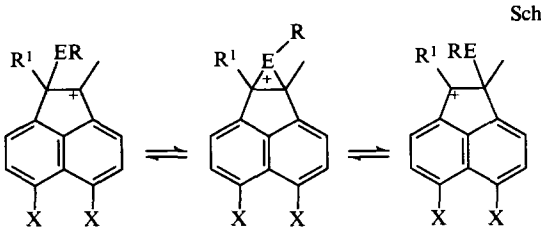
Ar = 2,4-$(O_2N)_2C_6H_3$ (**a**), 4-ClC_6H_4 (**b**).

The cleavage of the episulfonium ring is more difficult for ArS groups containing less electronegative substituents in the aromatic ring. For example, in the case where Ar is *p*-ClC_6H_4, more prolonged storage at ambient temperature (up to 24 h) is required to detect the interconversion shown in Scheme 17. This is probably caused by the fact that the stability of the π-complex relative to that of the σ-complex increases with decrease in the electron-withdrawing ability of the Ar groups.

Borodkin et al.[272] discovered a unique example of interconversion of the episulfonium ion **113f** and of the σ-complexes **114f** and **115f** isomeric to it (Scheme 18, see over).

The extremely high rate of the **113f** ⇄ **115f** interconversion even at −120 °C ($k_{114f \to 113f} \geq 10^8$ s^{-1})[273] implies easy cleavage of the episulfonium rings in the corresponding π-complexes. A similar σ,π-rearrangement has been found for selenium-centred ions at −80 °C: **113n** ⇄ **115n** ($k \geq 10^7$ s^{-1}).[274] The equilibrium between the σ- and π-complexes, **113** ⇄ **115**, is appreciably influenced by the nature of the substituents R, R^1, and X and the element E.[273–275] Analysis of these data resorting to those reported for 1-OR-1,2-dimethylacenaphthylenium ions[130] allowed Borodkin et al.[273–275] to draw the following conclusions:

Scheme 18



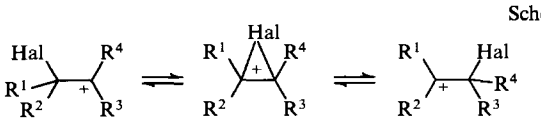
114a–s **113a–s** **115a–s**

	E	R	R^1	X
a	S	Me	Me	H
b	S	Me	CD_3	H
c	S	Ph	Me	H
d	S	Ph	CD_3	H
e	S	Ph	CH_2Cl	H
f	S	C_6F_5	Me	H
g	S	C_6F_5	CD_3	H
h	S	C_6F_5	CH_2Cl	H
i	S	C_6F_5	Me	Br
j	S	C_6F_5	Me	Me
k	S	C_6F_5	CH_2D	Me
l	Se	Ph	Me	H
m	Se	Ph	CD_3	H
n	Se	C_6F_5	Me	H
o	Se	C_6F_5	CD_3	H
p	Se	Ph	CH_2Cl	H
q	Se	Ph	CH_2Cl	H
r	Se	C_6F_5	Me	Me
s	Se	C_6F_5	CH_2D	Me

the proportion of the cationic π-complexes **113** in the equilibrium (see Scheme 18) increases with increase in the electron-donating properties of substituents R and R^1, with increase in the atomic number of the central element, and with diminution of the electron-donating properties of the substituents X. Using the **113f** ⇄ **115f** interconversion of the ions as an example, the authors cited showed that equilibria between cationic σ- and π-complexes with π-electron delocalisation in the ion core are not very sensitive to the effects of the medium.[275,276]

According to the kinetic scale of relative stabilities of σ- and π-complexes (see Table 6), the tendency to form bridged ions in the case of the halogen-centred complexes **116–118** (Scheme 19) should increase in the following sequence: F < Cl < Br < I.

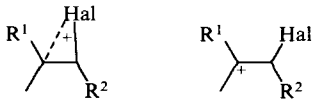
Scheme 19



116a–m **117a–m** **118a–m**

	Hal	R^1	R^2	R^3	R^4
a	Cl	H	H	H	H
b	Cl	Me	Me	Me	Me
c	Br	H	H	H	H
d	Br	Me	H	H	H
e	Br	Me	Me	H	H
f	Br	Me	H	Me	H
g	Br	H	Me	Me	H
h	Br	Me	Me	Me	H
i	Br	Me	Me	Me	Me
j	I	H	H	H	H
k	I	Me	H	Me	H
l	I	H	Me	Me	H
m	I	Me	Me	Me	Me

This is supported by the results of quantum-chemical calculations (see Table 6) and also by the ^1H and ^{13}C NMR spectroscopy data for the ions **116–118**.[2] The influence of substituents has been considered in a general form.[2] The vast majority of the spectral data can be accounted for by assuming the existence of static σ- and π-complexes, however some cases do not fit this concept. Indeed, it is difficult to explain large differences between the chemical shifts of C(1) and C(2) atoms for 1-methyl- and 1,1-dimethylethylenebromonium ions by the presence of symmetrical π-complexes of type **117**. As suggested,[2] this indicates either the formation of asymmetric π-complexes **119a,b** or rapid interconversion of these π-complexes and the corresponding σ-complexes **120a,b**.



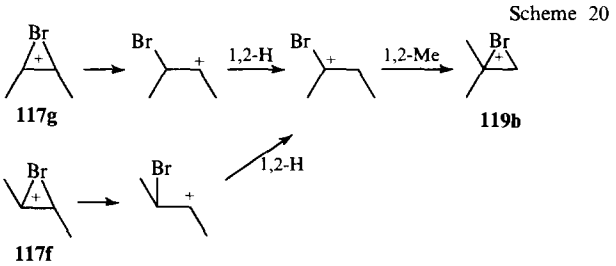
119a–d **120a–d**

	Hal	R^1	R^2
a	Br	H	H
b	Br	Me	H
c	Br	Me	Me
d	Cl	Me	H

This suggestion is supported by the substantial temperature dependence of the chemical shifts of the C(1), C(2) atoms in 1,1-dimethylethylenebromonium ion.[2] A similar interconversion of an asymmetric π-complex and a σ-complex has been suggested in the case of Hal = Br, R^1 = R^2 = Me (**119c** ⇄ **120c**). It is noteworthy that at Hal = Cl, R^1 = Me, R^2 = H, the σ-complex **120d** is more stable than the isomeric π-complex.[2]

The most probable structures for symmetrically substituted halogenonium ions must be either static symmetrical π-complexes of type **117** or σ-complexes **116**, **118** existing in a dynamic equilibrium with one another. Judging by the ^1H and ^{13}C NMR spectra, *cis*- and *trans*-2,3-dimethylethylenebromonium ions resulting from the action of SbF_5 on *meso*- or *d,l*-dibromobutanes in SO_2 do not undergo rapid interconversion on the NMR time scale. This allowed Olah et al.[2] to assign these structures to π-complexes. A similar situation occurs in the case of 1,2-dimethylethyleneiodonium ion in which the *cis* : *trans* ratio depends on the precursor used to generate the geometric isomers of the ion in a superacid medium.[2] Nevertheless, the π-complexes **117g** and **117f** are slowly converted at −40 °C into the complex **119b**, apparently, according to Scheme 20:[2]

Scheme 20



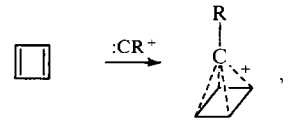
This confirms to the easy cleavage of the bromonium ring in these complexes.

An analysis of the ^{13}C NMR spectra of the tetramethylethylenebromonium ion led Olah et al.[2] to the conclusion that these spectra are inconsistent with a π-complex like **117** or the rapid **116** ⇄ **118** interconversion of σ-complexes. The interconversion of both forms of complexes according to Scheme 19[2,277] is the most likely. However, judging by the small value of isotopic perturbation, (δ = 1.81 ppm),[230] the proportion of σ-complexes **116** and **118** equilibrium with the π-complex **117** is very low.

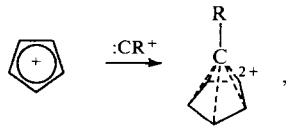
V. π,π-Rearrangements

Carbocations are frequently regarded as a connecting link between organic and organometallic chemistry.[45,278,279] Typical objects for investigation in the latter are π-complexes with multicentre metal-ligand bonds. These bonds are also found in carbocations. 'Long-lived' pyramidal carbocations (π-complexes) in which the coordination number of the carbon atoms can be 5 or more can serve as an example. These π-complexes may be formally regarded as resulting from the interaction of a $:CR^+$ fragment with antiaromatic or other four-electron systems (Scheme 21):[279]

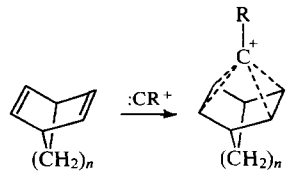
Scheme 21



121



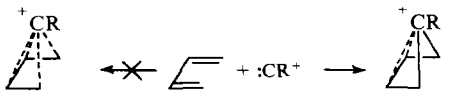
122



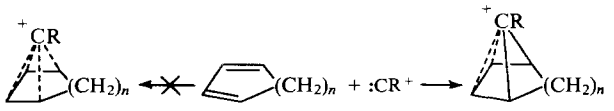
123

The main feature required for the formal construction of these systems from fragments is the similarity of the MO of these fragments as regards their symmetry.[45] If the four-electron component of the diene is not symmetrical, nonclassical ions of type **124a–c**, rather than pyramidal ions, are more stable (Scheme 22):[278,279]

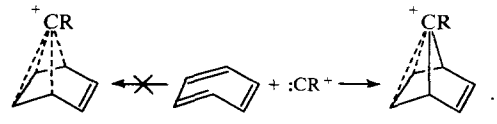
Scheme 22



124a



124b

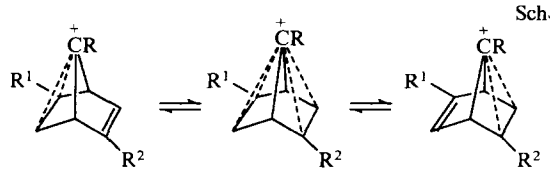


124c

Among the latter set of π-complexes, systems of type **124c** are the most interesting, since in these complexes there is a possibility that bonding of the CR^+ fragment 'switches' from one double bond to the other (π,π-rearrangement of the 'flipping' type[23,280]), in accordance to Scheme 23.

The apical atom in structures **126** has 10 electrons, two of which are located in an antibonding MO, which results in destabilisation of this structure.[45] According to MINDO/2 calculations,[281] the symmetrical structure **126a** corresponds to the transition state rather than to an intermediate state, the energy barrier to the π,π-rearrangement **125a** ⇄ **125'a** being rather high (26 kcal mol^{-1}). The theoretical data have been confirmed experimentally[280,282] (see Ref. 283).

Scheme 23



125a–h **126a–h** **125'a–h**

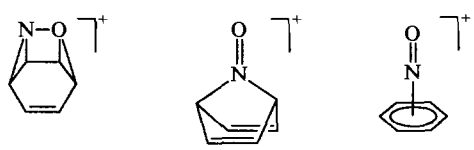
	R	R^1	R^2
a	H	H	H
b	Me	H	H
c	Ph	H	H
d	$HC=CH_2$	H	H
e	OH	H	H
f	OMe	H	H
g	H	Me	H
h	H	H	Me

A kinetic study of the rearrangement of the π-complex **125a** (see Scheme 23) by the radioactive tracer method made it possible to determine the lower limit of the free energy of activation ($\geq$19.6 kcal mol^{-1}).[280] High barriers to π,π-rearrangements are also characteristic of π-complexes **125g** and **125h** (>22.1 kcal mol^{-1} and > 16.6 kcal mol^{-1}, respectively).[280] The introduction in position 7 of a methyl group (π-complex **125b**) leads to a decrease in the activation free energy ($\Delta G^{\neq}_{-14\,°C}$ = 12.4 kcal mol^{-1}),[280] which is obviously due to the larger stabilising effect of this group in the transition state of type **126** compared with that in the ground state. This distinction is probably caused by the greater fraction of the positive charge on the C(7) atom in the symmetrical structure **126**, since, as was mentioned above, the simultaneous interaction of the two double bonds with this atom is unfavourable.

In the case where $R^1 = R^2 = H$ and R = Ph or $CH=CH_2$ rapid interconversion of π-complexes **125** ⇄ **125'** ($\Delta G^{\neq} < 5.2$ and < 8.2 kcal mol^{-1}, respectively) is more likely, whereas the presence in position 7 of a methoxy group having more pronounced electron-donating properties probably results in the formation of the symmetrical π-complex **126f**.[280,284] The latter is consistent with the results of a study of the basicities of 7-substituted norbornene derivatives, where it was shown that the introduction of an OH group in position seven of the 7-norborn-2-enyl cation removes the non-vertical interaction of the carbocationic centre with the double bond.[285]

To draw a parallel between the properties of carbocations and those of organometallic compounds, let us turn our attention to the rearrangements consisting in the migration of a π-bound fragment over a cyclic or open conjugated system. These rearrangements are rather typical of organometallic compounds (see, for example, Ref. 286), however, there is little information on these rearrangements in π-complexes derived from normal (not metal-centred) electrophilic reagents and unsaturated compounds.

Minkin et al.[287] have reported the results of MINDO/3 calculations of the structures of complexes derived from one of the classical electrophilic reagents, i.e. the nitrosonium cation, and benzene, indicating that minima on the potential energy surface correspond to π-complexes **127** and **128**, whereas the top of the hill corresponds to the centrally symmetrical π-complex **129** (see, however, Ref. 288).

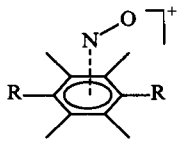


127 **128** **129**

The symmetry of π-complexes **127** and **128** was found to be substantially lower than could have been expected for the gaseous

phase and the solution.[289,290] In the latter case, in view of the isochronism of the protons of the aromatic ring in the ^{1}H NMR spectrum, the centrally symmetrical π-complex structure **129** was attributed to the complex. Although the π-complexes **127** and **128** possess much lower symmetries than the C_{6v} symmetry detected by NMR, this contradiction was eliminated by quantum-chemical calculations which showed that the complexes **127** and **128** can undergo a rapid degenerate rearrangement (with a barrier of < 3 kcal mol^{-1}) through 'sliding' of the NO group over the aromatic ring plane with 'switching' of the C–N bonds.[287]

Recent X-ray structural studies of π-complexes formed from durene[291] or hexamethylbenzene[291] (see Ref. 292) with the nitrosonium cation (with the $AlCl_4^-$ anion) have shown that the traditional view (see Refs 289, 290) that π-complexes of aromatic compounds with electrophilic reagents are highly symmetrical systems should be reconsidered.[47] It was found that the NO group in these complexes is displaced from the centre of the aromatic ring [towards two (2η) or three (3η) carbon atoms] and is arranged at an angle of ~50° with respect to the plane of the ring.



R = H (**130**), Me (**131**)

According to CNDO/2 calculations carried out using the real geometry of the complex **131**, the values of the positive charge on the basal C atoms of the aromatic ring (and on the methyl groups) are appreciably different.[291] Nevertheless, the ^{13}C NMR spectra recorded both for the liquid (HSO_3F–SO_2ClF, −130 °C)[293] and for the solid state (CPMAS spectra)[291] exhibit only two rather narrow singlets. This may be explained by the degenerate π,π-rearrangement of the complex occurring rapidly on the NMR time scale as 'sliding' of the NO group over the plane of the ring or as the rotation of this ring, about a normal to it, involving 'switching' of the C_{arom}–N bonds, and in the crystalline state the latter mechanism is the more likely.

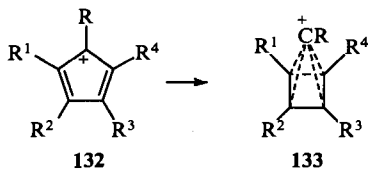
Mefed et al.[293] have studied a polycrystalline specimen of tetrachloroaluminate of complex **131** by relaxation NMR spectroscopy and determined the kinetic parameters of this rearrangement ($E_a = 10.2 \pm 0.6$ kcal mol^{-1}, $\lg A = 13.9 \pm 0.1$ kcal mol^{-1}). As shown by calculations of atomic interactions, the rotation of the hexamethylbenzene ring in the crystalline state should occur more easily ($E_a < 1$ kcal mol^{-1}) than that of the NO group, the latter being tightly clamped by the environment (20 or 150 kcal mol^{-1} depending on the direction of the rotation).

Judging by the NMR spectra, analogous rearrangements via 'sliding' of the NO^+ group over the aromatic ring are also realised in the case of complexes formed from nitrosonium cation and other alkyl-substituted benzene derivatives[292, 294] (see Ref. 295), fluorene,[296] and methyl-substituted naphthalenes.[297,298]

VI. On the possibility of 2-σ,π-rearrangements

The pyramidal cations like **133** can formally result from the rearrangement of cations **132** (Scheme 24) that consists in the cleavage of two σ-bonds to yield a conjugated cyclic π-system reacting with the apical :CR$^+$ fragment (2-σ,π-rearrangement (see Ref. 26).

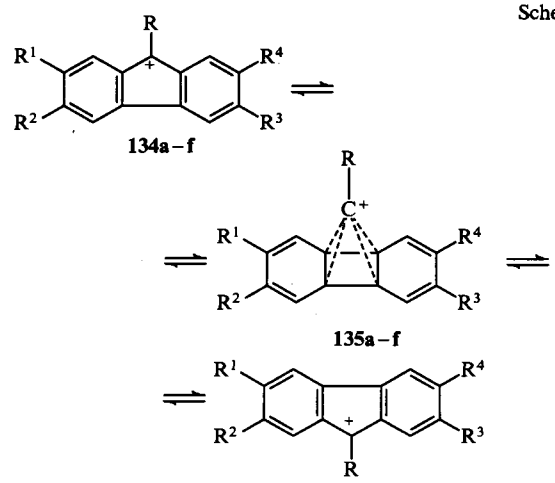
Scheme 24



132 **133**

The possibility of these rearrangements has been verified[299] experimentally for substituted fluorenyl cations **134** (Scheme 25).

Scheme 25



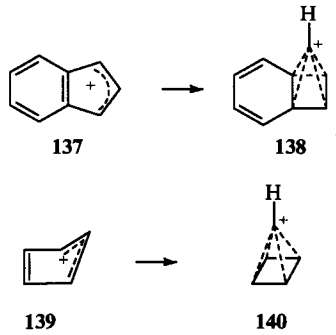
134a–f **135a–f** **136a–f**

	R	R^1	R^2	R^3	R^4
a	Me	D	H	H	H
b	Me	H	D	H	H
c	Me	H	Me	H	H
d	Me	Me	H	H	Me
e	Me	H	Me	Me	H
f	Me	Me	H	Me	H

It was found that the ion **134a** generated in the HSO_3F–SO_2ClF system is not converted into the cation **136b** at −78 °C. Similarly, no 2-σ,π-rearrangement shown in Scheme 25 proceeds in the case of the methyl-substituted fluorenyl ions **134c–f** up to 25°C.

Previously it had been shown that the 9-methyl- and 9-ethylfluorenyl cations are static on the ^{1}H NMR time scale up to −10°C.[194]

The possibility of the degenerate rearrangement of the fluorenyl cation in conformity with Scheme 25 has been studied by MINDO/3.[299] The energy of the pyramidal structure of type **135** was found to be 73.0 kcal mol^{-1} greater than that of the fluorenyl ion. However, the removal of benzoannelation leads to a decrease in the barrier.



137 **138**

139 **140**

Cation	**137**	**138**	**139**	**140**
ΔH_f/kcal mol^{-1}	247.8	296.9	255.3	269.7
	$\Delta\Delta H_f$ = 49.1		$\Delta\Delta H_f$ = 14.4	

The electronic structure of the fluorenyl ions **134** does not correspond to the ion **139**, but is more in agreement with the structure **141**.[299]



141 **140** **139**

We should note that the thermal rearrangement **139** → **140** is symmetry allowed, whereas the transformation **141** → **140** is a disallowed process.[299]

* * *

Thus, the cationic σ,σ-rearrangements have been most extensively studied to date. The σ,π- and π,π-rearrangements still remain poorly investigated. This reflects the fact that in general the chemistry of 'long-lived' π-complexes derived from ordinary electrophilic reagents and unsaturated systems lags behind the chemistry of σ-complexes. However, the number of studies of the structures and dynamics of π-complexes is rapidly increasing. This is because of the need to extend and deepen our theoretical views of the processes involving cationic π-complexes as well as to use the knowledge of their properties for developing methods of controlling organic reactions.

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Complex formation processes in 3*d* metal hexacyanoferrate(II) gelatin-immobilised matrices

O V Mikhailov

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Abstract. Data on nontraditional complex formation reactions in iron(II, III), cobalt(II), cobalt(III), nickel(II), and copper(II) hexacyanoferrate(II) gelatin-immobilised matrices with fixation of the immobilised substances by intermolecular forces are surveyed and described systematically. Such reactions proceed when the matrices come into contact with aqueous solutions of nitrogen-, oxygen-, and sulfur-containing polydentate ligands. The practical possibilities for complex formation reactions in metal hexacyanoferrate(II) gelatin-immobilised matrices are demonstrated. The bibliography includes 147 references.

I. Introduction

Investigators in the field of coordination chemistry have shown in recent years an increased interest in metal–ion ligand systems in which the initial complex formation conditions differ significantly from those in solutions and in the solid phase. One of the most promising aspects is the study of complex formation in the so called metal-containing immobilised matrix systems where the initial chemical compounds and the products formed in the process are more or less rigidly fixed in the bulk of a polymer. Theoretically it is possible to represent two types of immobilisation of the substance: via the functional groups of the polymer or as a result of the operation of intermolecular forces.

In the former case, the corresponding polymers must contain structural fragments capable of binding the metal ions chemically to the polymer; the type of the metal–polymer bonds formed under these conditions (ionic, covalent, etc. bonds) is determined exclusively by the nature of the reactants.[1]

The second version presupposes a kind of 'fixation' of the immobilised substance as a result of dispersion, orientation, inductive, and other similar types of interaction. The 'fixation' requires only the presence of a large surface of the polymer. This type of immobilisation can be achieved via operations such as dispersion, adsorption, or precipitation of the substance in the polymer layer, sputtering, impregnation etc.[1]

O V Mikhailov Kazan State Technological University, ul. K. Marksa 68, 420015 Kazan, Russian Federation. Fax (7-843) 276 54 03

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Naturally, there is also the possibility of an intermediate version where the 'fixation' as a result of the above types of interaction is accompanied also by the formation of fairly strong chemical bonds between the metal ions and the polymer molecules. The preparation of immobilised matrix systems of the first of the above types has promoted progress primarily in the field of metal complex catalysis; two parallel scientific fields began to develop simultaneously in this direction — immobilisation of coordination compounds on inorganic and organic bulk phase polymers.[1–5] Metal complex catalysis and organic synthetic reactions on polymer supports closely related to it[6–9] remain the main 'users' of the immobilised metal-containing matrix systems,[3] although to be fair one has to note that the range of their applications and their potential possibilities are much greater.[10–19] The extensive use of such systems has stimulated a series of specialised conferences during the last decade on problems of the synthesis and application of immobilised matrix systems.[20–23] The proceedings of these scientific forums constitute the contents of special issues of journals such as the *Journal of Molecular Catalysis* [**11**, 1, 2 (1981)] and the *British Polymer Journal* [**16**, 4 (1984)].

Analysis of the literature data makes it possible to claim that on the whole the immobilised matrix systems of the first type and the complex formation processes in them have by now been already fairly well investigated; at any rate, a whole series of monographs and review articles have been devoted to them and a list of these may be found, in particular, in Pomogailo's book.[1] On the other hand, complex formation in metal-containing immobilised matrices with fixation of the substance by intermolecular forces as well as the matrix systems themselves have not so far attracted any serious attention by investigators. The aim of the present review is to fill the existing gap to some extent.

II. Metal hexacyanoferrate(II) gelatin-immobilised matrices

The nature of both the polymer binder (which may influence significantly the selectivity of the complex formation reaction and the morphology of the reaction products) and of the immobilised chemical compound itself is of fundamental importance for the achievement and subsequent investigation of complex formation under the specific conditions created when chemical reactions take place in immobilised metal-containing matrices, where the substance is attached via intermolecular forces. The screening

which we carried out of natural and synthetic polymers in the immobilised substances showed that a low-molecular-mass polypeptide, namely gelatin, which is distinguished by the isotropic nature of its physicomechanical characteristics, transparency, hydrophilicity, and plasticity, is most suitable for the solution of the above problem. Among immobilised substances, preference should be given to 3*d* metal hexacyanoferrates(II) (MHCF), which successfully combine rigidity of attachment to the polymer, optimum kinetic lability, stability, and extremely low solubility in water.[24] Typical examples of such matrix systems are hexacyanoferrate(II) gelatin-immobilised matrices (MHCF-GIM), where iron(III), cobalt(II, III), nickel(II), and copper(II) hexacyanoferrates(II) are most often employed. In such matrices, the complex formation reactions take place as a result of the contact between the matrices and aqueous solutions of chelating ligands.[25]

1. Synthesis and structure

Despite its apparent simplicity, the synthesis of the MHCF-GIM is a specific and fairly laborious process.[24] Silver halide gelatin-immobilised matrices (AgHal-GIM), which are none other than the photosensitive emulsions in modern photographic materials, serve as a convenient starting material. Such matrices can be transformed fairly readily into silver-containing GIM, since the size of the silver particles is comparable to that of large clusters. For this purpose, one can employ the development and subsequent fixation processes well known in chemical photographic science and practice.[26-28] In its turn, it is possible to obtain from the silver-containing GIM, by means of specific chemical reactions, immobilised matrix systems with a very wide assortment of metal-containing compounds, retaining at the same time the quasi-molecular dispersity level of their particles which has been achieved for silver-containing GIM. The synthesis of the MHCF-GIM with iron(III), nickel(III), and copper(II) metal ions from the initial silver-containing GIM is carried out in two stages.[25,29-31]

In the first stage, the matrix is treated with a solution containing potassium hexacyanoferrate(III) and the oxalate, citrate, or tartrate complex of the corresponding 3*d* metal ion, as well as an agent for the establishment of the optimum pH in the precipitation of the target metal hexacyanoferrate(II). As a result, MHCF containing the given ion and silver(I) hexacyanoferrate(II) or other silver(I) compounds still less soluble in water, in particular AgCl or AgBr, are precipitated in the gelatin layer of the photographic material.

In the second stage, the GIM obtained are treated with an aqueous solution of sodium thiosulfate, as a result of which $Ag_4[Fe(CN)_6]$ or AgHal is transformed into the readily water-soluble compound $Na_3[Ag(S_2O_3)_2]$, which is removed from the bulk of the polymer to the solution. On decomposition of the polymeric binder in the resulting metal-containing GIM by protolytic enzymes, the complexes $KFe[Fe(CN)_6]$, $Ni_2[Fe(CN)_6]$, and $Cu_2[Fe(CN)_6]$ can be isolated from these matrices.[24] Bearing in mind the factors noted above as well as data on the compositions of the oxalate, citrate, and tartrate complexes of the corresponding 3*d* elements,[32-34] the transformation of the silver-containing GIM into the target iron(III), nickel(II), and copper(II) hexacyanoferrate(II)-GIM can be described with the aid of the following reactions[35]

$$\{2\,AgHal\} + HO\text{-}C_6H_4\text{-}OH + 2\,OH^- \longrightarrow \{2\,Ag\} + HO\text{-}C_6H_4\text{=O} + 2\,Hal^- + H_2O, \quad (1)$$

$$\{Ag + AgHal\} + 2S_2SO_3^{2-} \longrightarrow \{Ag\} + Ag(S_2O_3)_2]^{3-} + Hal^-, \quad (2)$$

$$2Fe_2(HCt)(HTr) + 4\{Ag\} + 4[Fe(CN)_6]^{3-} + 3K^+ \longrightarrow \{3KFe[Fe(CN)_6] + Ag_4[Fe(CN)_6]\} + 2HCt^{3-} + [Fe(HTr)_2]^{3-}, \quad (3)$$

$$\{3KFe[Fe(CN)_6] + Ag_4[Fe(CN)_6]\} + 8S_2O_3^{2-} \longrightarrow \{3KFe[Fe(CN)_6]\} + 4[Ag(S_2O_3)_2]^{3-} + [Fe(CN)_6]^{4-}, \quad (4)$$

$$6[Ni(HCt)_3]^{7-} + \{Ag\} + 4[Fe(CN)_6]^{3-} + 4Cl^- \longrightarrow \{3Ni_2[Fe(CN)_6] + 4AgCl\} + [Fe(CN)_6]^{4-} + 18HCt^{3-}, \quad (5)$$

$$\{3Ni_2[Fe(CN)_6] + 4AgCl\} + 8S_2O_3^{3-} \longrightarrow \{3Ni_2[Fe(CN)_6]\} + 4Ag(S_2O_3)_2]^{3-} + 4Cl^-, \quad (6)$$

$$6[Cu(Ox)_2]^{2-} + 4\{Ag\} + 4[Fe(CN)_6]^{2-} \longrightarrow \{3Cu_2[Fe(CN)_6] + Ag_4[Fe(CN)_6]\} + 12Ox^{2-}, \quad (7)$$

$$\{3Cu_2[Fe(CN)_6] + Ag_4[Fe(CN)_6]\} + 8S_2O_3^{2-} \longrightarrow \{3Cu_2[Fe(CN)_6]\} + 4[Ag(S_2O_3)_2]^{3-} + [Fe(CN)_6]^{4-}, \quad (8)$$

where H_2Ox, H_4Ct, and H_4Tr are oxalic, citric, and tartaric acids respectively, the immobilised chemical compounds being indicated in braces.

The synthesis of the cobalt(II) hexacyanoferrate(II)-GIM is more complex and includes three stages:[35-37]

$$4\{Ag\} + 4[Fe(CN)_6]^{3-} \longrightarrow \{Ag_4[Fe(CN)_6]\} + 3[Fe(CN)_6]^{4-}, \quad (9)$$

$$\{Ag_4[Fe(CN)_6]\} + 2CoCl_2 \longrightarrow \{Co_2[Fe(CN)_6] + 4AgCl\}, \quad (10)$$

$$\{Co_2[Fe(CN)_6] + 4AgCl\} + 8S_2O_3^{2-} \longrightarrow \{Co_2[Fe(CN)_6]\} + 4[Ag(S_2O_3)_2]^{3-} + 4Cl^-. \quad (11)$$

As regards cobalt(III) hexacyanoferrate(II) matrices, the nature of the immobilised substance contained in them still cannot be regarded as finally established. It has been suggested that the compound present in the GIM is the simple cobalt(III) hexacyanoferrate(II) $Co_4[Fe(CN)_6]_3$,[24,35,38] but the latest data indicate that $KCo[Fe(CN)_6]$ should be regarded as a more probable compound. This compound is diamagnetic,[24] which indicates the presence in the latter of Fe(II) and Co(III) ions in an octahedral environment of CN-ligands with O_h symmetry. This complex should be considered as a kind of intermediate between $KCo^{III}[Fe^{II}(CN)_6]$ and $KFe^{II}[Co^{III}(CN)_6]$. Like the $KFe[Fe(CN)_6]$, $Ni_2[Fe(CN)_6]$ or $Cu_2[Fe(CN)_6]$-GIM, the KCo.[Fe(CN)$_6$]-containing GIM may be synthesised from silver-containing gelatin-immobilised matrices in a two-stage treatment in accordance with the equations

$$3[Co(HCt)_2]^{3-} + 4\{Ag\} + 4[Fe(CN)_6]^{3-} + 4Cl^- + 3K^+ \longrightarrow \{3KCo[Fe(CN)_6] + 4AgCl\} + 6HCt^{3-} + [Fe(CN)_6]^{4-}, \quad (12)$$

$$\{3KCo[Fe(CN)_6] + 4AgCl\} + 8S_2O_3^{2-} \longrightarrow \{3KCo[Fe(CN)_6]\} + 4[Ag(S_2O_3)_2]^{3-} + 4Cl^-. \quad (13)$$

The technological processes involving the preparation of the target MHCF-GIM and the compositions of the solutions with which the system was treated in each of the stages have been described in detail.[39-84]

It is known that, in terms of its chemical nature, gelatin is a polydisperse mixture of low-molecular-mass polypeptides ($M = 50\,000 - 70\,000$) and their aggregates ($M = 200\,000 - 300\,000$).[27,28,85,86] According to the literature,[87,88] gelatin molecules consist of three α-type polypeptide chains with almost identical molecular masses, two α-chains being usually almost identical as regards the set and sequence of the aminoacids (α1-chains), while the third (the α2-chain) differs in this respect from the other two. A structure has been proposed for such molecules,[89,90] in which a left-handed helical structure of the α-type was attributed to each polypeptide chain. Within the framework of such a structure, all three helices are 'plaited' with one another to form a single 'right-handed' helix, hydrogen bonds playing a significant role in the stabilisation, as was to be expected.[87] The α2-chains are characterised overall by the same set of polypeptide fragments as the α1-chains, but their aminoacid sequence contains fewer aminoacids such as proline, hydroxyproline, and lysine, the predominating aminoacids being tyrosine, valine, leucine, isoleucine, histidine, and hydroxylysine.[28]

The sequence of the peptide fragments in the α1-chains with more than 700 aminoacid residues has now been fully elucidated.[27,28] It is of interest that, in contrast to other proteins, where no common features in the alternation of the aminoacids in the peptide fragments have been found, in gelatin, starting with the 17th residue, glycine invariably occupies each third position, so that the overall formula of the polypeptide units in the α1-chain can be written in the form Gly–X–Y, where Gly = glycine, while X and Y are other aminoacid residues. The glycine–proline–hydroxyproline combination is most frequently encountered.[27] The sequence of the aminoacid residues in the α2-chain has still not been accurately established.[28]

Like other proteins, gelatin is an ampholyte because it includes 'free' acid and basic groups (i.e. groups which can be titrated in aqueous solution) such as the β-carboxy-group of aspartic acid, the β-carboxy-group of glutamic acid, the β-imidazolyl group of histidine, the ε-amino-group of lysine, the δ-guanidino-group of arginine, and the phenolic hydroxy-group of tyrosine.[27,28] Their nitrogen and oxygen atoms can play the role of donor centres in relation to various *d* element ions, but, overall, gelatin is a fairly weak complex-forming agent.[27,28]

The present author's electron microscope studies of the MHCF-GIM classified above have shown that all these matrices are transparent to the electron flux and hence the particles of the immobilised MHCF attain a quasi-molecular level of dispersity. They can therefore be regarded as coordination polymers with a relatively low molecular mass and a fairly regular structure, being located in the cavities between the polypeptide units of the gelatin molecules.[35] Such polymers have a face-centred lattice with the *Fm*3 or the *Fm*3*m* symmetry space group and unit cell dimensions of 9.93 Å (Co), 10.18 Å (Ni), and 10.03 Å (Cu).[91] The coordination number (C. N.) of Fe(II) is 6 and an octahedral envirnonment comprising the CN-groups is characteristic of this ion. The ions of the other 3*d* element in the MHCF have coordination numbers of 4 and 6 (tetrahedral and octahedral environments).

Quantum-chemical calculations for the CN^- ions have shown that the electron density on the carbon atom is almost three times greater than on the nitrogen atom,[92] so that the carbon atom is a harder donor centre than nitrogen. Since Fe(II) is a harder Pearson acid than Co(II), Ni(II), and Cu(II) (their orbital electronegativities in solution are +0.69, +0.52, +0.29, and −0.55 eV respectively)[93] and exhibit a lower affinity for nitrogen, the Fe–CN–M (M = Co, Ni, Cu) structural fragments are formed. Similar group of atoms arise also in the complex $KCo[Fe(CN)]$ or $Co_4[Fe(CN)]_3$ because the affinity of Co(III) for nitrogen is much higher than that of Fe(II), while the affinity of Fe(II) for carbon greatly exceeds the affinity of Co(III) for this element. Some of the iron atoms in $KFe[Fe(CN)]$ are coordinated via the carbon atom, whilst others are coordinated via the nitrogen atom, so that the Fe–CN–Fe groups are produced.[91] Thus, in all the MHCF coordination polymers considered here, iron is coordinated to the cyano-group via the carbon atom, whilst all other *d* elements are coordinated via the nitrogen atom.[92]

The elastic properties of bulk-phase gelatin resemble those of rubber; this is quite natural for infinite chains formed by long chains of molecules connected by a limited number of cross links.[94] This structure is potentially suitable for the formation of polymer-immobilised matrices because it does not permit the formation of any kind of rigid crystalline blocks and furthermore contains a fairly large number of cells for the reception and subsequent fixation of the molecules of the immobilised substance. When filled with the molecules of the corresponding chemical compund, these cells retain a certain freedom of migration in space. With a polymer of such a structure it is possible, in principle, to obtain immobilised matrices characterised by a fairly uniform distribution of the metal-containing substance in some part of the bulk-phase polymer. Furthermore, such matrices are sterically accessible for the occurrence of diverse chemical processes, in particular complex formation. Gelatin has an extremely high surface area and an extensive system of micropores, so that when it comes into contact with any kind of aqueous solution the permeation of both the solvent molecules and of the solute into the bulk-phase polymer is as a rule ensured comparatively readily.[27,28]

2. Specific features of the complex formation reactions

Taking into account the entire set of data concerning gelatin as a polymeric material and also the topography of the immobilised matrix system obtained on its basis, one can discern the following features of complex formation reactions occurring in these systems:[24,35] hindered contacts between the reactants; the presence of a charge on the polymer molecules in contact with the ligand solution because gelatin is an ampholyte; an extremely small reaction volume in which the complex formation process takes place; limited mobility of the complex-forming agent [i.e. of the immobilised metal hexacyanoferrate(II)]; a low rate of 'supply' of the ligand to the bulk-phase polymer; the nonequilibrium nature of the complex formation process.

The above factors make it possible to predict the preferential formation and accumulation in the GIM of the following coordination compounds which are not characteristic of complex formation in solution and in the solid phase:[24,35] intermediate complex forms, ligand-deficient complexes, coordination dimers and polymers, and chelates with a pronounced deficiency of protons. Complex formation in MHCF-GIM systems should therefore be regarded as a completely specific phenomenon in coordination chemistry, requiring for its description a model different from that of complex formation in solution and in the solid phase.

The methodological foundations of such a model have been considered.[95] Although all the MHCF-GIM–aqueous chelating ligand solution systems are typically heterogeneous, complex formation reactions in them can be regarded, to a satisfactory approximation, as quasi-homogeneous because they take place not at the solid–liquid (matrix–ligand solution) interface but in the bulk phase of the polymer.

The point is that, according to electron microscope data, the hexacyanoferrate(II) in the MHCF-GIM is present in the massive gelatin in the form of a layer 10–20 μm thick, above which there is a layer of gelatin with a thickness ranging from 2 to 15 μm.[35] On this basis, the MHCF-GIM can be regarded as the reaction microvolume present in the solid phase and in contact with the aqueous ligand solution, on the one hand, and as a kind of intermediate state between the solution and the solid phase, on the other. When this matrix comes into contact with an aqueous ligand solution capable of forming with the ion of the metal M

thermodynamically more stable coordination compounds of the hexacyanoferrate complex, the ligand, diffusing in the massive polymer, reacts with M and binds it in the corresponding chelate complex. On the other hand, the iron(II) in the metal hexacyanoferrate(II) coordination polymer is transformed into the kinetically extremely inert and thermodynamically stable anion $[Fe(CN)]^{4-}$, which passes from the MHCF-GIM to the solution in contact with it.

When Fe–CN–M (M = Fe, Co, Ni, Cu) groups are attacked by an alkaline solution of the ligand, their fate is determined by the ratio of the M–N and M–O bond energies. One may predict that, for $E_{M-N} > E_{M-O}$, the metal hexacyanoferrate(II) will prove resistant to the action of the OH^- ions present in the alkaline solutions of the ligands and will enter into a direct interaction with the corresponding ligand. For $E_{M-N} < E_{M-O}$, the M–N bonds will initially dissociate and will be replaced by the M–O bonds, so that the metal ion–ligand interaction in the MHCF-GIM will be preceded by the decomposition of the hexacyanoferrate(II) by the OH^- ions, which will be accompanied by the formation of coordination polymers of the corresponding oxides, oxide hydroxides, and hydroxides with O or OH bridging groups.[24] The version with $E_{M-N} > E_{M-O}$ occurs in the case of the $Ni_2[Fe(CN)]$ and KCo[Fe(CN)] matrices, while that with $E_{M-N} < E_{M-O}$ occurs in the case of KFe[Fe(CN)], $Co_2[Fe(CN)]$, and $Cu_2[Fe(CN)]$ matrices.

It may be expected that, in the first two matrices, interaction between the hexacyanoferrates(II) of the 3*d* elements and moderately soft and soft Pearson bases (the nitrogen-, nitrogen- and oxygen-, and nitrogen-containing ligands considered below are in fact of this kind) is accompanied by the dissociation of the M–NC bonds and the formation of stronger bonds between the metal and the donor centres of the ligand, the Fe–CN bonds being retained under these conditions. When the coordination number of Fe(II) in the structures of the hexacyanoferrates(II) of 3*d* elements is 6, there is no steric hindrance to the formation of the very stable inert anion $[Fe(CN)]^{4-}$ of configuration $t_{2g}(\pi^2_{d_{xy}}\pi^2_{d_{xz}}\pi^2_{d_{yz}})$ and ligand field stabilisation energy (LFSE) equal to $+24D_q$.[91,96] However, in the case of matrix systems with KFe[Fe(CN)], $Co_2[Fe(CN)]$, and $Cu_2[Fe(CN)]$, the hexacyanoferrates(II) interact with the OH^- ion, the process being accompanied by dissociation of M–NC bonds and formation of M–O bonds with retention of the Fe–CN bonds and hence the formation of the anion $[Fe(CN)]^{4-}$.[24,91]

Special studies by the present author showed that gelatin does not interact with any of the (N, O)-, (N, S)-, (O, S)-, and (S, S)-ligands or with any of the hexacyanoferrates(II) of 3*d* elements.[24,35,95,97,98] Furthermore, the complex formation products diffusing from the matrix to the solution also do not interact with any of these ligands or with gelatin. One can therefore claim that the solid–solution interface should not influence complex formation processes occurring in the GIM.[95] Previously it was mentioned that the substance contained in the MHCF-GIM is not located on the surface of the matrix and is not dispersed uniformly throughout the massive polymer, but is, as it were, 'imbedded' at a certain depth. This factor and also the inertness of gelatin to the ligands suggests that the ligand diffusion process is not accompanied by a chemical reaction over the entire path traversed and that the MHCF–ligand interaction occurs only after the ligand 'diffusion path' has been traversed. It has therefore been suggested that complex formation in the MHCF–GIM systems be described in terms of the mathematical procedures of the so called external problem of diffusion kinetics.[24,95,99]

3. Kinetic aspects of the complex formation

The complex formation process in the MHCF–GIM systems can occur theoretically either via an associative mechanism (S_N2) or via a pseudo-dissociative mechanism (S_N1).[24,25,35,95] In the former case, the MHCF is stable towards OH^- ions and the ligand molecules therefore gradually enter the inner sphere of the MHCF coordination polymer and $[Fe(CN)]^{4-}$ is then eliminated; this version occurs on complex formation in the KCo[Fe(CN)]–GIM [25,38] and $Ni_2[Fe(CN)]$–GIM [25,30,96,97] systems. The rate of complex formation is governed by a bimolecular reaction. In the second case, the MHCF present in the matrix undergoes alkaline degradation by the OH^- ions to the corresponding oxide or oxide hydroxide, which are involved in the subsequent reaction between the metal ion and the ligand.

On the one hand, the rate of formation of the oxide or hydroxide depends on the MHCF concentration in the matrix but is independent of the ligand concentration in solution and this reflects the clear analogy with typical dissociative processes. On the other hand, the rate of complex formation proper is in this case also limited by a bimolecular reaction. The mechanism of this version of complex formation in the MHCF–GIM has in fact been referred to as of the 'pseudo-S_N1' type;[25,31] it operates in complex formation reactions in the KFe[Fe(CN)]–GIM [25,29,70] and $Cu_2[Fe(CN)]$–GIM [25,32,76] systems and partly in the $Co_2[Fe(CN)]$–GIM.[37]

The model of complex formation in the MHCF–GIM which combines the mathematical procedures of the external diffusion kinetic problem with the kinetic equations within the framework of the Guldberg–Waage law has been used to analyse the experimental relations

$$D' = f(c_F,\ c_L^0,\ t),$$

where D' is the optical density of the metal chelate GIM, c_F the molar concentration of the MHCF in the matrix, c_L^0 the molar concentration of the ligand in solution, and t the duration of the complex formation reaction.

In the case of an associative mechanism, the set of proposed computational equations is

$$\lg\left(c_F\frac{d\alpha}{dt}\right) = \lg k_1 + m\lg c_F(1-\alpha) + l\lg c_L^0 + l\lg\left[1-\exp\left(-\frac{\Delta t}{Mh^2}\right)\right], \quad (14)$$

$$\lg\left(c_F\frac{d\beta}{dt}\right) = \lg k_2 + p\lg c_F(\alpha-\beta) + q\lg c_L^0 + q\lg\left[1-\exp\left(-\frac{\Delta t}{Mh^2}\right)\right], \quad (15)$$

$$\lg\left(c_F\frac{d\omega}{dt}\right) = \lg k_i + y\lg c_F(\psi-\omega) + z\lg c_L^0 + z\lg\left[1-\exp\left(-\frac{\Delta t}{Mh^2}\right)\right]. \quad (1)$$

The following set of equations correspond to a dissociative mechanism:

$$\lg\left(c_F\frac{d\alpha'}{dt}\right) = \lg k_{OH} + m'\lg c_F(1-\alpha') + l'\lg c_L^0 + l'\lg\left[1-\exp\left(-\frac{\delta t}{Mh^2}\right)\right], \quad (17)$$

$$\lg\left(c_F\frac{d\beta'}{dt}\right) = \lg k_1 + p'\lg c_F(\alpha'-\beta') + q'\lg c_L^0 + q'\lg\left[1-\exp\left(-\frac{\Delta t}{Mh^2}\right)\right], \quad (18)$$

$$\lg\left(c_F\frac{d\omega'}{dt}\right) = \lg k_j + y'\lg c_F(\psi'-\omega') + z'\lg c_L^0 + z'\lg\left[1-\exp\left(-\frac{\Delta t}{Mh^2}\right)\right]. \quad (19)$$

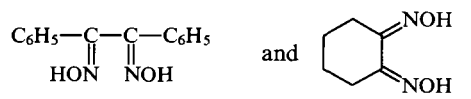
In these equations, k_1, k_2, k_i, and k_j are the rate constants for the consecutive complex formation stages, k_{OH} is the rate constant for the alkaline degradation of the MHCF, *m*, *l*, *p*, *q*, *y*, *z*, *m'*, *l'*, *p'*, *q'*, *y'*, and *z'* are the stoichiometric coefficients in the equations for the complex formation reactions, α' is the degree of accumulation of the hydroxide (or oxide hydroxide) of the corresponding metal ion in the GIM, α, β, ψ, ω, β', ψ', and ω' are the degrees of accumulation of various complexes in the matrix, Δ and δ are the diffusion coefficients of the ligand molecules and OH^- ions for diffusion from the solution to the bulk-phase polymer respectively, *M* is the molecular mass of the ligand, and *h* is the length of the 'diffusion path' traversed by the ligand from the surface of the matrix to the surface of the layer of the MHCF present in it.[35] A program for the computer-mathematical treatment of the experimental relations $D' = f(c_F, c_L^0, t)$ has been compiled with the aid of these equations. It made it possible to calculate the stoichiometric coefficients in the equations for the elementary steps and the overall complex formation processes for a whole series of MHCF-(N), (O), (S), (P)-ligand systems. The theoretical aspects of the kinetics of the complex formation reactions in the MHCF-GIM have been studied in detail.[24,95]

III. Complex formation in the nickel(II) hexacyanoferrate matrix

1. Complex formation in the Ni(II)-(N, O)-ligand systems

According to the available data,[100-105] nickel(II) forms a fairly large number of sparingly soluble chelate complexes with various (N, O)-ligands. Despite this, there are only isolated instances of their employment for complex formation in the $Ni_2[Fe(CN)_6]$-GIM. The Ni(II)-dimethylglyoxime system has been indisputably characterised in greatest detail among the systems considered.

The study of complex formation in a MHCF-GIM system was first reported by Mikhailov and Polovnyak.[40] The results of their study as well as those of later and detailed investigations[24,35,77] indicate the formation in this system of four different dimethylglyoximate complexes, namely $Ni(HL)_2$ (purple), $NiL(H_2O)_2$ (carmine red), $[Ni(H_2L)]Cl_2$ (yellow-green), and $[Ni(H_2L)_2]Cl_2$ (blue) (H_2L = dimethylglyoxime). In two other systems, containing ligands related to dimethylglyoxime, namely benzil glyoxime [diphenylglyoxime] and nioxime [1,2-cyclohexanedione dioxime]

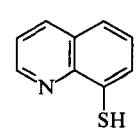


the complex formation processes proceed in approximately the same way as in the Ni(II)-dimethylglyoxime system, as was to be expected. However, the number of coordination compounds formed in this process {$Ni(HL)_2$ and $[Ni(H_2L)_2]Cl_2$} is smaller than in the Ni(II)-dimethylglyoxime system.[24]

The formation of only one complex NiL_2 (L^- = deprotonated form of the ligand) has been detected in the Ni(II)-1-nitroso-2-naphthol, Ni(II)-2-nitroso-1-naphthol, Ni(II)-8-hydroxyquinoline, and Ni(II)-8-hydroxy-5-methylquinoline systems.[24] It is remarkable that the nature of the complex formation in all the systems enumerated remains virtually the same both in aqueous solutions and in the solid phase; the number and compositions of the complex species formed in both cases are the same.[35]

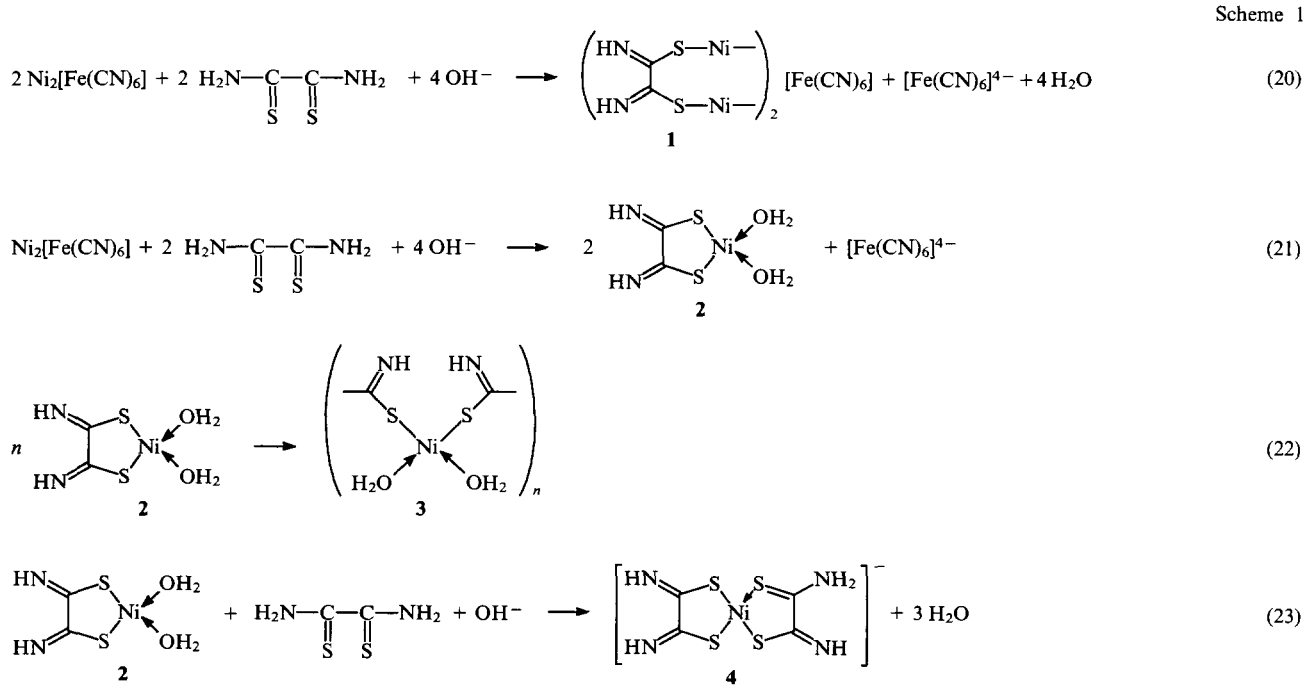
2. Complex formation in the Ni(II)-(N, S)-, (O, S)-, (S, S)-ligand systems

The rule governing the formation of the Ni(II)-ligand complexes in the $Ni_2[Fe(CN)_6]$-GIM system noted above holds also when any kind of (N, S)-, (O, S)-, or (S, S)-ligand capable of giving rise to only one deprotonated species in aqueous solution participates in this process.[24,35] As an example, one may quote 8-mercaptoquinoline



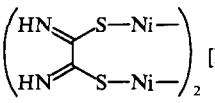
and its alkyl, aryl, and halo-derivatives. A number of studies have been devoted to the formation of complexes in the $Ni_2[Fe(CN)_6]$-GIM with participation of such ligands.[25,30,60,68,74,81] Only coordination compounds having the composition NiL_2, where L^- = singly deprotonated ligands, are formed in the Ni(II)-8-mercaptoquinoline system, exactly as in the systems Ni(II)-alkyl, aryl, and halo-derivatives of 8-mercaptoquinoline (in particular 2-methyl, 5-methyl, 2,7-dimethyl-, 2,4,6-trimethyl-, 5-phenyl-, 6-phenyl-, 5-bromo-, and 5-methylthio-8-mercaptoquinoline) at pH > 9.

Scheme 1



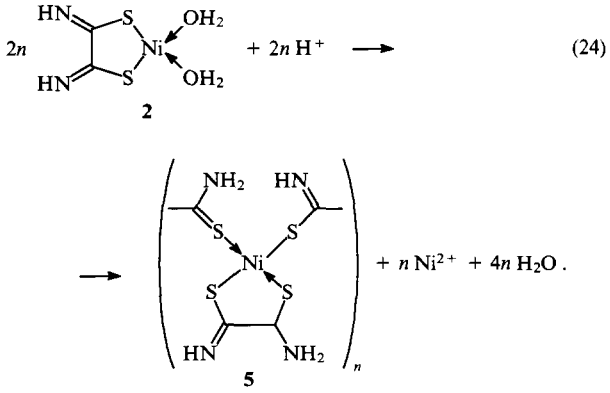
The conclusion reached in the studies quoted above concerning the number and composition of the complex species formed agrees completely with data for complex formation with the 8-mercaptoquinolines listed above in solution and in the solid phase. These are presented in a monograph[106] and in later communications, in particular in Refs 107–109. However, the situation changes significantly when the (N, S)-ligand is capable of forming several species with different degrees of deprotonation, for example HL^- and L^{2-}.[35] In conformity with the prediction made above, in this case ligand- and proton-deficient metal chelates do indeed arise on complex formation in the $Ni_2[Fe(CN)_6]$ matrix. Incidentally many of them have still not been detected in the corresponding Ni(II)–(N, S)-, (O, S)-, (S, S)-donor atom ligand systems in solution and in the solid phase.

The formation of the complex



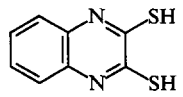
in the $Ni_2[Fe(CN)_6]$–GIM system, considered in detail in a number of investigations,[25,30,40,58,66,69,71,97] constitutes the most striking example. Analysis of relations of the type $D' = f(c_F, c_L^0, t)$ in various coordination regimes in the Ni(II)–dithiooxamide system[25,30,97] shows that the anions $[Fe(CN)_6]^{4-}$ are gradually eliminated from the inner sphere of the $Ni_2[Fe(CN)_6]$-coordinated polymers during complex formation, the process being accompanied by an increase in c_L^0 in accordance with the S_N2 mechanism. The ligand-deficient complex $(Ni_2L)_2[Fe(CN)_6]$ (grey-blue) **1**, the monomeric (complex **2**), the polymeric (complex **3**) proton-deficient complexes $NiL(H_2O)_2$ **2** (pink-violet) and $[NiL(H_2O)_2]_n$ **3** (violet), and a soluble complex having the probable composition $[Ni(L)HL]^-$ **4** with the ratio Ni(II) ion : ligand = 1 : 2, where H_2L = dithiooxamide, are formed in succession under these conditions. According to literature data,[30,97,110] their formation in the GIM can be represented with the aid of Scheme 1 (see previous page).

It is striking that the monomeric chelate is rapidly and irreversibly transformed at pH<5 into the coordination polymer $[Ni(HL)_2]_n$ (dark blue)[30,97,110] in accordance with the scheme



(24)

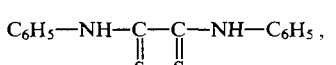
Thus, in the formation of the Ni(II)–dithiooxamide complexes in the $Ni_2[Fe(CN)_6]$–GIM system, at least five different coordination compounds arise, whereas in solution only one complex, namely $[Ni(HL)_2]_n$, is produced.[111–119] The diversity of coordination compounds arising during complex formation in the Ni(II)–quinoxaline-2,3-dithiol system is somewhat smaller.



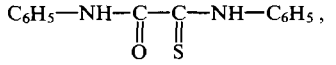
Quinoxaline-2,3-dithiol can be regarded as a rigidly structured analogue of dithiooxamide, which is invariably coordinated to Ni(II) via two sulfur atoms.

According to the results of the mathematical analysis of the $D' = f(c_F, c_L^0, t)$ curves and the chemical analysis of the compounds isolated from the corresponding metal chelate GIM, the complexes $(Ni_2L)_2[Fe(CN)_6]$ (orange), $NiL(H_2O)_2$ (pink), and the soluble complex $[NiLHL]^-$ are formed in succession with increase in c_L^0 in the Ni(II)–quinoxaline-2,3-dithiol system, as in the Ni(II)–dithiooxamide system.[30,69,120,121] Like the monomeric chelate $NiL(H_2O)_2$ with dithiooxamide, the chelate $NiL(H_2O)_2$ with quinoxaline-2,3-dithiol is readily transformed at pH < 5 into a 1 : 2 chelate with a singly deprotonated ligand. However, in contrast to the Ni(II)–dithiooxamide system, in this case the conversion of complex **2** into complex **5** is reversible and at pH > 9 the chelate **5** is converted reversibly into $NiL(H_2O)_2$. According to the literature data,[25,30,120] this difference is associated with the fact that the 1 : 2 complex with the HL^- form of quinoxaline-2,3-dithiol is a monomer whereas the chelate, having a similar composition, with the HL^- form of dithiooxamide is a coordination polymer. The formation of the polymeric chelate $[Ni(HL)_2]_n$ with quinoxaline-2,3-dithiol is sterically hindered because the ligand is cumbersome; for the same reason, quinoxaline-2,3-dithiol does not form with Ni(II) the coordination polymer $[NiL(H_2O)_2]_n$ either.[25,35] On the other hand, data[122,127] concerning complex formation in the Ni(II)–quinoxaline-2,3-dithiol system in solution indicate unambiguously the formation of only one coordination compound, namely $Ni(HL)_2$.

All that has been said about the Ni(II)–dithiooxamide and Ni(II)–quinoxaline-2,3-dithiol systems permits the conclusion that, with the aid of complex formation processes in the $Ni_2[Fe(CN)_6]$–GIM systems, it is indeed possible to synthesise many more coordination compounds than in solution or in the solid phase. On the other hand, the complex formation process in the system containing Ni(II) and another cumbersome structural analogue of dithiooxamide, namely *N*,*N*′-diphenyldithiooxamide



results in the formation of only one coordination compound — $Ni(HL)_2$, as in complex formation in solutions.[69,71,98,128] However, when another ligand, namely *N*,*N*′-diphenylthiooxamide



which differs from the preceding one only by the fact that one of its sulfur atoms has been replaced by an oxygen atom, is used in the complex formation process in the nickel(II) hexacyanoferrate(II)–GIM, a much greater number of coordination compounds (namely four) can again be obtained than on complex formation in solution or in the solid phase (one complex).[78,98]

The causes of such a sharp difference in the nature of complex formation in the Ni(II)–(N, O)-ligand and the Ni(II)–(N, S)-, (O, S)-, or (S, S)-ligand systems in the $Ni_2[Fe(CN)_6]$–GIM have been considered.[24,98] The small tendency of the Ni(II) chelates with the HL^- forms of the (N, S)-, (O, S)-, and (S, S)-ligands to split off protons even at high

pH (13 and above) and the fact that (N, S)-, (O, S)-, and (S, S)-ligands of the type H_2L, the proton-donating capacity of which is usually much smaller compared with their (N, O)-analogues even in a highly alkaline medium, generate insufficient amounts of the L^{2-} forms of the ligands for the formation of complexes with Ni(II) were specified as the most important causes. The deficiency of the L^{2-} form prevents the formation of the Ni(II) chelates with this species on complex formation in solution.

However, the migration of some of the protons from the inner coordination sphere of the Ni(II) chelates with the HL^- forms of the (N, S)-, (O, S)-, and (S, S)-ligands and their binding by the negatively charged gelatin molecules become possible on complex formation in the $Ni_2[Fe(CN)_6]$-GIM system where the molecules of the massive polymers have a negative charge (see Section II, 2).

By virtue of this factor, the possibility of the formation of metal chelates with a pronounced deficiency of protons, which is ruled out in solution and in the solid phase, appears on complex formation in the $Ni_2[Fe(CN)_6]$-GIM system. On the other hand, in the case of the (N, O)-donor atom ligands of the type H_2L, the ligands themselves are capable of generating sufficient amounts of the L^{2-} species for the formation of Ni(II) complexes in a highly alkaline solution. This ensures the possibility of formation in solution of chelates both with the HL^- and L^{2-} species. Therefore in the case of the (N, O)-ligands the formation of any new complex species, which would not be detected on complex formation in the Ni(II)-(N, O)-donor atom ligand systems in solution, is not observed in the $Ni_2[Fe(CN)_6]$-GIM system.[24,77] Thus the study of the complex formation processes in the $Ni_2[Fe(CN)_6]$-GIM has fully confirmed the prediction that ligand-deficient complexes, coordination polymers, and chelates with a pronounced proton deficiency may be formed under these specific conditions.[25,30,97,98,111]

IV. Complex formation in the copper(II) hexacyanoferrate matrix

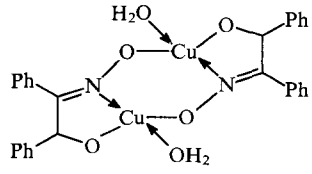
1. Complex formation in the Cu(II)-(N, O)-ligand systems

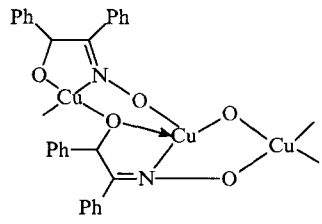
Like Ni(II), Cu(II) belongs to the class of fairly soft Pearson acids.[129] Nevertheless Cu(II) forms an extremely large number of chelate complexes with organic ligands, the donor centres of which are the 'hard' nitrogen and oxygen atoms, in particular with complexones,[96,100,130-132] oximes,[104] 8-hydroxyquinoline, nitrosonaphthols and their substituted derivatives,[105] and Schiff bases.[96,100] Therefore comparison of the possibilities for the formation of Ni(II) and Cu(II) complexes with (N,O)-ligands in the corresponding MHCF-GIM systems is particularly interesting because in the case of the $Ni_2[Fe(CN)_6]$-GIM system the process proceeds via an associative S_N2 mechanism,[25,30] while in the case of the $Cu_2[Fe(CN)_6]$-GIM system it proceeds via a pseudo-dissociative S_N1 mechanism.[25,31] The available literature data on this subject, in particular data concerning the formation of complexes in the Cu(II)-8-hydroxyquinoline, Cu(II)-8-hydroxy-2-methylquinoline, Cu(II)-8-hydroxy-2-methylquinoline,[24,35] and Cu(II)-α-benzoin oxime[24,35,80] systems in the $Cu_2[Fe(CN)_6]$-GIM show that the alkaline degradation of copper(II) hexacyanoferrate(II) take place initially in all cases with its transformation in the first stage into polymeric copper(II) hydroxo-complexes and ultimately into the polymeric hydroxide $[Cu(OH)_2]_n$.

$$\{Cu_2[Fe(CN)_6]\}_n + 2m\,OH^- \longrightarrow \longrightarrow 2[Cu_n(OH)_m]^{(2n+m)+} + n[Fe(CN)_6]^{4-}, \quad (25)$$

$$[Cu_n(OH)_m]^{(2n+m)+} + (2m-n)\,OH^- \longrightarrow [Cu(OH)_2]_n \quad (2)$$

The polymeric copper hydroxide formed as a result of these processes becomes a kind of 'starting area' for the subsequent interaction of copper(II) with the (N, O)-ligands indicated above, which causes the latter to enter the coordination sphere of Cu(II). The validity of processes (25) and (26) is indicated by the results of the mathematical analysis of the corresponding $D' = f(c_F, c_L^0, t)$ kinetic curves in the Cu(II)-(N,O)-ligand systems indicated, according to which for $t < 1$ min the chemical process proceeds without the attachment of ligand molecules to copper(II) ions over the entire range of c_F and c_L^0 investigated. Furthermore, the results of chemical analysis indicate unambiguously that, for $c_L^0 < 10^{-5}$ M and $t < 10$ min, only the polymeric hydroxo-complex $[Cu(OH)_2]_n$ is formed in all these systems in the GIM.[24,35] The clear predominance of the process involving the formation of copper(II) complexes with the ligands compared with the alkaline degradation of the $Cu_2[Fe(CN)_6]$-GIM has been noted only for $c_F < 1.0$ M, $c_L^0 > 1.0 \times 10^{-2}$ M, and $t >$ min.[24,35] In all the Cu(II) systems considered with 8-hydroxyquinoline and its derivatives, it has been possible to establish reliably the existence of only one complex species—CuL_2 (L^- is the deprotonated form of the ligand). In the Cu(II)-α-benzoin oxime system, only one coordination compound is also formed in the $Cu_2[Fe(CN)_6]$-GIM. Judging from the results of elemental analysis, the compound has an empirical formula close to CuL, where L^{2-} is the doubly deprotonated form of the ligand. Either a dimeric structure with two five-membered and one six-membered metallocycles and two coordinated water molecules[80] or a polymeric structure with a three-dimensional macrostructure, incorporating five-membered rings without coordinated water molecules,[24] may be attributed to the compound.





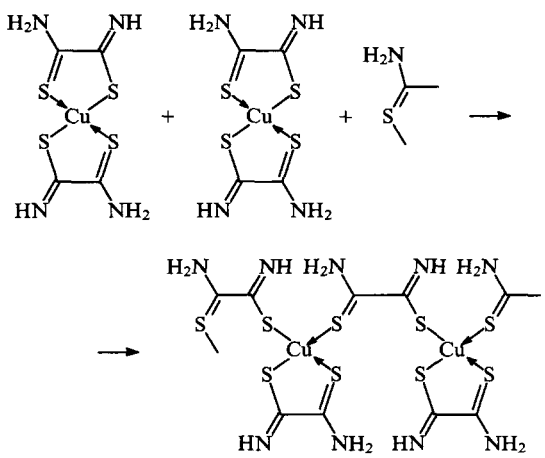
An unambiguous choice between them on the basis of the results of physical research methods is so far impossible. It is remarkable that the ligand in the system inhibits fairly appreciably the alkaline degradation of copper(II) hexacyanoferrate(II).[24,80] If (N, O)-ligands participate in the complex formation process in the $Cu_2[Fe(CN)_6]$-GIM, as in the $Ni_2[Fe(CN)_6]$-GIM, no new coordination compounds unknown for the corresponding Cu(II)-ligand systems in solution or in the solid phase are detected. The possible causes of this phenomenon have been discussed.[24] They resemble the causes discussed for the Ni(II)-(N, O)-donor atom ligand system (see Section III, 2).

2. Complex formation in the Cu(II)-(N, S)-, (O, S)-, (S, S)-ligand systems

The Cu(II)-dithiooxamide system is the most interesting and most thoroughly investigated.[25,31,58,67,72,79,133]

Analysis of the $D' = f(c_F, c_L^0, t)$ kinetic curves in terms of various coordinates[25,31] as well as the results of physicochemical studies of the substances isolated from the corresponding metal chelates matrices[79,133] permitted the conclusion that three coordination compounds are formed in the $Cu_2[Fe(CN)_6]$-GIM system, namely $[CuL(H_2O)_2]_n$,

$[Cu(HL)_2]_n$, and $[Cu(HL)_2(HL)]^-$ (H_2L^- = dithiooxamide), the first two of which are insoluble whilst the third is soluble in water. It is striking that, as for the Cu(II) – (N, O)-ligand systems, in this case complex formation in the $Cu_2[Fe(CN)_6]$ – GIM system involves the initial alkaline degradation of the MHCF in accordance with reactions (25) and (26) and only then does the incorporation of the singly deprotonated form of the ligand (HL^-) in the inner sphere of the copper(II) hydroxide coordination polymer begin.[25,31,79,133] The fact that compounds analogous to $[CuL(H_2O)]_n$ and $[Cu(HL)_2]_n$ are formed also in the complex formation reactions in the Ni(II) – dithiooxamide system is striking (see Section III, 2). According to the literature,[31,133] the monomers $CuL(H_2O)_2$ and $Cu(HL)_2$ arise initially in the Cu(II) – dithiooxamide system and then polymerise as a result of the 'cross-linking' of their molecules. In particular, for $[Cu(HL)_2]_n$ the process takes place in the following way:

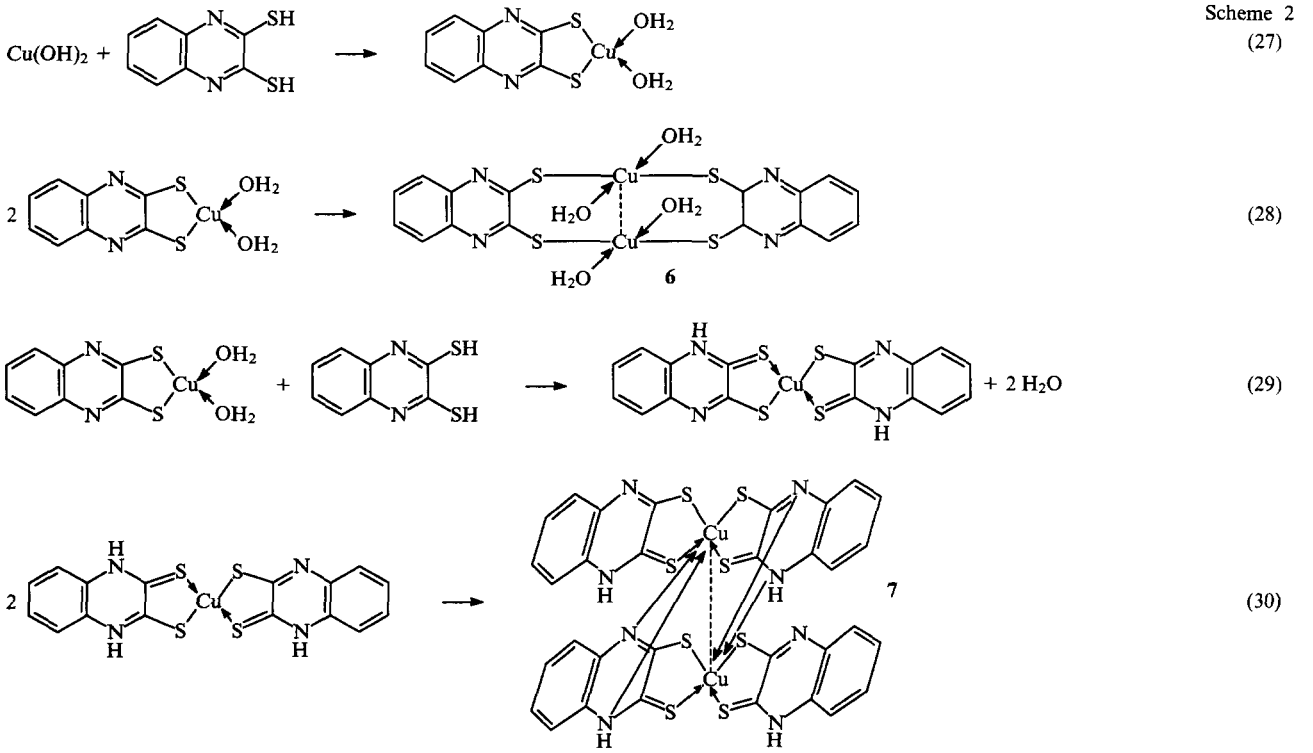


The monomeric intermediates $CuL(H_2O)_2$ and $Cu(HL)_2$ are also formed in the Cu(II) – quinoxaline-2,3-dithiol system, but ultimately the products formed in the matrix are not coordination polymers, as in the Cu(II) – dithiooxamide system, but the dimers $Cu_2L_2(H_2O)_4$ **6** and $Cu_2(HL)_4$ **7**. The diamagnetism of these compounds indicates the presence of a Cu – Cu bond in them.[31] In the case of the $Cu_2L_2(H_2O)_4$ chelate, the appearance of this bond is accompanied by the formation of two additional six-membered chelate rings ensuring a lower ground state energy than in the initial $CuL(H_2O)_2$ monomers. The formation of the dimer $Cu_2(HL)_4$ is promoted by the donor – acceptor interaction of Cu(II) with the nitrogen atoms of the quinoxaline ring, as a result of which the mutual approach of the copper chelate rings (and hence of the copper atoms), accompanied by the $\delta(3d_{xy} - 3d_{xy})$ overlap of the atomic orbitals of the Cu(II) atoms, enables the formation of the metal – metal bond.[24] The formation of the coordination compounds indicated above, based on the present author's data,[24,31] is illustrated in Scheme 2.

We may note that the ν(N – H) band in the IR spectrum of $Cu_2(HL)_4$ occurs at 3380 cm^{-1}, this frequency being characteristic of the N – H groups coordinated around the metal ion.[134] This serves as yet another piece of evidence in support of the dimeric structure of the copper(II) chelate with singly deprotonated quinoxaline-2,3-dithiol and of the presence in the latter of additional weak copper – 'quinoxaline' nitrogen coordinate bonds. It is striking that, for $c_L^0 > 10^{-1}$ M, a third ligand molecule becomes attached to the 1:2 chelates both in the Cu(II) – quinoxaline-2,3-dithiol system and in the Cu(II) – dithiooxamide system considered previously, this being accompanied by the formation of soluble compounds of the type $[Cu(HL)_2(HL)]^-$.[24,31,133] A tetragonal-pyramidal structure, in which two molecules of the ligand are bidentate, their donor atoms being located in the base of the pyramid, whilst the third molecule is monodentate and the sulfur atom coordinated to the metal ion is at the apex of the pyramid, has been postulated for these complexes.[24,133] However, neither chelate accumulates in any appreciable amounts either in the metal chelate GIM or in the solutions of the corresponding ligands in contact with them, so that the mechanism of their formation has still not been investigated in detail.

As can be seen from the foregoing, exactly as in the Cu(II) – dithiooxamide system, complex formation in the $Cu_2[Fe(CN)_6]$ – GIM in the Cu(II) – quinoxaline-2,3-dithiol system results in the formation of three coordination compounds, whereas complex formation reactions in solution or in the solid phase give rise only to chelates with the ratio H : L = 1 : 2.[98,100,102,135,136] However, in the case of the

Scheme 2

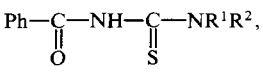


Cu(II)–*N*,*N*′-diphenylthiooxamide and Cu(II)–*N*,*N*′-diphenyldithiooxamide systems, complex formation in the Cu_2.[$Fe(CN)_6$]–GIM leads to the formation of only the paramagnetic monomeric compounds $Cu(HL)_2$, as happens also under the traditional conditions.[31,79] The formation of polymeric complexes of these systems is subject to steric hindrance, as for the analogous system containing Ni(II).[31,79]

The causes of the formation in the Cu(II)–*N*,*N*′-diphenylthiooxamide and Cu(II)–*N*,*N*′-diphenyldithiooxamide systems of the monomers $Cu(HL)_2$ rather than the dimers $Cu_2(HL)_4$ [although both these ligands have, like quinoxaline-2,3-dithiol, electron-donating nitrogen atoms capable of being coordinated to Cu(II) in the complex formation reaction] are not entirely understood. It is most likely that in the monomers $Cu(HL)_2$ free rotation of the phenyl groups about the C–N bonds is possible, which hinders the mutual approach of the planar fragments of these monomeric molecules (particularly when the phenyl groups have rotated by an angle of 90° relative to the plane of the chelate ring). A similar situation arises also in the copper(II) chelate complex of dithiooxamide.[24,133] On the other hand, in the case of the monomeric $Cu(HL)_2$ complex of quinoxaline-2,3-dithiol, the phenylene groups are in the same plane as the metal chelate rings, so that steric hindrance to the mutual approach of the $Cu(HL)_2$ fragments is absent.

The formation of Cu(II) complexes with 1,2-dithiocarbamoylhydrazine and 1-carbamoyl-2-thiocarbamoylhydrazine may serve as yet another piece of evidence for the greater synthetic possibilities of complex formation in MHCF–GIM systems.[31,82] Two Cu(II) complexes have been detected in these systems—an insoluble dimeric complex and a soluble monomeric complex; on the other hand, in solution and in the solid phase only one coordination compound is produced.[100,137] These systems are of interest because with their aid it is possible to obtain nonsilver photographic images, the colour and optical-sensitometric characteristics of which are very close to the corresponding characteristics of the initial black and white silver images on silver halide light-sensitive materials.[82]

A series of new coordination compounds, previously undetected on complex formation under traditional conditions, have been discovered in the complex formation reactions of 3-benzoylthiourea derivatives having the general formula [75,76]

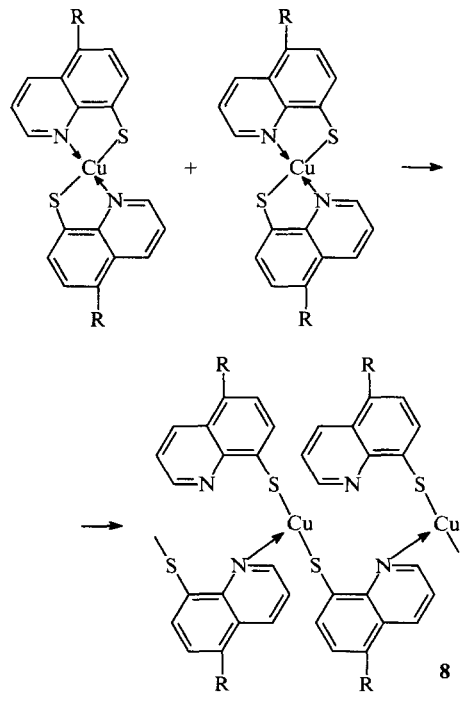


R^1, R^2 = aryl or arylalkyl.

In this connection, it is remarkable that, when the Cu_2[$Fe(CN)_6$]–GIM system is brought into contact with alkaline solutions of 1-naphthyl- and 1-(3,5-di-*tert*-butyl-4-hydroxy)phenetyl-3-benzoylthiourea, neither the formation of Cu(II) complexes with the above organic compounds nor even the alkaline degradation of copper(II) hexacyanoferrate(II) were detected in the systems.[75,76] Clearly the cumbersome nature of these ligands strongly hinders their diffusion into the polymer layer of the matrix and they therefore accumulate at the matrix–solution interface, where they create a kind of 'protecting shell', which in fact prevents the permeation of the OH^- ions into the bulk of the polymer. This phenomenon evidently requires further studies.

Under traditional conditions, the nature of complex formation in the Cu(II)–8-mercaptoquinoline and Ni(II)–8-mercaptoquinoline systems is known to be similar and only one chelate ML_2 (M = Ni, Cu; L^- = deprotonated form of 8-mercaptoquinoline) is formed in both cases.[107] A similar picture is observed also in the complex formation reaction between Ni(II) and 8-mercaptoquinoline in the corresponding metal hexacyanoferrate gelatin-immobilised matrices.[25,31] In the majority of the Cu(II)–alkyl, aryl-, or halo-8-mercaptoquinoline systems, the chelates CuL_2 are also the only products of the complex formation reaction in the MHCF–GIM.[31,35] The few exceptions include the Cu(II)–2-methyl-8-mercaptoquinoline, Cu(II)–2,7-dimethyl-8-mercaptoquinoline, and Cu(II)–2,4,6-trimethyl-8-mercaptoquinoline systems, in which the Cu(II) → Cu(I) redox process occurs, as in complex formation in solution, and hence complexes of the type CuL are formed.

In the Cu(II)–5-bromo-8-mercaptoquinoline and Cu(II)–5-methylthio-8-mercaptoquinoline systems, the formation of the monomeric chelates CuL_2 in the complex formation reaction in MHCF–GIM is accompanied by the formation at fairly high concentrations c_F and c_L^0 (>1.5 M and $>1.5 \times 10^{-2}$ M respectively) of coordination polymers having the same stoichiometric composition, which arise, according to the present author's data,[24] as a result of the 'cross-linking' of the CuL_2 monomers in accordance with the scheme



(31)

R = Br, SMe.

Such a polymer is stable only so long as it is in the reaction space of a matrix having a small volume. On the other hand, when attempts are made to isolate it from the GIM, it instantly depolymerises. However, in a gelatin-immobilised matrix at high concentrations c_F and c_L^0, the association of the CuL_2 monomers in accordance with Scheme (31) is energetically more favourable than the dissociation of the polymer formed in this way into the initial CuL_2 fragments. In contrast to the CuL_2 monomer, the coordination polymer synthesised is not a chelate and its absorption in the visible part of the spectrum is much weaker than that of the monomer. As a result of this, the $D' = f(c_F, c_L^0, t)$ (c_L^0 = const.) relations for the two systems Cu(II)–5-bromo-8-mercaptoquinoline and Cu(II)–5-methylthio-8-mercaptoquinoline systems are much more complex and have distinct maxima.[24]

It is easy to note that steric hindrance to the formation of type **8** polymeric complexes of Cu(II) with various substituted 8-mercaptoquinolines is smallest precisely when the substituent is in the 5-position, so that the formation of these polymers specifically when 5-bromo-8-mercaptoquinoline and 5-methylthio-8-mercaptoquinoline are used in the complex formation

reaction in the $Cu_2[Fe(CN)_6]$–GIM can be fully accounted for. However, the formation of such polymers in the $Cu_2[Fe(CN)_6]$–GIM has not been detected in the Cu(II)–5-chloro-8-mercaptoquinoline and Cu(II)–5,8-dimercaptoquinoline systems, as in the Cu(II)–8-mercaptoquinoline system.[24]

Presumably the absence of the polymers $(CuL_2)_n$ from the first of the above systems is associated with the lower donor capacity of the nitrogen atom in the 5-chloro-8-mercaptoquinoline molecule compared with that of 5-bromo-8-mercaptoquinoline because the chlorine atom is more electronegative and hence has a greater capacity for electron density withdrawal from the nitrogen atom. On the other hand, in 5,8-dimercaptoquinoline the sulfur atom in the 5-thiol group is a more effective electron pair donor than the sulfur atom in the methylthio-group. Because of this, at high concentrations c_F and c_L^0 in the Cu(II)–5,8-dimercaptoquinoline system, the formation of the polymer $[Cu_2L_2(H_2O)_{2n}]$, where L^{2-} is a doubly deprotonated ligand, rather than the $(CuL_2)_n$ coordination polymer indicated by Scheme (31), is more likely.[138]

It follows from the foregoing that, in complex formation reactions in the $Cu_2[Fe(CN)_6]$–GIM systems containing Cu(II) and (N, S)-, (O, S)-, and (N, S)-ligands capable of giving rise to two species differing in the degree of deprotonation, the same tendency towards the formation of coordination compounds with L^{2-} in the inner sphere is observed as in the formation of complexes in the $Ni_2[Fe(CN)_6]^-$–GIM. However, one may note at least two differences. Firstly, the complex formation reaction in the $Cu_2[Fe(CN)_6]$–GIM system proceeds in accordance with a pseudo-S_N1 mechanism and is preceded by the alkaline degradation of copper(II) hexacyanoferrate(II) in accordance with Eqns (25) and (26). For this reason, even before the start of the interaction of Cu(II) with the corresponding (N, O)- or (N, S)-ligand, the $[Fe(CN)_6]^{4-}$ anion is removed from the reaction sphere and does not enter the inner coordination sphere of the Cu(II) complexes formed. A direct consequence of this is the absence from all the Cu(II)–(N, O)-, (N, S)-, (O, S)-, or (S, S)-ligand systems investigated hitherto of 'mixed' complexes of the type $(M_2L)_2[Fe(CN)_6]$, observed in a series of Ni(II)–(N, S)-ligand systems (see Section III, 2). Secondly, the more marked tendency towards the formation of dimeric and polymeric complex species by Cu(II) compared with Ni(II) [92,96,139] is still more pronounced in the complex formation reaction in the MHCF–GIM than in solution or in the solid phase. On the other hand, overall, the data for complex formation in the $Cu_2[Fe(CN)_6]$–GIM confirm primarily the prediction that coordination dimers and polymers may be formed under these specific conditions.[35]

V. Complex formation in cobalt(II) and cobalt(III) hexacyanoferrate matrices

In contrast to nickel and copper, which form stable hexacyanoferrate(II) and stable chelate complexes with specific (N, O)-, (N, S)-, (O, S)-, or (S, S)-donor atom ligands in only one oxidation state (namely the +2 state), cobalt is capable of forming two fairly stable hexacyanoferrate complexes, $Co_2[Fe(CN)_6]$ and $KCo[Fe(CN)_6]$, and fairly stable complexes with the above ligands in which it is present in the +2 and +3 oxidation states. It is therefore useful to examine complex formation reactions in the $Co_2[Fe(CN)_6]$–GIM and $KCo[Fe(CN)_6]$–GIM systems.

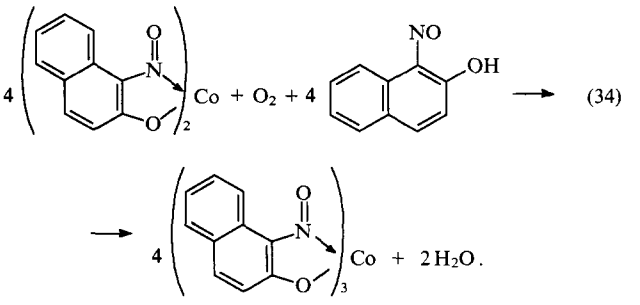
1. Complex formation in the Co(II)/Co(III)–(N, O)-ligand systems

Judging from its orbital electronegativity in aqueous solutions (+0.52 eV),[92] Co(II) is a somewhat harder Pearson acid than Ni(II) and Cu(III). Cobalt(II) belongs to the class of hard Pearson acids.[129] Both these ions have a fairly high affinity for nitrogen. They therefore form extremely readily coordination compounds with a fairly large series of (N, O)-donor atom ligands.[96,139] So far, however, more or less detailed data on complex formation in the MHCF–GIM are available only for the Co(II)–1-nitroso-2-naphthol[24,37] and Co(II)–2-nitroso-1-naphthol[24,36,37] systems. When the $Co_2[Fe(CN)_6]$–GIM comes into contact with alkaline solutions of these ligands (pH ≃ 12), the alkaline degradation of cobalt(II) hexacyanoferrate(II) takes place initially in accordance with the equations

$$\{Co_2[Fe(CN)\ ]\}_n + 2m\,OH^- \longrightarrow \longrightarrow 2[Co_n(OH)_m]^{(2n-m)+} + n[Fe(CN)\ ]^{4-}, \quad (32)$$

$$[Co_n(OH)_m]^{(2n-m)+} + (2m-n)OH^- \longrightarrow [Co(OH)_2]_n. \quad (33)$$

It is easy to see that Eqns (32) and (33) are analogous to Eqns (25) and (26) describing the degradation of $Cu_2[Fe(CN)_6]$ by OH^- ions. Subsequently, the polymeric cobalt(II) hydroxide interacts both with 1-nitroso-2-naphthol and with its isomer 2-nitroso-1-naphthol; the only product is then CoL_2.[24,36,37] It was shown in the studies quoted above that, for $c_F < 0.15$ M, $c_L^0 > 1.0 \times 10^{-2}$ M, and $t \geqslant 10$ min, CoL_2 is partially oxidised by atmospheric oxygen to the corresponding cobalt(III) chelate. In particular, in the case of 1-nitroso-2-naphthol this process proceeds in accordance with the equation[24]



In terms of the nature of the $D' = f(c_F, c_L^0, t)$ relations, the Co(II)–8-hydroxyquinoline and Co(II)–α-benzoin oxime systems are close to the Co(II)–1-nitroso-2-naphthol and 2-nitroso-1-naphthol systems. Similar complex formation reactions probably take place in them.[37] When the $Co_2[Fe(CN)_6]$–GIM system comes into contact with an alkaline solution of dimethylglyoxime, the gelatin layer initially acquires a violet colour, which vanishes after 20 s. According to Mikhailov and Polovnyak,[37] this unusual phenomenon is associated with the oxidation of the dimethylglyoxime chelate $Co(HL)_2$ (violet in colour) formed initially to the corresponding colourless and water-soluble chelate $Co(HL)_3$, which is removed from the matrix when the latter comes into contact with the ligand solution.

In contrast to the Co(II)–(N, O)-ligand systems already considered, complex formation in the $Co_2[Fe(CN)_6]$–GIM has not been detected in any of the Co(III)–(N, O)-ligand systems [where the (N, O)-ligands were 1-nitroso-2-naphthol, 2-nitroso-1-naphthol, 8-hydroxyquinoline, and α-benzoin oxime]. It has been suggested that the reason for this phenomenon arises from the extremely high thermodynamic stability of cobalt(III) hexacyanoferrate(II) and the fact that ligand exchange between the inner sphere of the cobalt(III) hexacyanoferrate(II) coordination polymer and the (N, O)-ligands is difficult.

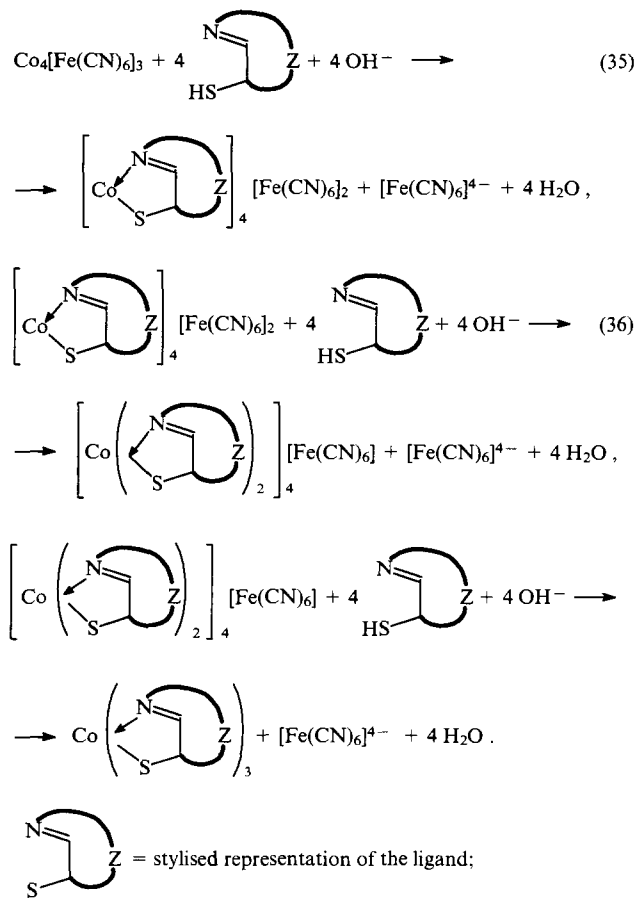
2. Complex formation in the Co(II)/Co(III)–(N, S)-, (O, S)-, (S, S)-ligand systems

According to the present author's data,[24] the nature of the $D' = f(c_F, c_L^0, t)$ relations in the Co(II)–dithiooxamide, Co(II)–*N,N'*-diphenyldithiooxamide, Co(II)–*N,N'*-diphenyldithiooxamide, Co(II)-quinoxaline-2,3-dithiol, and Co(II)-8-mercaptoquinoline systems for complex formation in the $Co_2[Fe(CN)_6]$–GIM is the same as that discussed above in the Co(II)–(N, O)-donor atom ligand systems. Accordingly, the

alkaline degradation of $Co_2[Fe(CN)_6]$ in accordance with Schemes (32) and (33), the formation of the chelates $Co(HL)_2$ (HL^- is the singly deprotonated ligand), and their subsequent oxidation by atmospheric oxygen to the corresponding chelates $Co(HL)_3$ are observed in all these systems when the $Co_2[Fe(CN)_6]$-matrix comes into contact with solutions of the (N, S)-ligands listed above. However, in contrast to complex formation in the MHCF–GIM in the Co(II)–(N, O)-ligand systems, in the case of the (N, S)-ligands the cobalt(II) complexes are in fact intermediates and do not accumulate in any appreciable amounts in the matrices whatever the values of c_F, c_L^0, and t.[24,35] In this connection, one should note that, according to the results of a whole series of investigations,[116,118,119,127,140,141] the complex formation reactions between cobalt(II) and dithiooxamide, its *N*,*N*′-substituted derivatives, and quinoxaline-2,3-dithiol in solution result in the formation of the chelates $Co(HL)_2$ or CoL_2, which are fairly resistant to oxidation. The fact that the chelates CoL_2 formed in the $Co_2[Fe(CN)_6]$–GIM are detected only as intermediates has been attributed[24] to the high dispersity of cobalt(II) hexacyanoferrate(II) in the matrix and the high concentration of OH^- ions in the system, which increases the probability of the oxidation of Co(II) to Co(III) in the MHCF–GIM compared with solution. As in the $Cu_2[Fe(CN)_6]$–GIM, the complex formation reaction in the $Co_2[Fe(CN_6]$–GIM takes place in accordance with a pseudo-S_N1 mechanisms.[25,35] For the same reasons as in the case of the $Cu_2[Fe(CN)_6]$–GIM, no sphere complexes of any kind with OH^- or $[Fe(CN)_6]^{4-}$ anions arise in the $Co_2[Fe(CN)_6]^-$–GIM on complex formation in the Co(II)–(N, S)-, (O, S)-, and (S, S)-ligand systems.[24,25,35]

As regards complex formation in the Co(III)–(N, S)-, (O, S)-, and (S, S)-ligand systems in the cobalt(III) hexacyanoferrate(II)–GIM, the situation is on the whole much more complex.[25,35] The clearer evidence for this is provided by the complex formation reaction in the Co(III)–dithiooxamide system, which has been investigated in detail.[25,38,65] It was noted that the complex formation in this system proceeds in accordance with an S_N2 mechanism and is accompanied by multistage elimination of the $[Fe(CN)_6]^{4-}$ anion from the inner sphere of the cobalt(III) hexacyanoferrate(II) coordination polymer. This results in gradual complex formation, giving rise to the sparingly soluble chelates $[Co(HL)]_4[Fe(CN)_6]_2$, $[Co(HL)_2]_4[Fe(CN)_6]$, and $Co(HL)_3$ (HL^- is the singly deprotonated ligand). The ratios of these complexes in the matrix depend both on the values of c_F, c_L^0, and t and on the degree of dispersity of elemental silver in the silver-containing matrices from which the cobalt(II) hexacyanoferrate(II) matrices have been obtained.[25,38,65] It is therefore extremely difficult to predict the final result of the complex formation reaction for a particular set of parameters c_F, c_L^0, and t.

The situation is complicated further also by the fact that, at fairly high ligand concentrations in solution and for prolonged contact between the matrix and the solution in the Co(III)–dithiooxamide system, the soluble complex $[Co(HL)_2(HL)_2]^-$ also appears. An octahedral structure of this compound with two monodentate and two bidentate ligand molecules has been postulated.[38] The bidentate molecules are coordinated to Co(III) via the nitrogen and sulfur atoms, while the monodentate ligands are coordinated via the sulfur atoms. Similar sparingly soluble chelates with the metal : ligand = 1 : 1, 1 : 2, and 1 : 3 ratios have been detected also in the Co(III)–*N*,*N*′-diphenylthiooxamide, Co(III)–*N*,*N*′-diphenyldithiooxamide,[25,38] and Co(III)-8-mercaptoquinoline[24,25] systems. According to data of Mikhailov and Budnikov,[25] their formation reactions can be described by the following general equations:



Z = open chain or cyclic group of atoms.

It is noteworthy that that 1 : 1 and 1 : 2 chelates have not been detected in the complex formation reactions in solution and in the solid phase.[106,140] Apart from these types of complexes, the formation of the complex $(Co_2L)_2[Fe(CN)_6]$ in the Co(III)–*N*,*N*′-diphenylthiooxamide system has also been postulated.[38] The following remarkable factor is striking in this connection. As already stated above, Ni(II) and Cu(II) form fairly stable coordination chelate compounds with the L^{2-} forms of dithiooxamide and *N*,*N*′-diphenylthiooxamide. However, Co(III) has a higher charge and a smaller radius than Ni(II) and Cu(II), so that the Co(III) chelates formed with the HL^- forms of both these ligands should be more effective proton donors, like the chelates with the corresponding form of *N*,*N*′-diphenyldithiooxamide, than the analogous Ni(II) and Cu(II) chelates. It can therefore be expected that the probability of the formation of the Co(III) chelates with the L^{2-} forms of all the above three ligands is much greater than the probability of the formation of the corresponding Ni(II) and Cu(II) chelates.

However, the HL^- forms and not the L^{2-} forms of the above ligands are in fact present in the inner spheres of virtually all the Co(III) compounds with dithiooxamide *N*,*N*′-diphenylthiooxamide, and *N*,*N*′-diphenyldithiooxamide synthesised by the complex formation reactions in the cobalt(II) hexacyanoferrate(II)–GIM. This paradox may be accounted for by the fact that theoretically the *trans*-HL^- or *trans*-L^{2-} forms of the above ligands with nitrogen and sulfur donor atoms should participate in the formation of the complexes of Co(III), since the latter is a harder Pearson acid than Ni(II) and Cu(II), and not the *cis*-HL^- or *cis*-L^{2-} forms (with two donor sulfur atoms), as happens in the case of Ni(II) and Cu(II).[24] On the other hand, the participation of the *trans*-L^{2-} forms in the complex formation reaction automatically presupposes that any of the above ligands is tetradentate and hence this should lead theoretically to the formation of polymeric chelates. However, the formation of

polymeric structures by Co(III), involved exclusively in octahedral coordination, with the tetradentate *trans*-L^{2-} forms of such ligands is sterically hindered, whereas the formation of chelates with the bidentate *trans*-HL^- forms does not encounter such hindrance. In all the Co(III) chelate complexes with dithiooxamide, *N*,*N'*-diphenylthiooxamide, and *N*,*N'*-diphenyldithiooxamide formed by complex formation reactions in the cobalt(III) hexacyanoferrate(II) matrix, the ligands are coordinated to the metal ion via the nitrogen and sulfur atoms.[24,35] One can therefore expect that complex formation in the MHCF–GIM should not occur in the Co(II)-quinoxaline-2,3-dithiol system, where the ligand is a structurally rigid analogue of dithiooxamide and contains only sulfur atoms as the donor centres.[24,35,38]

In conclusion one should note that the nature of complex formation in the cobalt(III) hexacyanoferrate(II)–GIM in all the Co(III)–(N, S)-ligand systems investigated is independent of the number of species with different degrees of deprotonation formed by the ligand.[24,25,35,38] This constitutes a sharp difference between complex formation reactions in the cobalt(III) hexacyanoferrate(II)–GIM, on the one hand, and in the nickel(II) and copper(II) hexacyanoferrate(II) matrices, on the other, where such a dependence can be seen (see Sections III, 2 and IV, 2) to be quite distinct. One can also conclude that, overall, the characteristic features of complex formation in the cobalt(III) hexacyanoferrate(II)–GIM clearly confirm the validity of the prediction that intermediate coordination compounds, which are not detected under the 'traditional' conditions (see Section II, 2), can be formed under the specific conditions of the MHCF–GIM.

VI. Complex formation in the iron(III) hexacyanoferrate(II) matrix

The uniqueness of the situation consists in the fact that the metal-containing components of this MHCF–GIM contain ions of the same 3*d* element in different oxidation states [Fe(II) and Fe(III)]. Each of them is potentially capable of forming complexes mainly with 'hard' donor centres.

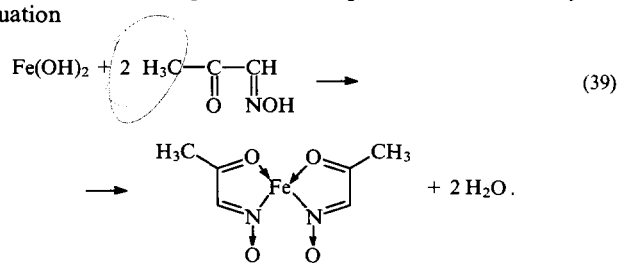
1. Complex formation in Fe(II, III)–(N, O)-ligand systems

The Fe(II) and Fe(III) atoms present in $KFe[Fe(CN)_6]$ belong to the category of moderately hard and hard Pearson acids respectively[129] (their orbital electronegativities in aqueous solution are +0.69 and +2.22 eV respectively).[92] Their extremely stable complexes with (N, O)-ligands such as 8-hydroxyquinoline, nitrosonaphthols and their derivatives,[105] oximes,[104] and complexones,[100,101] are known. However, only two of these — 8-hydroxyquinoline[70,72] and isonitrosoacetone $H_3CC(O)CH{=}NOH$ — have so far been used in complex formation reactions in the $KFe[Fe(CN)_6]$–GIM. The study of complex formation in the $KFe[Fe(CN)_6]$–GIM system is extremely seriously restricted by the fact that the Fe(II) and Fe(III) complexes formed with ligands containing both nitrogen and oxygen usually absorb extremely weakly in the visible part of the spectrum, have relatively low stability constants, and dissolve appreciably in water.[29,72] It has been shown in the studies quoted that, when the $KFe[Fe(CN)_6]$–GIM comes into contact with alkaline solutions of the above ligands ($pH \geqslant 12$), the alkaline degradation of the metal-containing component of the MHCF–GIM takes place initially in accordance with the equations

$$KFe[Fe(CN)]+3OH^- \longrightarrow \longrightarrow FeO(OH)+[Fe(CN)]^{4-}+K^++H_2O\ , \quad (37)$$

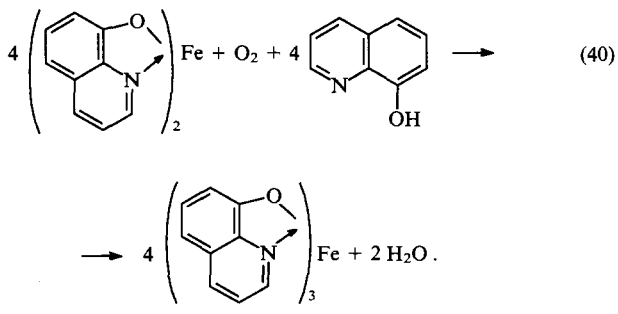
$$KFe[Fe(CN)]+2OH^- \longrightarrow \longrightarrow Fe(OH)_2+[Fe(CN)]^{3-}+K^+\ . \quad (38)$$

This results in the formation of a mixture of Fe(II) and Fe(III) oxide hydroxides in the GIM, the ratio of which probably depends very significantly both on the experimental conditions and on the degree of dispersity of iron(III) hexacyanoferrate(II) in the immobilised matrix.[24] However, only the Fe(II) hydroxo-complexes interact with each of the ligands indicated above.[29,70] The $D'=f(c_F, c_L^0, t)$ curves for the Fe(II)–isonitrosoacetone system are extremely simple: with increase in $c_F t$ and c_L^0 (at a fixed concentration c_F), the optical densities of the polymer layer of the matrix increase monotonically, tending to certain limiting values which depend on c_F.[70] According to Mikhailov and Polovnyak,[70] the complex formation process is described by the equation



(39)

The chelate FeL_2 is virtually the only complex formation product also in the Fe(II)–8-hydroxyquinoline system.[70] However, in this case the $D'=f(c_F, c_L^0, t)$ relations are somewhat more complex than in the Fe(II)–isonitrosoacetone system: in particular, for $c_F < 0.3$ M and $c_L^0 > 1.0 \times 10^{-2}$ M, with increase in t the quantities D' begin to decrease after attaining a certain maximum value.[70,72] This finding has been attributed[29,70,98,142] to the occurrence in the system under consideration of the Fe(II) → Fe(III) redox process in accordance with the overall scheme

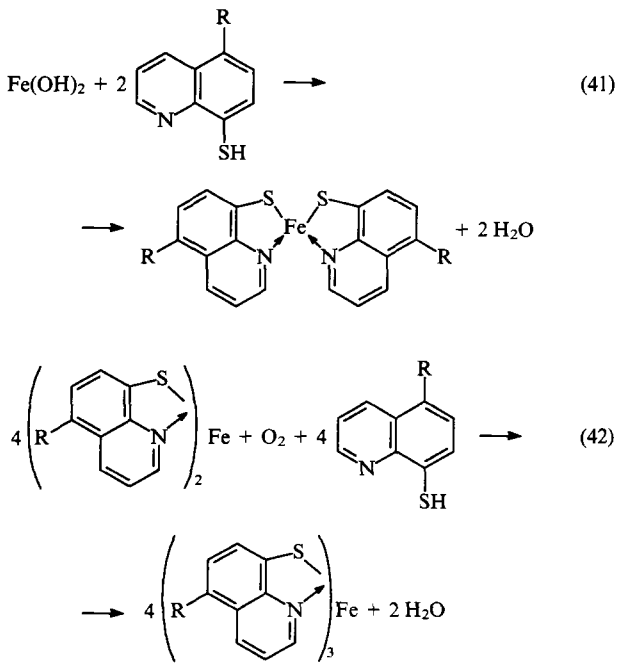


(40)

It has been stated that the natures of the $D'=f(c_F, c_L^0, t)$ curves for the Fe(II)–1-nitroso-2-naphthol and Fe(II)–2-nitroso-1-naphthol systems are similar to those for the Fe(II)–isonitrosoacetone system, but these systems have not been characterised in greater detail.[24,70]

2. Complex formation in the Fe(II), (III)–(S, S)-, (N, S)-, and (O, S)-ligand systems

There are also hitherto extremely few examples of complex formation in the Fe(II)–(N, S)-ligand systems under the specific conditions which obtain in the $KFe[Fe(CN)_6]$-GIM. There are data on complex formation in the iron(III) hexacyanoferrate(II) matrix when the latter comes into contact with aqueous alkaline solutions of 8-mercaptoquinoline and its 5-bromo- and 5-methylthio-derivatives.[24] In all three cases, three ligand molecules become attached in succession to one $Fe(OH)_2$ fragment during the complex formation process, the third molecule being attached much more slowly than the first two. It has been suggested that initially Fe(II) complexes with the corresponding ligands arise in all the iron(II)–ligand systems indicated, but the complexes are instantaneously oxidised by atmospheric oxygen to the corresponding Fe(III) coordination compounds.



(41)

(42)

It is striking that the chelates FeL_3 are formed in all these cases actually from $Fe(OH)_2$ and not from FeOOH or some other iron(III) oxide hydroxide.[24] On the other hand, one should note that, when the $KFe[Fe(CN)_6]$-GIM comes into contact with alkaline solutions of ligands such as dithiooxamide, *N*,*N*′-diphenylthiooxamide or *N*,*N*′-diphenyldithiooxamide, quinoxaline-2,3-dithiol, 1,2-dithiocarbamoylhydrazine, and 1-carboxyl-2-thiocarbamoylhydrazine, only the alkaline degradation of iron(III) and potassium hexacyanoferrates(II) is detected and no Fe(II) and Fe(III) coordination compounds with the ligands indicated are produced.[25,29] In contrast to complex formation in the $M_2[Fe(CN)_6]$-GIM [M = Ni(II), Cu(II), Co(II)] and the $KCo[Fe(CN)_6]$-GIM, in the complex formation reaction in the $KFe[Fe(CN)_6]$ matrices it was not possible to detect in any of the systems considered any kind of new coordination compounds which had not been detected previously in the interaction of Fe(II) with the corresponding ligands in solutions or in the solid phase.[35,70,98] The high lability of the high-spin Fe(II) and Fe(III) chelates and also the low probability of the formation of dimeric and polymeric species with the ligands considered by both iron(II) and iron(III) have been specified as the probable causes of this phenomenon.[24,29]

To a first approximation, all the 3*d* element-chelating (N,O)-, (N,S)-, (O,S)-, and (S,S)-ligand systems described in the literature can be quite definitely assigned to one of two types of complex formation: in the first of these, the process proceeds by a formal S_N2 mechanism [systems in which the metal-containing components are nickel(II) and cobalt(III) hexacyanoferrates(II)], while in the second it proceeds via a formal pseudo-S_N1 mechanism [systems in which the metal-containing components are copper(II), iron(III), and cobalt(II) hexacyanoferrates(II)]. Both homoligand and heteroligand {i.e. containing ligand molecules deprotonated to a particular extent and the $[Fe(CN)_6]^{4-}$ anion} chelate complexes may be formed in systems of the first type. Only homoligand coordination compounds are formed in systems of the second type and, despite the fact that theoretically there is a possibility in this instance of the existence of complexes containing in the inner coordination sphere any of the forms of the ligands indicated above as well as the OH^- group, their appearance has not been detected in the complex formation reaction in the MHCF-GIM in any of the systems examined in the literature.

Only one variant of complex formation is as a rule characteristic of each of the metal hexacyanoferrate(II)-GIM considered. Depending on the nature of the ion of the 3*d* element (but regardless of the nature of the ligand), the formation of the above heteroligand complexes in such a variant either always occurs [in the complex formation reaction occurring in the cobalt(III) hexacyanoferrate(II)-GIM] or, on the contrary, it never occurs [in the complex formation reaction in the cobalt(II) hexacyanoferrate(II)-GIM]. Only the $Ni_2[Fe(CN)_6]$-GIM is an exception, where complex formation can take place in accordance with one or another variant depending on the nature of the ligand. The first variant occurs for ligands containing nitrogen, which are capable of generating under the complex formation conditions at least two species with different degrees of deprotonation, while the second occurs in the case of ligands containing both nitrogen and sulfur, which give rise to only one deprotonated species, and also in the case of ligands containing both nitrogen and oxygen. One can therefore conclude that the nature of the differences between the complex formation reactions in solutions and in the metal hexacyanoferrate(II) gelatin-immobilised matrix systems is fully consistent with the predictions which can be made on the basis of the considerations described in Section II, 2.

VII. Practical possibilities for complex formation reactions in metal hexacyanoferrate(II) matrices

1. The production of nonsilver photographic images on silver halide photosensitive materials

The process involving the formation of nonsilver photographic images consists of three stages: (1) bleaching of the silver image obtained on the photographic material by means of its standard treatment[26-28] in a solution containing potassium hexacyanoferrate(III), the soluble salt of a 3*d* element ion (as a rule the chloride or sulfate), and any organic hydroxyacid (citric, oxalic [sic], or tartaric); (2) fixation of the bleached image by treating the photographic emulsion with an aqueous solution of sodium thiosulfate; (3) toning of the image by treating the photographic emulsion with an alkaline solution of the corresponding chelating organic compound. In terms of the composition of the solutions used to treat the photographic materials and the chemistry of the processes occurring, the first two stages correspond to the synthesis of the MHCF-GIM and the third to the complex formation reaction in such GIM.[35] It is noteworthy that in a number of instances the nonsilver photographic image obtained from the metal chelates can be produced also by a shorter procedure: the exposed silver halide photographic material is initially developed and then subjected to treatment involving the successive operations 1-3. It is then possible to shorten the time required to obtain the nonsilver metal chelate image and also to improve the efficiency and accelerate the oxidation of the elemental silver to the corresponding silver(I) compounds [the hexacyanoferrate(II) or the chloride).[143] Several tens of technological processes of this type have already been described in the literature. The main bulk of the publications have been devoted to the synthesis of nonsilver images from nickel(II) chelates;[40,41,43,49,53,57,58,60,66,68,69,71,72,74,77,78,81] and a somewhat smaller number have been devoted to the synthesis of images from copper(II) chelates;[36,39,42,46,50,51,54,55,58,62,67,72,75,76,79,80] on the other hand, instances of the employment of the chelates of other 3*d* elements are the carriers of nonsilver images are encountered much more rarely.[36-38,44,47,48,56,63,65,72] In particular, technologies for the production of nonsilver images by means of carriers such as the nickel(II) chelate complexes of dimethylglyoxime,[40,77] dithiooxamide and its *N*,*N*′-diphenyl derivatives,[41,57,58,64,66,69,71] and *N*,*N*′-diphenylthiooxamide,[53,78] the copper(II) chelate complexes of α-benzoin oxime,[46,60] 8-hydroxyquinoline,[50] and dithiooxamide,[39,64,72,79] the cobalt(II) chelate complexes of nitrosonaphthols,[36,37,44] the cobalt(III) chelate complex of dithiooxamide,[38,45,65] and the iron(II) complex of 8-hydroxyquinoline.[45,70]

The formation of nonsilver images from nickel(II) chelate complexes of dithiooxamide is the most interesting process.[40,58,64,66,69,71,72] It has been used, in particular, for the preparation of 'blue slides'.[58] This procedure for the preparation of 'blue slides' is less laborious and, what is most important, is less demanding as regards external conditions compared with the familiar traditional processes based on organic dyes.[143] The dark blue or blue images obtained from the $[Ni(HL)_2]_n$ chelate complexes of dithiooxamide are distinguished by a greater purity of the light lines, greater contrast, and greater photostability. Yet another important quality of this procedure is that, in contrast to all the other processes for the intensification of photographic images known hitherto,[26] in many cases it does not increase but actually diminishes the degree of fogging compared with the initial silver image.[40,58,64] The cause of this phenomenon is closely associated with the occurrence of process (23).

The above phenomenon is fairly typical for technologies for the synthesis of nonsilver images from the chelates of 3*d* elements. It is observed, in particular, also in the formation of images from the copper(II) chelate complex of dithiooxamide (dark-green),[39,64,79] the copper(II) chelate complex of 1,2-dithiocarbamoylhydrazine (black),[50,82] the copper(II) chelate complex of 1-carbamoyl-2-thiocarbamoylhydrazine (black-brown),[51,82] and the cobalt(III) chelate complex of dithiooxamide (amber-yellow).[38,48,65] It is striking that the images generated by the copper(II) chelate complex of 1,2-dithiocarbamoylhydrazine[50,82] and the iron(III) complex of 8-hydroxyquinoline[45,70] are very close to the initial neutral grey silver images. This is particularly effective in those cases where after intensification it is desirable to retain the black or grey-black colour of the image.

One should note especially that the employment of all these technologies makes it possible to vary widely the photographic characteristics of the treated materials. In particular, by altering the concentrations and the duration of the toning stage, it is possible to both decrease and increase the photographic sensitivity achieved in the formation of the initial silver image.[72] Review articles have been published on the problem under consideration.[72,143]

2. Synthesis of test objects for the measurement of optical absorption spectra

A fundamentally new variant of the preparation of test objects has been developed with the aid of complex formation in the MHCF–GIM systems. Its significant features reduce to the fact that the substance analysed is synthesised in a gelatin layer as a result of a series of specific chemical reactions.[144–146] In particular, test objects comprising nickel(II)–dimethylglyoxime, copper(II)–dithiooxamide, cobalt(II)-2-nitroso-2-naphthol, and iron(II)–8-hydroxyquinoline coordination compounds have been prepared in this way. In principle, the ideas underlying this method can be used to prepare also test objects comprising a series of other inorganic compounds, in particular oxides and sulfides.[144] This method is probably fairly promising also for the preparation of test objects comprising certain organic compounds which absorb intensely in the visible part of the spectrum.[145]

3. Modelling of complex formation in bulk-phase polymers

There are indications in the literature that complex formation in a MHCF–GIM system may serve as a useful model for the interpretation of the stabilising effect of certain antioxidants for polymeric materials, in particular derivatives of 3-benzoylthiourea. Such a stabilising effect reduces to the 'complexing' of the microimpurities comprising the ions of the 3*d* elements, for example copper(II), present in bulk-phase polymers.[138,147] However, the study of this problem is in the initial stage.

VIII. Conclusion

It follows from the foregoing that complex formation in the metal hexacyanoferrate(II) gelatin-immobilised matrix systems is a specific phenomenon in chemical science in general and in coordination chemistry in particular. A new field of science has arisen — involving the study of the reactivities of polymer-immobilised coordination compounds with fixation of the substance by means of intermolecular forces and the study of the characteristics of complex formation involving such compounds. In essence, only the first steps have been taken on these lines, but it is already evident that complex formation under the nontraditional conditions described can lead to the formation of coordination compounds the existence of which investigators have sometimes not even suspected. There is no doubt that, as the range of the metal–ligand systems employed within the framework of the 'classical' complex formation expands, the very considerable potential synthetic possibilities of complex formation in metal hexacyanoferrate(II)-GIM as well as its possible practical applications will be manifested to a much greater extent.

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Uronic acids: synthesis and reactions

V A Timoshchuk

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Abstract. The review describes the methods of synthesis of uronic acids involving both the catalytic oxidation of sugars and their oxidation by nonspecific oxidants. The principal paths in the transformations of uronic acids and their derivatives, characteristic of compounds of this class, which make it possible to synthesise new compounds that are otherwise difficult to obtain are considered. The bibliography includes 217 references.

I. Introduction

By definition, the term uronic acid is applied to monosaccharides in which the primary hydroxy-group has been transformed as a result of oxidation into a carboxy group. Uronic acids are usually understood only as alduronic acids, which are derivatives of aldoses, while the preferred name for keturonic acids is ketoaldonic acids. However, in the present review the term 'uronic acids' is used in a wide sense for all polyhydroxy-compounds containing carbonyl and carboxy-groups simultaneously. The presence of the carboxy-group in the structure of uronic acids is reflected in the relative reactivities of the hydroxy-groups, in the resistance to hydrolysis of the *O*- and *N*-glycosidic bonds, and also in their tendency to undergo β-elimination, leading to the formation of unsaturated sugars, which frequently serve as valuable intermediates in the synthesis of compounds which are difficult to obtain. The chemistry of uronic acids abounds with examples of the successful employment of the carboxy-group in monosaccharides in the construction of molecules having a specified structure.

The aim of the present review is to give a systematic account and to survey the extensive and interesting data on the synthesis and reactions of uronic acids. The review summarises data on the methods of synthesis of uronic acids with different carbon chain lengths, attention being concentrated on the oxidation reactions of monosaccharide derivatives. The methods of synthesis of diverse derivatives of uronic acids, which may be of interest in experimental studies and which may serve as synthons in the synthesis of optically active noncarbon compounds, are also examined.

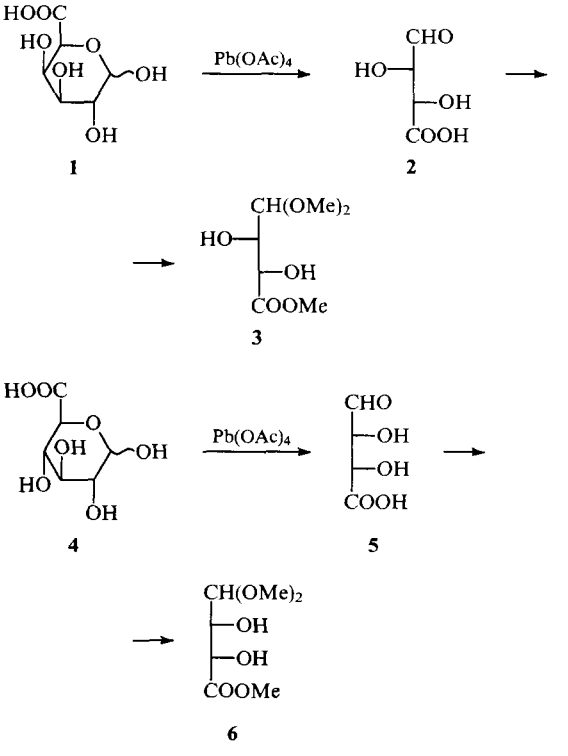
The last section of the review is devoted to numerous chemical reactions of uronic acids, which illustrate the extensive synthetic possibilities of compounds of this class.

V A Timoshchuk Radiation Chemistry Laboratory, Faculty of Chemistry, Belorussian State University, prosp. F. Skoriny 4, 220050 Minsk, Belarus. Fax (7-017) 220 82 72, Tel. (7-017) 220 67 56

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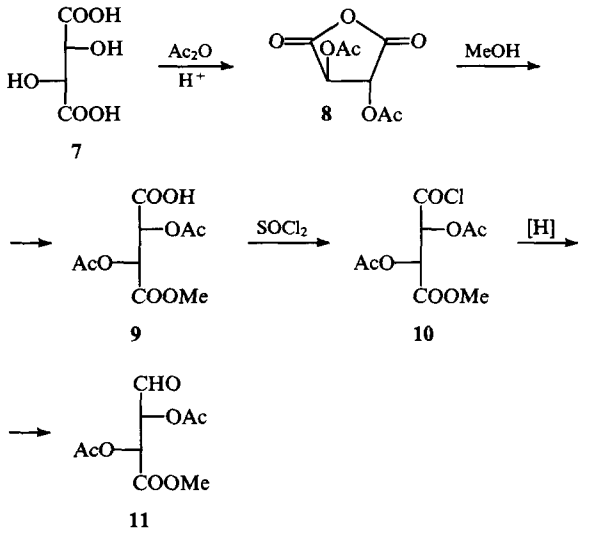
II. Tetruronic acids

D-*threo*-Tetruronic acids **2** and D-*erythro*-tetruronic acids **5** are readily formed when D-galacturonic acid **1** and D-glucuronic acid **4** are treated with two equivalents of $Pb(OAc)_4$. Tetruronic acids have been isolated and characterised as the dimethyl acetals of their methyl esters **3** and **6**.[1]

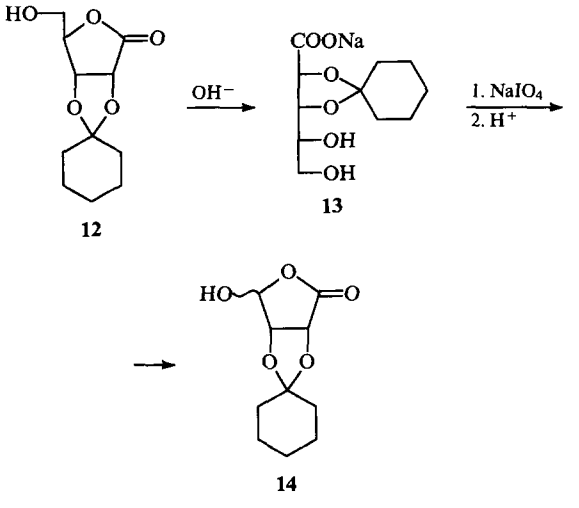


1 **2** **3** **4** **5** **6**

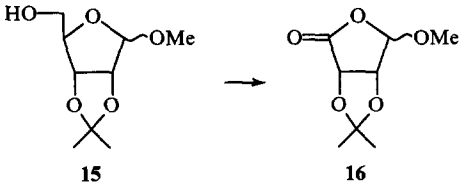
The source of L-*threo*-tetruronic acid is L-tartaric acid **7**, which is converted, as a result of treatment with acetic anhydride, into the anhydride **8**, affording the monomethyl ester **9** in methanol. The Rosenmund reduction of the acid chloride **10** leads to the methyl ester of 2,3-di-*O*-acetyl-L-*threo*-tetruronic acid **11**.[2]



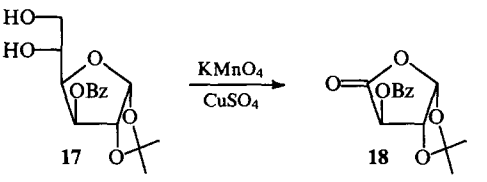
The cyclohexylidene derivative of the lactone of L-*erythro*-tetruronic acid **14** has been obtained in 93% yield by the periodate oxidation of the salt **13** formed from D-ribonolactone **12**.[3]



An unexpected result has been obtained in the oxidation of the methyl riboside **15**. Refluxing it with pyridinium chlorochromate in benzene, using a Dean–Stark procedure, leads to D-erythruronolactone **16**.[4]

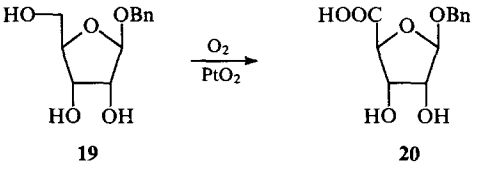


The lactone of L-*threo*-tetruronic acid **18** is formed smoothly on oxidation of 3-*O*-benzoyl-1,2-*O*-isopropylidene-α-D-glucofuranose **17** by $KMnO_4$ in the presence of $CuSO_4$.[5]

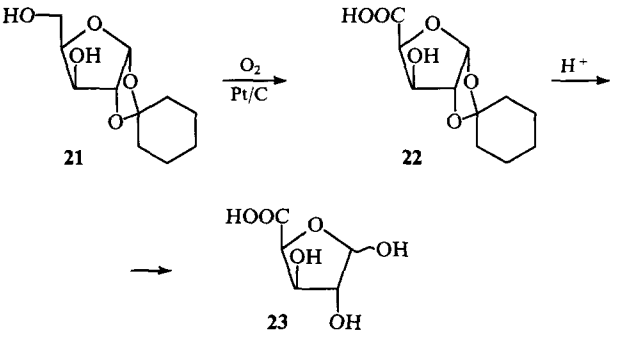


III. Penturonic acids

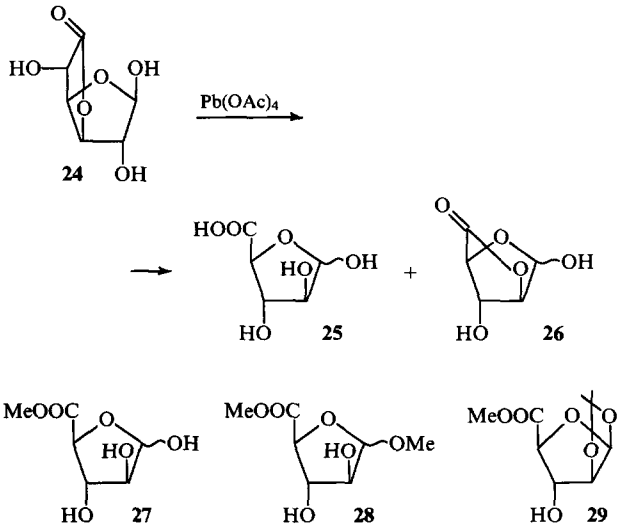
A convenient, albeit expensive and not always satisfactorily reproducible, method of synthesis of penturonic acids is the oxidation of pentofuranosides by oxygen over platinum or platinum black. The catalytic oxidation of benzyl β-D-ribofuranoside **19** over platinum black leads to the corresponding riburonide **20** in 48% yield. Oxidation by oxygen in the presence of platinum on charcoal affords a less satisfactory result (yield 13%).[6]



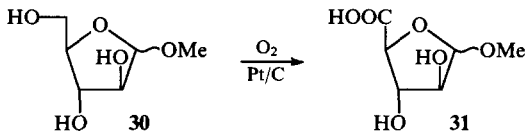
The acid **22**, the acid hydrolysis of which gives rise to D-xyluronic acid **23**, has been synthesised by the catalytic oxidation of 1,2-*O*-cyclohexylidene-α-D-xylofuranose **21**.[7]



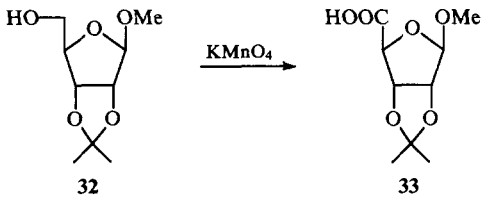
Treatment of the glucurone **24** with one equivalent of $Pb(OAc)_4$ leads to the formation of D-arabinuronic acid **25** and its lactone **26**, which has been identified as the methyl ester **27**, its glycoside **28**, and its acetal **29**.[1]



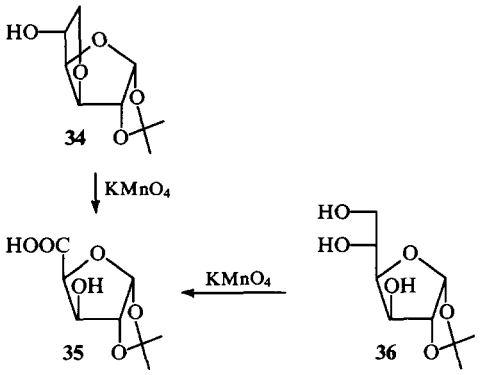
The catalytic oxidation of the arabinoside **30** to the arabinuronide **31** has been described.[8]



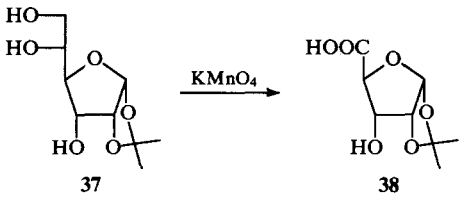
$KMnO_4$ has been used successfully for the oxidation of appropriately protected pentoses. The acetal of the methyl riboside **32** is oxidised to the acid **33** in 31% yield in an aqueous alkaline solution.[9] Acidification of the reaction mixture and rapid removal of the acid **33** formed by extraction with ether makes it possible to increase its yield to 65%.[10] Oxidation in a mixture of acetone and acetic acid leads to the formation of the acid **33** in 54% yield.[11]



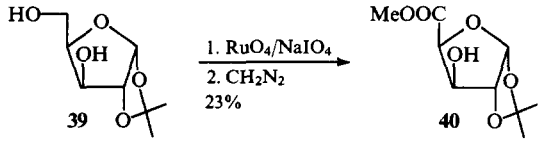
Anhydroglucofuranose **34** is oxidised by $KMnO_4$ to xyluronic acid **35**.[12]



The acid **35** is formed readily when the acetal of glucofuranose **36** is treated with $KMnO_4$. Riburonic acid **38** has been obtained from the acetal of allofuranose **37** under similar conditions.[13]

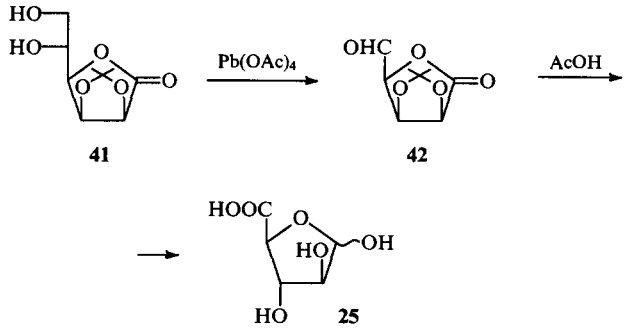


Ruthenium tetroxide in the presence of sodium metaperiodate can be used as the oxidant in the synthesis of penturonic acids. The acid **33** has been synthesised from compound **15** by this method.[14] The xyluronic acid ester **40** has been obtained by the oxidation of [the acetal of] xylofuranose **39** with subsequent esterification.[15]

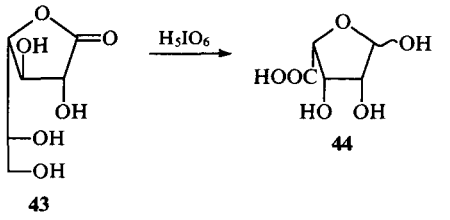


The preparation of the acid **35** by the successive oxidation of the glucofuranose acetal **36** by $Pb(OAc)_4$ and bromine in the presence of $BaCO_3$ has been described.[16]

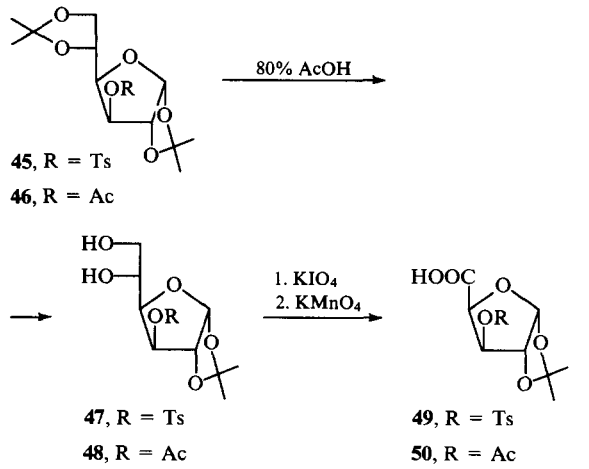
One of the sources for the synthesis of penturonic acids is glyconic acid γ-lactones. An example of such synthesis has been demonstrated by Mashida.[16] The aldehyde **42** has been obtained by oxidising the mannonolactone **41** by $Pb(OAc)_4$ and was then transformed in 10% acetic acid into arabinuronic acid **25**.



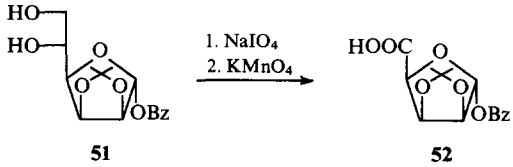
This approach has been used successfully in the synthesis of L-lyxuronic acid **44** from D-gulonolactone **43**.[17]



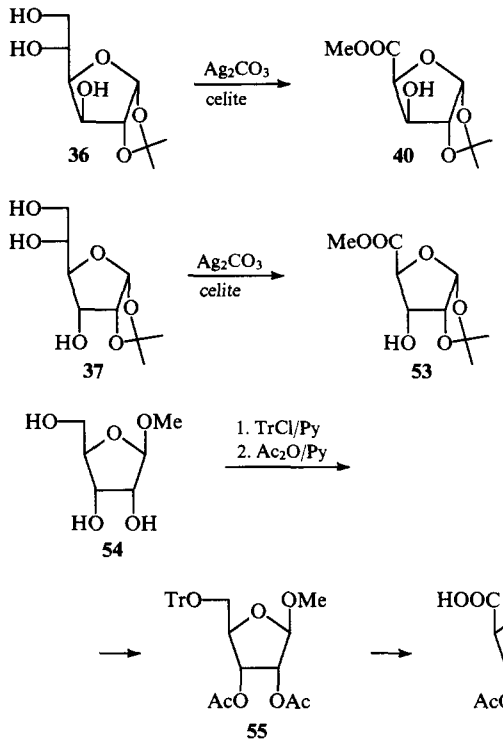
The derivatives of glucofuranose diacetals **45** and **46** are readily available starting compounds for the synthesis of penturonic acids with various substituents at C(3). The diols **47** and **48** obtained from them by mild acid hydrolysis are oxidised in succession by potassium metaperiodate and permanganate. The yield of the acids **49** and **50** is 50%.[18]



The successive oxidation of 1-*O*-benzoyl-2,3-*O*-isopropylidene-α-D-mannofuranose **51** initially with $NaIO_4$ and then $KMnO_4$ leads to the formation of the D-lyxuronic acid derivative **52**.[19]

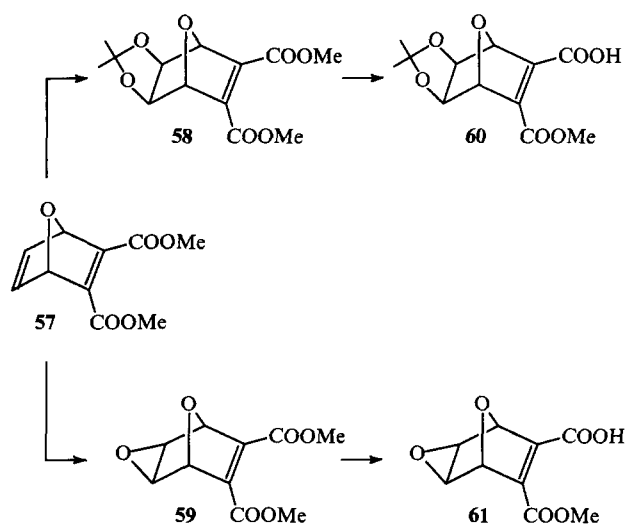


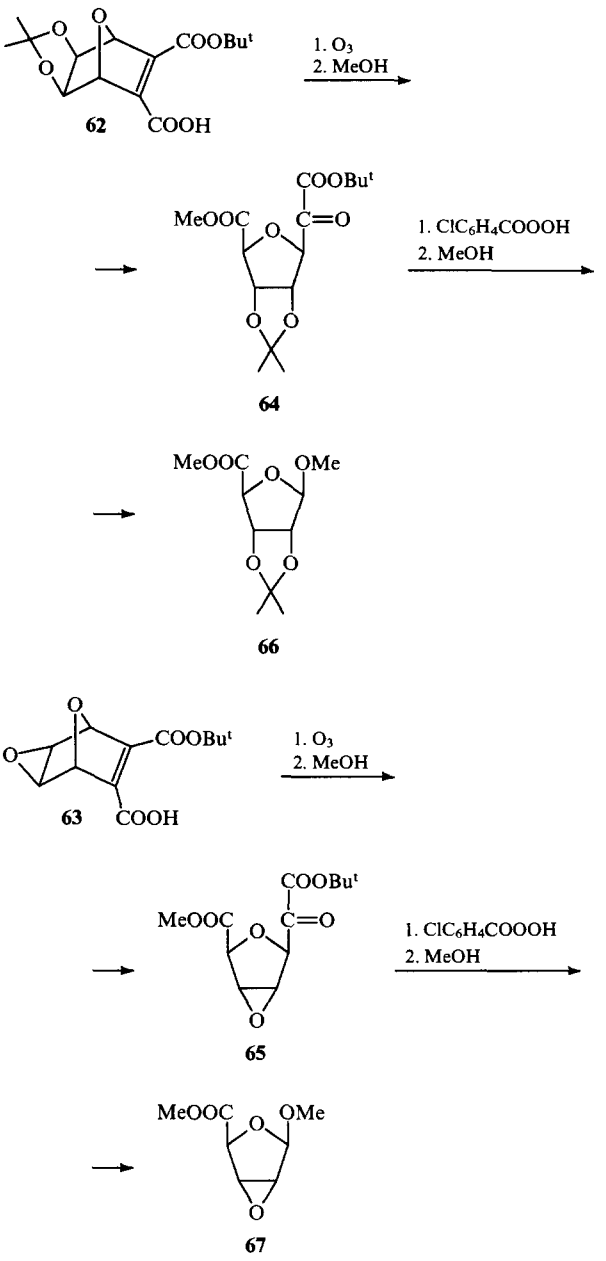
Silver carbonate on celite has been used as the oxidant for the synthesis of penturonic acids. Methyl D-xyluronate **40** and methyl D-riburonate **53** have been obtained by oxidising the hexofuranose acetals **36** and **37** in methanol.[20]



A procedure has been developed for the transformation of *O*-glycosides into *O*-glycuronides.[21] The successive tritylation and acetylation of the methyl riboside **54** afforded a fully protected derivative **55**, the oxidation of which with CrO_3 in acetone in the presence of sulfuric acid (the Jones reagent) gives rise to the D-riburonide acetate **56** in 67% yield.

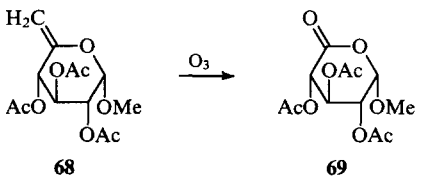
A chemical-enzymic strategy has been used in the total enantioselective synthesis of riburonides.[22] The Diels–Alder adduct **57** (the result of the condensation of furan with dimethyl ethynedicarboxylate) was transformed into the unsaturated esters **58** and **59**. Their asymmetric hydrolysis by pig liver esterase gave the half-esters **60** and **61** in fairly high optical yields. The *tert*-butyl esters **62** and **63** obtained from them were converted by ozonisation in methanol into the ketoacids **64** and **65**, the Baeyer–Villiger oxidation of which followed by methanolysis, afforded derivatives of D-riburonic acid — the acetal **66** and the epoxide **67**.





The L-enantiomer of the riburonide **66** has been obtained by the ozonolysis of the half-ester **60** and oxidation with *m*-chloroperbenzoic acid.

The conversion of the glucosene **68** into the 1,5-lactone of D-xyluronic acid **69** may serve as an example of a nontrivial and fairly general method of synthesis of penturonic acids.[23]

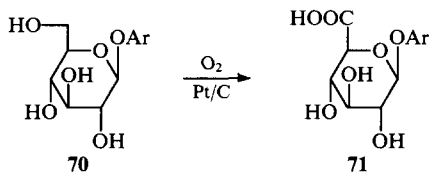


IV. Hexuronic acids

Like penturonic acids, hexuronic acids are obtained either by the catalytic oxidation of *O*-glycosides or by treating appropriately protected sugars with nonselective oxidants.

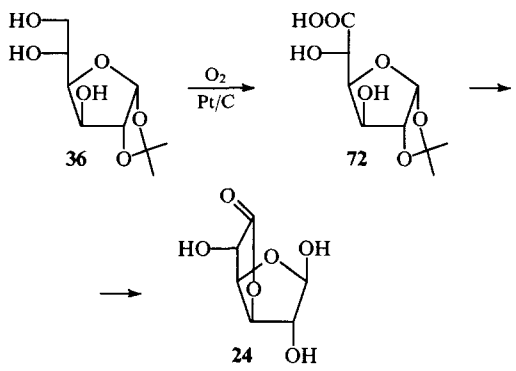
The conditions for the catalytic oxidation and the methods for the isolation and identification of alkyl *O*-glucuronides,

O-galacturonides, and *O*-mannuronides have been described.[24-26] Methyl α- and β-2-deoxyglucuronides and galacturonides have been synthesised by catalytic oxidation.[27] The methods of synthesis of phenyl and naphthyl β-D-glucuronides **71** from the corresponding aryl glycosides **70** have been described.[28,29]



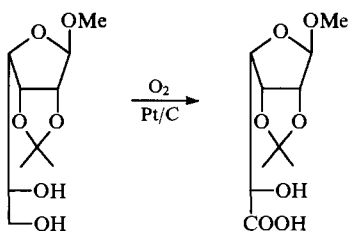
70 **71**

Derivatives of hexofuranoses can also be used for the preparation of uronic acids. Thus the oxidation of the glucofuranose acetal **36** with oxygen over platinum leads to the acid **72**, which is converted by lactone-formation into the glucurone **24** on heating in water.[30]



36 **72** **24**

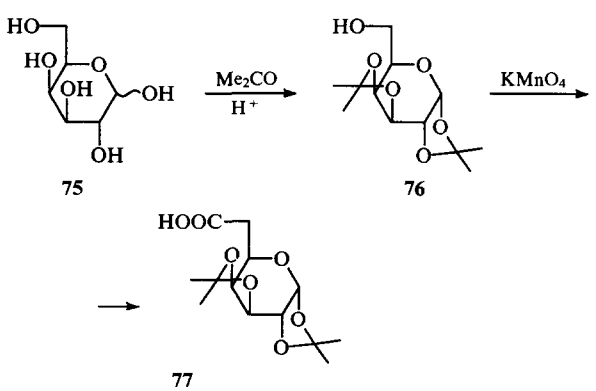
The catalytic oxidation of the D-gulofuranoside acetal **73** has been used in the synthesis of the D-guluronide **74**.[31]



73 **74**

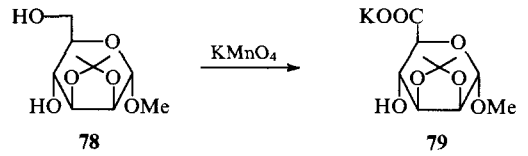
A review presenting more detailed data has been devoted to the catalytic oxidation of sugars.[32]

Appropriately protected sugars with a free primary hydroxy-group are smoothly oxidised to uronic acids by nonselective oxidants. The oxidation of the diacetal **76** obtained from D-galactose by $KMnO_4$ affords the galacturonic acid derivative **77**.[33]



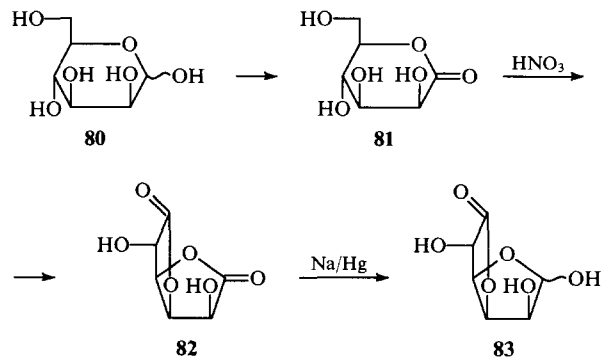
75 **76** **77**

The D-mannopyranoside acetal **78** can be oxidised by $KMnO_4$ to the acid **79** in an acceptable yield even in the presence of a free secondary hydroxy-group.[34]



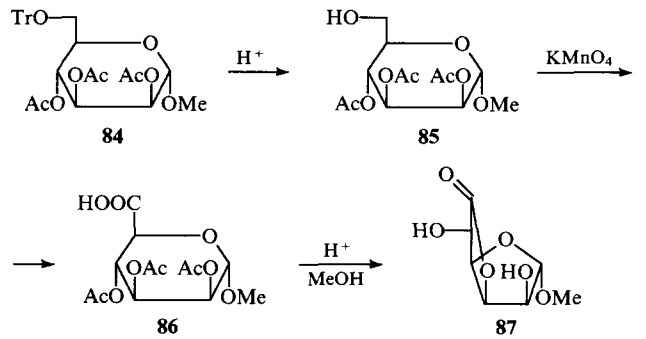
78 **79**

The electrolytic oxidation of D-mannose **80** leads to the formation of δ-mannonolactone **81**, the treatment of which with nitric acid gives rise to the dilactone of D-mannosaccharic acid **82**, while the reduction of the latter with sodium amalgam results in the formation of the 6,3-lactone of D-mannuronic acid **83**.[35]



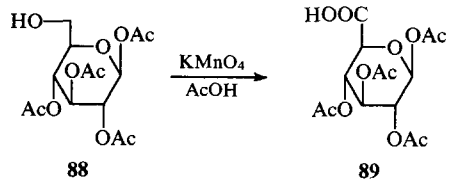
80 **81** **82** **83**

The oxidation with potassium permanganate in an acetone–acetic acid mixture of the sugar **85**, obtained from its 6-*O*-trityl precursor **84**, is yet another example of the synthesis of derivatives of D-mannuronide **86** and its lactone **87**.[36]



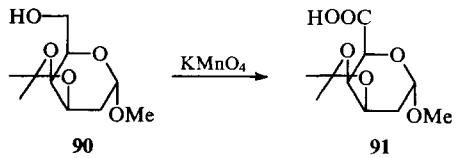
84 **85** **86** **87**

A similar synthetic scheme has been used in the oxidation of β-D-glucopyranose tetraacetate **88** to the full acetate of D-glucopyranuronic acid **89**.[37]

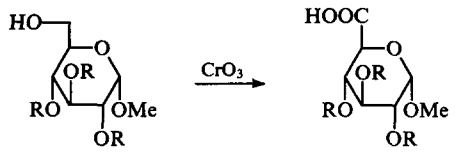


88 **89**

$KMnO_4$ has been used to oxidise the acetal of methyl 2-deoxy-α-D-galactopyranoside **90** to the acid **91**.[38]



90 **91**

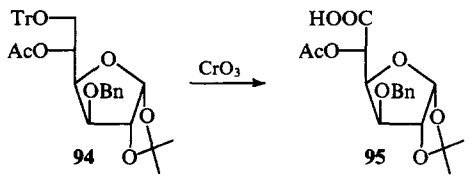


92 93

R = Me, Bn.

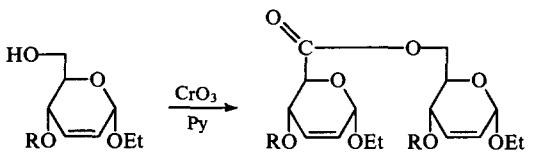
CrO_3 may be used as the oxidant in the synthesis of glucuronic acid derivatives **93** from the partly protected glucopyranosides **92**.[39,40]

A convenient method of synthesis of the D-glucofuranuronic acid derivative **95** involves the oxidation of the fully protected glucofuranose **94** by CrO_3 in acetone in the presence of sulfuric acid.[41]



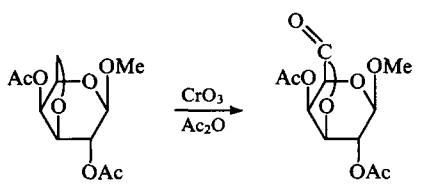
94 95

The formation of the ester **97** has been observed in the oxidation of the unsaturated sugar **96** with CrO_3 in pyridine.[42]



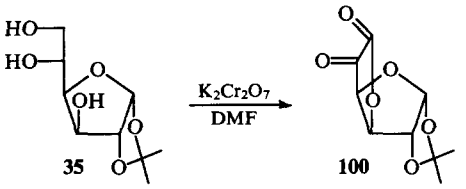
96 97

The oxidation of 3,6-anhydrogalactopyranoside **98** with CrO_3 in acetic anhydride leads to the 6,3-lactone **99**.[43]



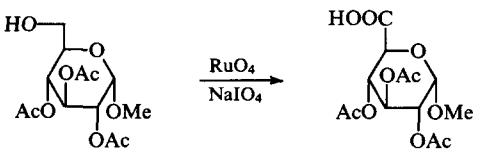
98 99

The sugar **35** can be oxidised by potassium dichromate in dimethylformamide (DMF) to the ketolactone **100**.[44]

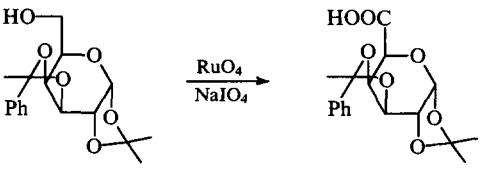


35 100

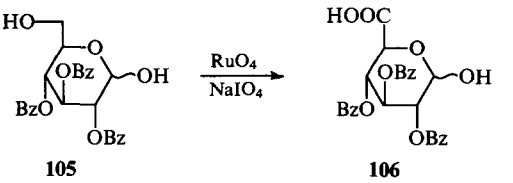
Ruthenium tetroxide together with sodium metaperiodate has found an application as the oxidant in the synthesis of hexuronic acids. The acids **103** and **104** have been obtained by this method from the sugars **101** and **102**. It has been shown for sugar **105**, with free primary and hemiacetal hydroxy-groups, that the oxidation does not involve the anomeric centre and leads to the acid **106**.[15]



101 103

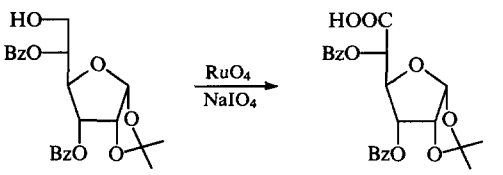


102 104



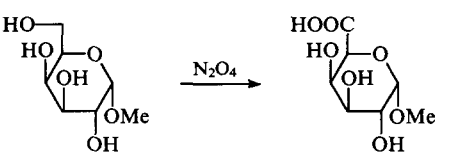
105 106

D-Allofuranose **107** is transformed into D-allofuranuronic acid **108** on oxidation with RuO_4.[45]



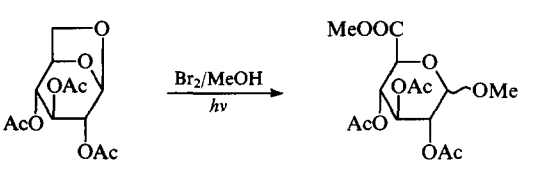
107 108

When the D-galactopyranoside **109** is treated with nitrogen(IV) oxide, the latter exhibits an oxidative selectivity, affording the D-galacturonide **110**.[46]



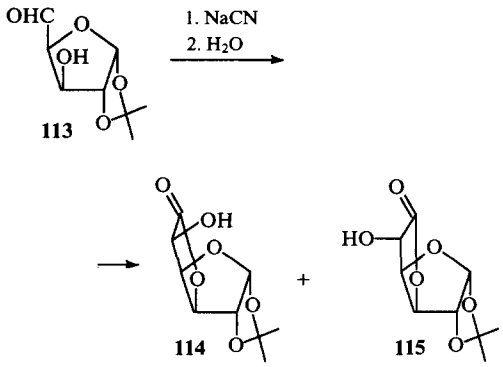
109 110

Despite the low yield, the oxidation of the levoglucosan acetate **111** with bromine on irradiation with UV light to give the ester **112** is nevertheless of interest.[47]

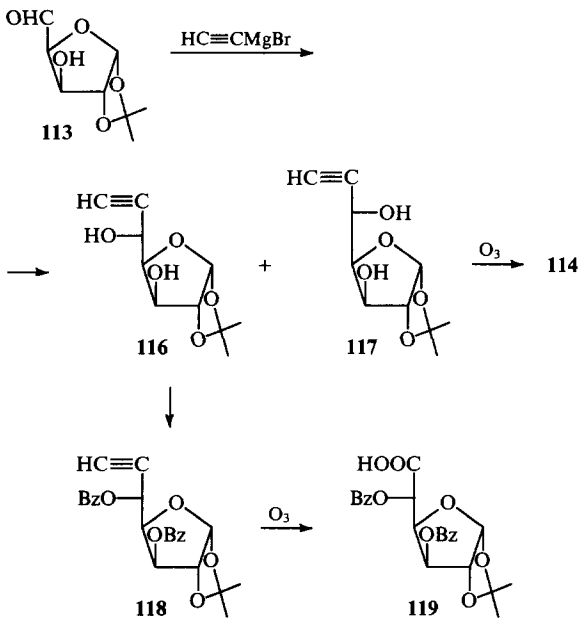


111 112

The introduction of a carboxy-group is achieved in a number of instances by the addition of nucleophiles to the aldehyde group. Two lactones — L-iduronolactone **114** and D-glucuronolactone **115** — have been obtained from 1,4-pento-dialdoxylofuranose **113** by the cyanohydrin synthesis.[48]

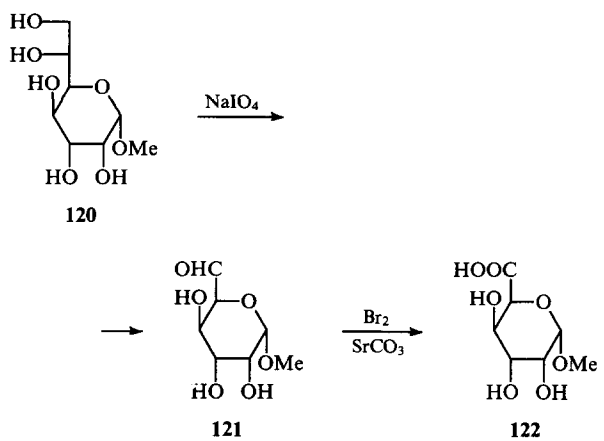


The addition of ethynylmagnesium bromide to the aldehyde **113** affords ethynyl sugars with D-gluco- and L-ido-configurations (compounds **116** and **117** respectively). The lactone **115** and the acid **119** have been obtained by the ozonolysis of compound **116** and the dibenzoate **118**.[49]

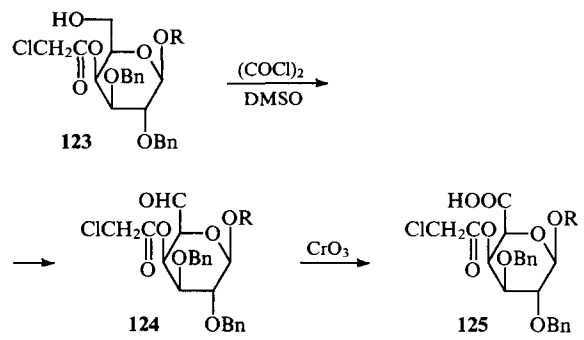


1,4-Pentodialdoribofuranose has also been used for reactions of a similar type.[50]

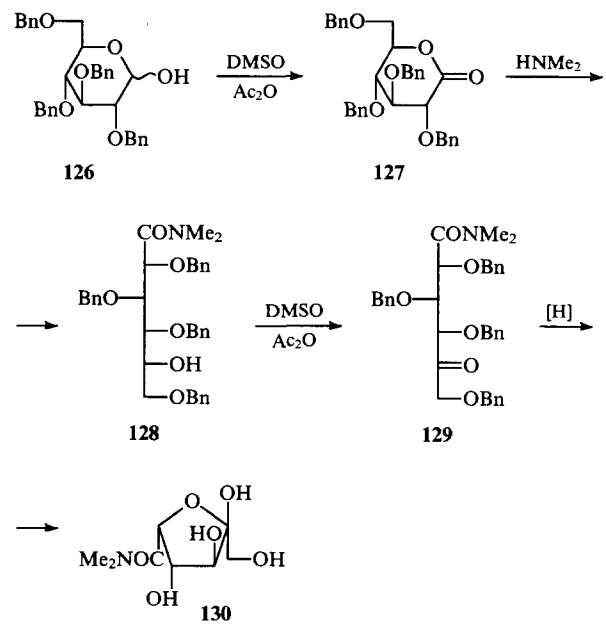
Heptopyranosides can also serve as a source of hexuronic acids. Thus oxidation of the sugar **120** (the product of the cyanohydrin synthesis from D-glucose) with sodium metaperiodate results in the formation of the aldehyde **121**, the treatment of which with bromine in the presence of strontium carbonate gives the D-guluronide **122**.[51]



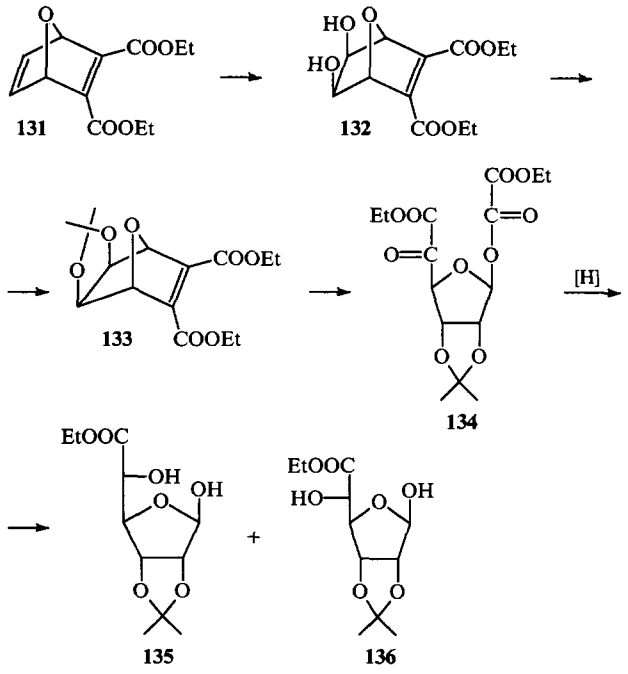
The Swern oxidation of the primary hydroxy-group in sugars to the aldehyde group followed by the conversion of the latter in one way or another into a carboxy-group constitutes yet another procedure for the preparation of uronic acids. Treatment of the galactopyranoside **123** with the dichloride of oxalic acid in dimethyl sulfoxide (DMSO) at −78 °C leads to the aldehyde **124**, the oxidation of which by the Jones reagent affords the acid **125**.[52]



A rare example of the synthesis of uronic acids in a series of ketoses has been demonstrated by Kuzuhara and Fletcher.[53] The glucopyranose **126** with the free hemiacetal hydroxy-group was oxidised by Pfitzner–Moffatt method to the D-gluconolactone **127**. The gluconamide **128** obtained from it was oxidised by the same method to the ketone **129**. The removal of the protecting benzyl groups from the latter leads to the amide of L-sorburonic acid **130**.

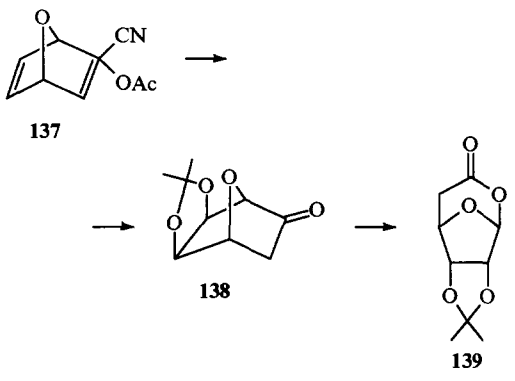


Fairly effective methods have been developed for the preparation of hexuronic acids by the diene synthesis. The total synthesis of uronic acids with the D,L-talo- and allo-configurations has been described.[54] The adduct **131**, obtained as a result of the condensation of furan with methyl ethynedicarboxylate, is oxidised by OsO_4 to the diol **132**. The ozonolysis of its acetal **133** followed by a thermal rearrangement leads to the ester of the ketoacid **134**, the hydrogenation of which over platinum affords the D,L-taluronate **135** and the D,L-alluronate **136**.



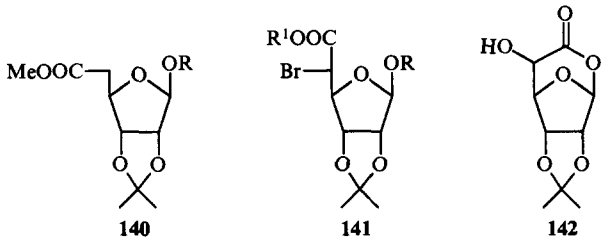
131 132 133 134 135 136

The condensation of furan with α-acetoxyacrylonitrile leads to the formation of the adduct **137**, which is transformed into the ketone **138** by successively: oxidation with OsO_4, acetal formation, and treatment with MeONa. Its oxidation with *m*-chloroperbenzoic acid leads to the acetal of 5-deoxy-D,L-ribo-hexofuranurono-6,1-lactone **139**.[55]



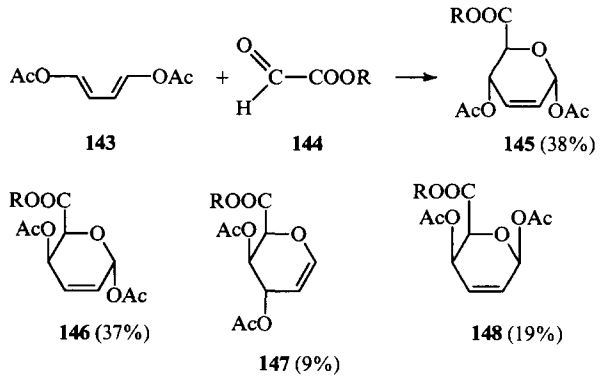
137 138 139

The use of cyanovinylcamphanate for the condensation makes it possible to obtain, as a result of total asymmetric synthesis, the optically active uronic acid derivatives **140**–**142**.[56–60]



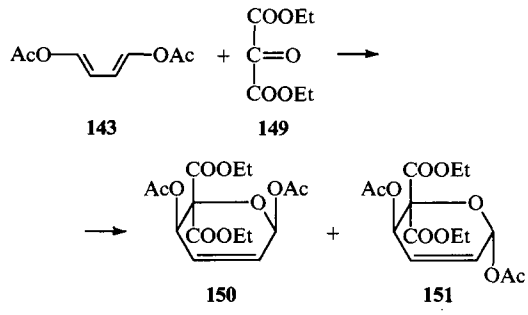
140 141 142

The Diels–Alder reaction between 1,4-diacetoxybuta-1,3-diene **143** and the alkyl glyoxylate **144** leads to a way of synthesising racemic unsaturated hexopyranuronic acids **145**–**147**.[61] When the reaction is carried out under mild conditions, the isomer **148** with an admixture of compound **145** (13%) is formed.



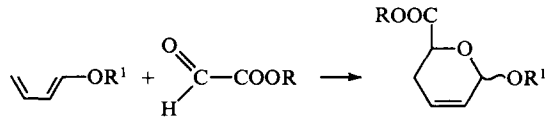
143 144 145 (38%) 146 (37%) 147 (9%) 148 (19%)

The condensation of the substituted butadiene **143** with diethyl mesoxalate **149** leads to the formation of the isomeric compounds **150** and **151**,[61] which are related to uronic acids.



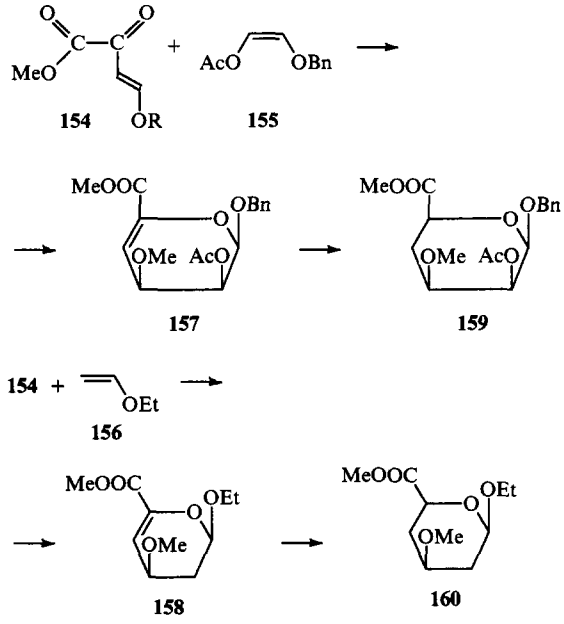
143 149 150 151

The unsaturated 2,3,4-trideoxyuronides **153** are formed on condensation of the glyoxylates **144** with 1-alkoxybuta-1,3-dienes **152**.[62–64]



152 144 153

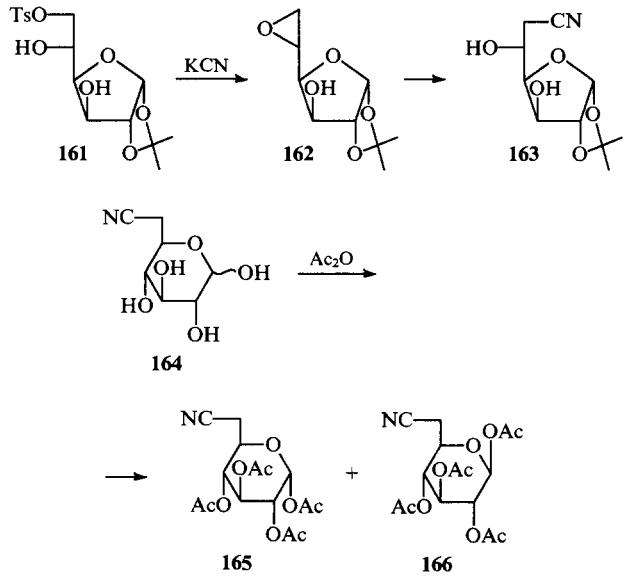
The 4-deoxy- and 2,4-dideoxy-D,L-mannopyranuronides **159** and **160** have been obtained by the hydrogenation of the Diels–Alder adducts **157** and **158** formed as a result of the condensation of compound **154** with the dienophiles **155** and **156**.[65]



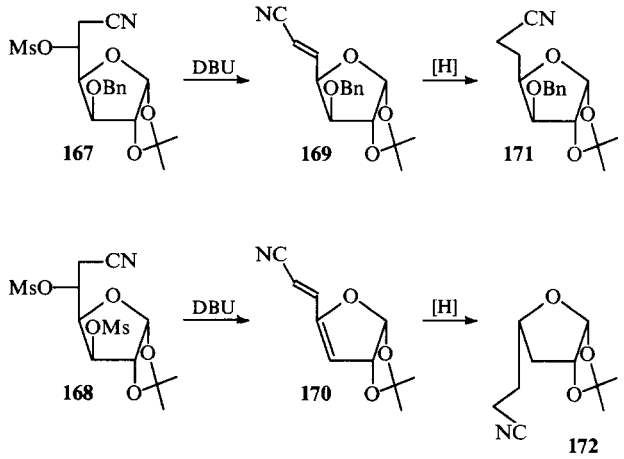
154 155 157 159 156 158 160

V. Higher and branched uronic acids

The substitution of primary tosyloxy-groups in sugars by potassium cyanide is used to obtain uronic acids with a lengthened carbon chain. It has been shown[66] that the interaction of D-glucofuranose tosylate **161** with potassium cyanide in acetone leads to the formation of the α-epoxide **162**, while the reaction in ethanol affords the nitrile **163**. The acetates of the α- and β-anomers of 6-deoxyhepturonitrile **165** and **166** have been obtained by the acid hydrolysis of the nitrile **163** and the acetylation of the D-pyranuronitrile **164** formed.



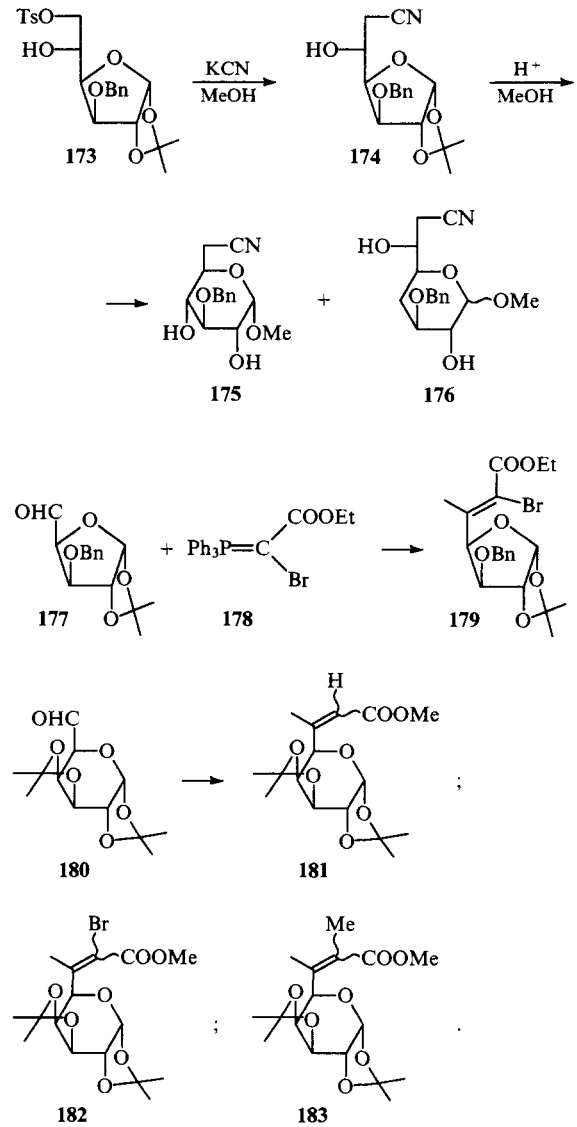
The monomethanesulfonyl derivative **167** and the di(methanesulfonyl) derivative **168** of the nitrile **163** are readily transformed on treatment with 1,5-diazabicyclo[5.4.0]undec-5-ene (DBU) into the unsaturated nitriles **169** and **170**, the reduction of which gives rise to D-dideoxyheptofuranurono-nitrile **171** and L-trideoxyheptofuranurononitrile **172**.



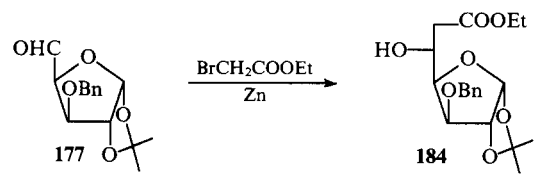
The interaction of the tosylate **173** with potassium cyanide in methanol leads to the 6-deoxyurononitrile **174**, the methanolysis of which results in the formation of the nitriles of the hexopyranuronide **175** and the hexofuranuronide **176**.[67]

The carbon chain of sugars can be built up by several units at once with the aid of the Wittig reaction. Treatment of the aldehyde **177** with bromoethoxycarbonylmethylenetriphenylphosphorane **178** affords a satisfactory yield of the unsaturated uronic acid ester **179**.[68]

This approach has been used to obtain the analogues of lincomycin **181**–**183** from the aldehyde **180**.[69]



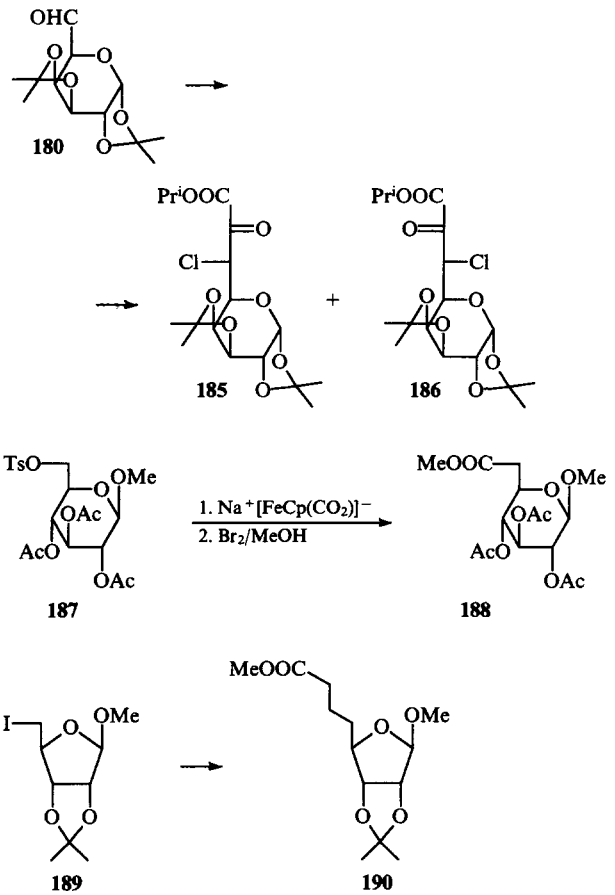
The Reformatskii reaction has been used to synthesise higher uronic acids. The condensation of the aldehyde **177** with ethyl bromoacetate and zinc gives rise to the ethyl 6-deoxyheptofuranuronate derivative **184**.[70]



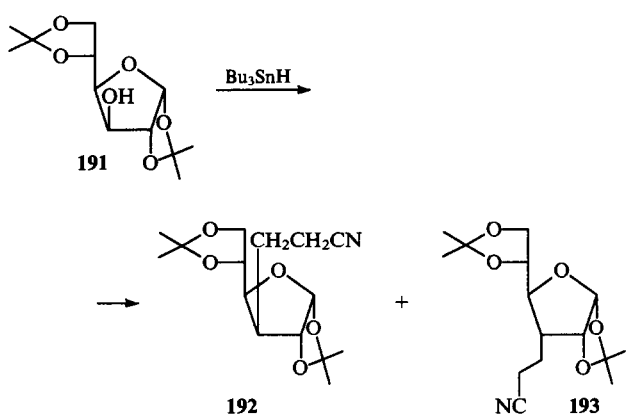
Under the conditions of the Darzens condensation, the aldehyde **180** condenses with dichloroacetic acid ester to form a diastereoisomeric mixture of glycidic esters, which are converted by treatment with $MgCl_2$ into the chlorodeoxyketouronic acid esters **185** and **186**.[71]

A method for lengthening the carbon chain of sugars with formation of uronic acids has been demonstrated.[72] It was shown that the interaction of the tosylate **187** with sodium dicarbonylcyclopentadienylferrate and then with bromine in methanol leads to the hepturonic acid ester **188**.

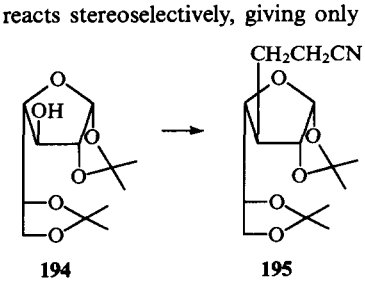
The free radical species generated from the iododeoxysugar **189** in the Zn–$FeCl_3$–NaI–Py system adds to methyl acrylate, affording the trideoxyoctofuranuronic acid ester **190**.[73]



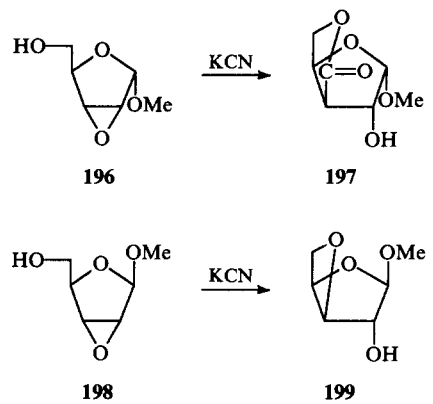
Alkyl halides form a C–C bond with electron-deficient alkenes in the presence of tributyltin hydride. It has been shown[74] that this reaction can be extended also to alcohols. The interaction of glucose diacetal **191** with acrylonitrile and tributyltin hydride results in the formation of a mixture of the isomeric uronic acid nitriles **192** and **193** branched at the C(3) carbon atom.



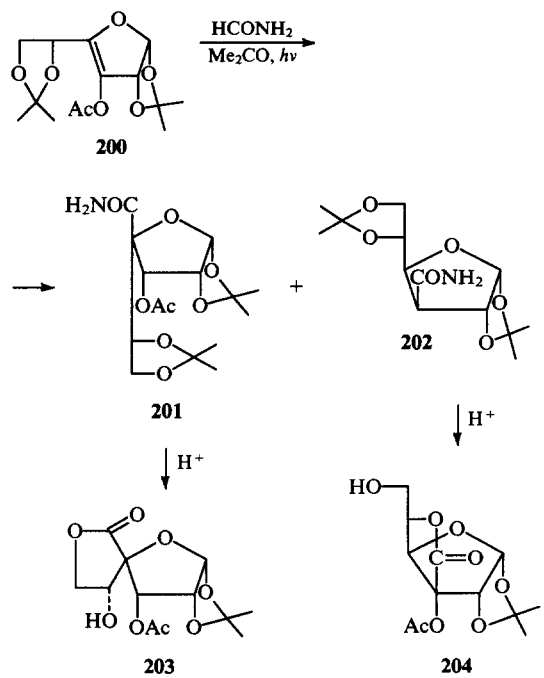
In contrast to the sugar **191**, the galactofuranose diacetal **194** reacts stereoselectively, giving only the nitrile **195**.



The opening of the oxirane ring on treatment with potassium cyanide can be used to obtain branched uronic acids.[75] Thus heating of 2,3-anhydro-α-D-riboside **196** in an aqueous solution of KCN gives rise to the lactone **197**. The β-D-riboside **198** is converted under these conditions into the 3,5-anhydro-β-D-riboside **199**.

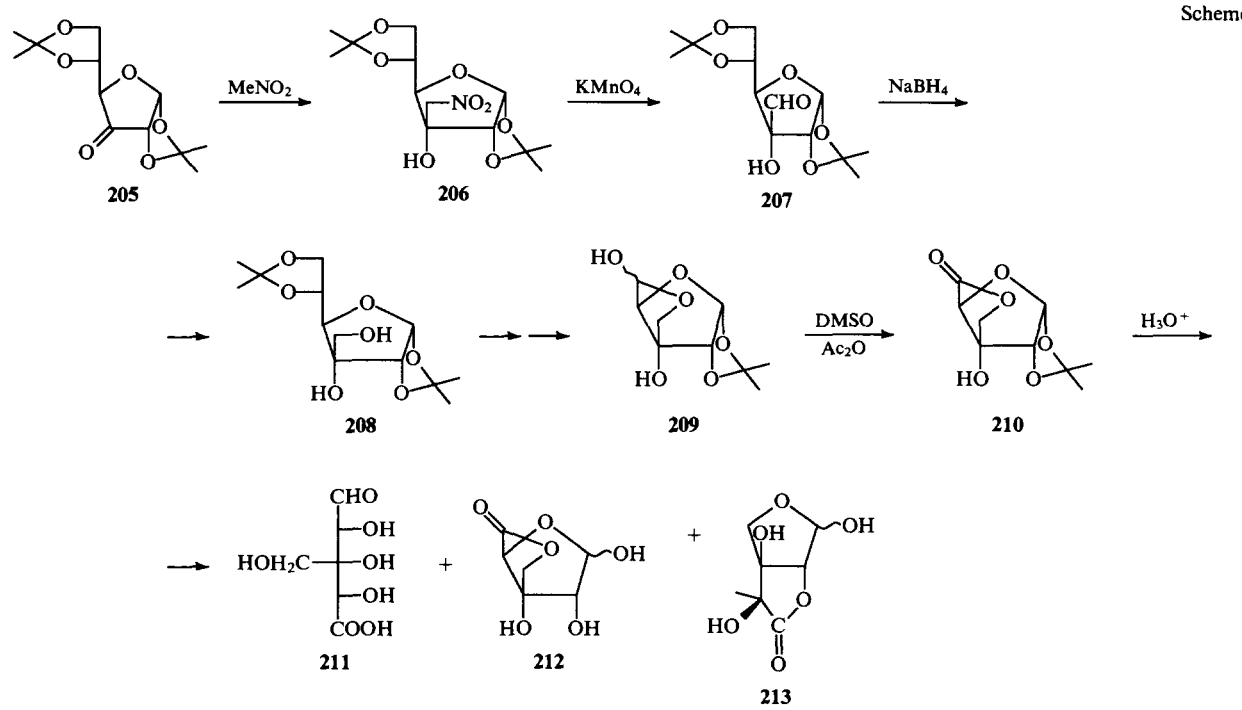


The photoamidation of the unsaturated sugar **200** leads to the formation of the two isomeric carbamoylation products **201** and **202**.[76] Mild acid hydrolysis results in the formation of the spirolactone **203** from the amide **201** and of the lactone **204** from the isomer **202**.

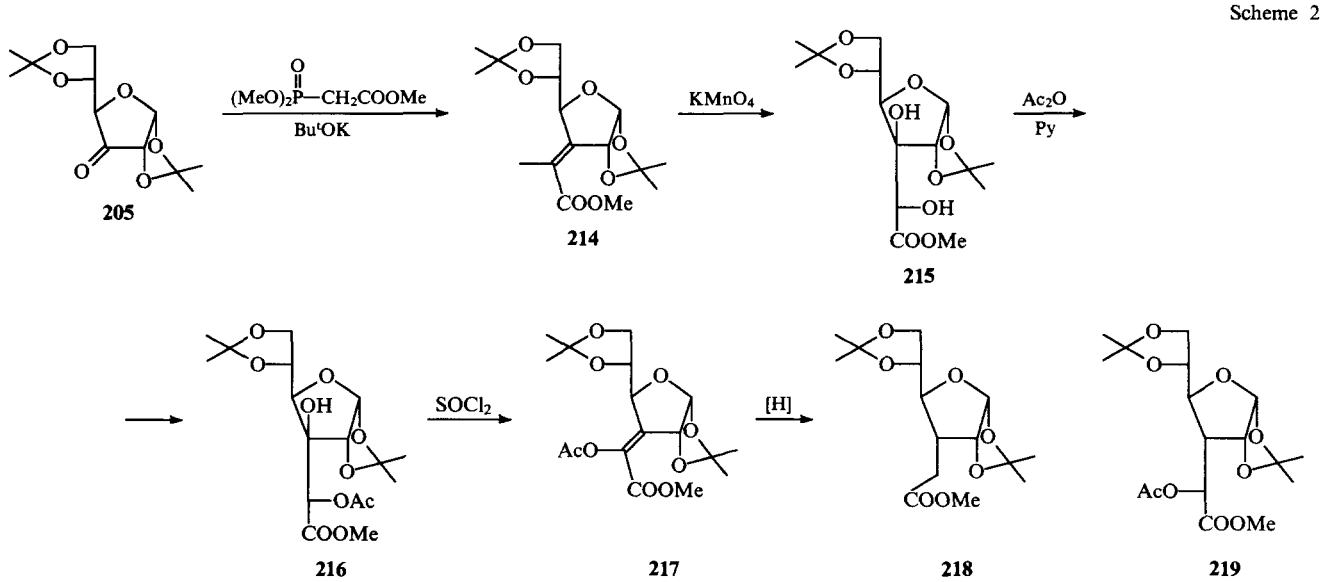


3-*C*-Hydroxymethyl-D-riburonic acid **211** has been detected in human bile as a complex of bilirubin glycosides. It was synthesised by treating the keto-derivative **205** with nitromethane and Bu^{t}OK. The Nef oxidation of the resulting nitroalcohol **206** with $KMnO_4$ led to the formation of the aldehydoalcohol **207**, which was smoothly reduced with $NaBH_4$ to the alcohol **208**. Successive acylation of the primary hydroxy-group in compound **208**, the removal of the isopropylidene protecting group, and the metaperiodate oxidation of the 5,6-diol group, and deacetylation led to the synthesis of the hemiacetal **209**. Its Pfitzner–Moffatt oxidation leads to the lactone **210**, the mild acid hydrolysis of which affords the acid **211** together with two of its isomeric lactones—**212** and **213** (Scheme 1).[77]

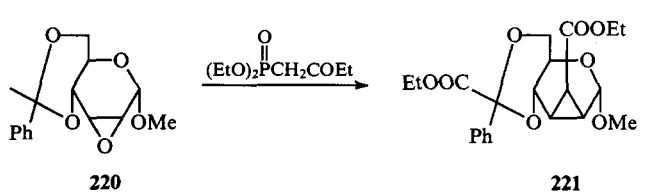
Scheme 1



Scheme 2

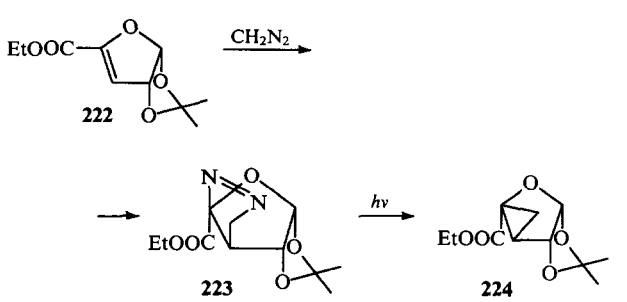


The condensation of the hexulose **205** with trimethyl phosphonoacetate in the presence of Bu^{t}OK leads to the unsaturated ester **214**, the hydroxylation of which with $KMnO_4$ in pyridine leads stereospecifically to the diol **215**. Its monoacetate **216** is transformed on treatment with thionyl chloride in pyridine into the enol acetate **217**, the reduction of which with hydrogen over platinum in methanol affords the deoxyacid ester **218**. The hydrogenation of the enol acetate **217** over palladium in ethyl acetate produces the acetate of the ester **219** (Scheme 2).[78]

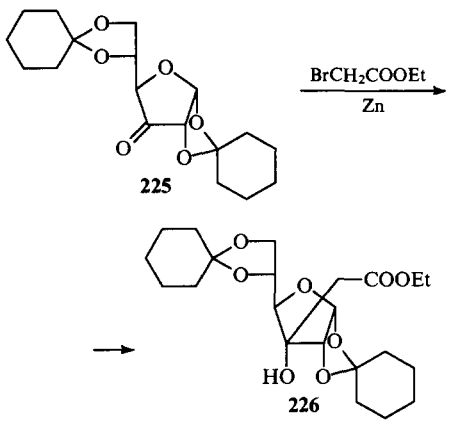


The ethyl ester of the branched uronic acid **221** has been obtained by treating the oxirane **220** with triethyl phosphonoacetate.[79]

The interaction of the eneuronate **222** with diazomethane and subsequent photolysis of the pyrazoline **223** formed give rise to the uronic acid ester **224** with a cyclopropane ring.[80]

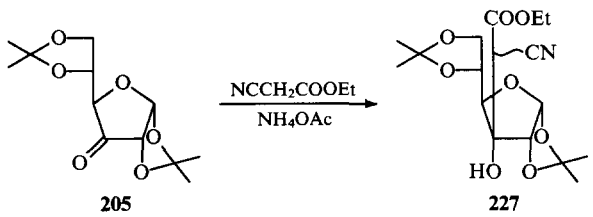


The applicability of the Reformatskii reaction in the synthesis of branched deoxyuronic acid esters has been demonstrated.[81] The condensation of the ketone **225** with ethyl bromoacetate and zinc affords the deoxyacid ester **226**.



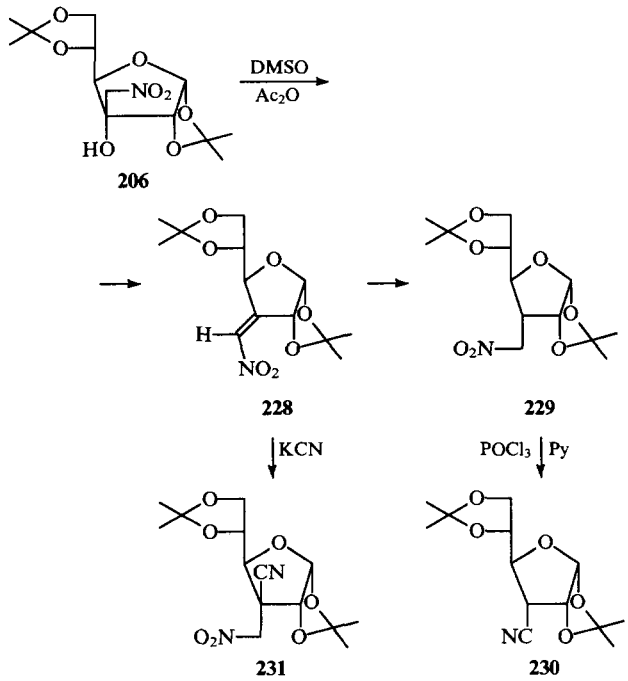
225 **226**

The Knoevenagel reaction between the carbonyl compound **205**, cyanoacetic ester, and ammonium acetate leads to the ester nitrile **227**, which gives rise to the possibility of synthesising branched uronic acids with an additional carboxy-group.[82]



205 **227**

The nitroalcohol **206**, formed as a result of the condensation of compound **205** with nitromethane, leads to extensive possibilities for the synthesis of a whole series of derivatives of branched uronic acids.[83] The dehydration of the nitroalcohol by acetic anhydride in DMSO affords the 3-*C*-methylene derivative **228**. The product of its reduction **229** is converted into the nitrile **230** on treatment with phosphoryl chloride in pyridine. The alkene **228** readily combines with potassium cyanide, giving the nitrile **231**.

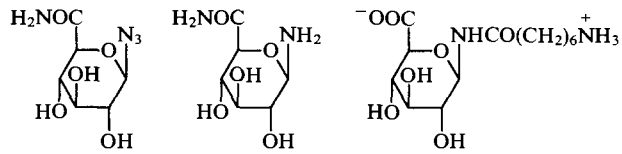


206 **228** **229** **231** **230**

VI. Aminodeoxyuronic acids

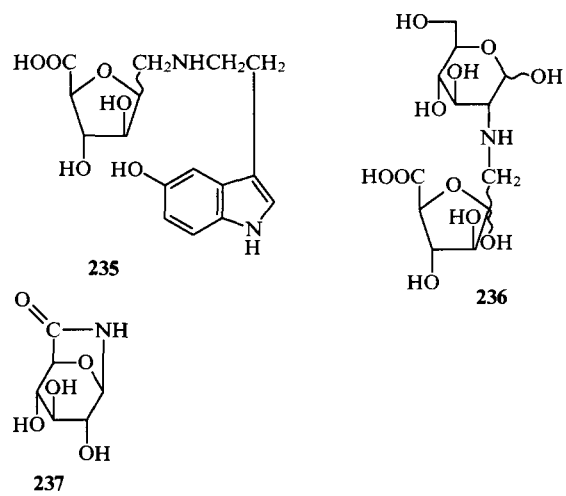
Aminodeoxyuronic acids are fairly common in nature. They have been detected in many bacterial polysaccharides and in nucleoside antibiotics.

The glycosylamines derived from uronic acids, which on the grounds of formal considerations can be considered in this section, are obtained by reducing the corresponding glycosyl azides; the latter are formed in their turn from acetylated halogenoses and sodium azide. The azide **232** and the amine **233** synthesised in this way exhibit antitumour activity.[84]



232 **233** **234**

The ω-aminoheptanoyl derivative of β-D-glucuronopyranosylamine **234** is an effective inhibitor of β-D-glucuronidase.[85] Direct treatment of uronic acids with amines is accompanied by the Amadori rearrangement. Thus the condensation of glucuronic acid with serotonin and glucosamine afforded the derivatives **235** and **236** of 1-amino-1-deoxy-D-fructuronic acid,[86,87] although the lactam **237** could be isolated on treatment with ammonia.[88]



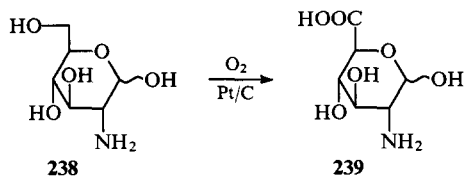
235 **236**

237

The synthesis and reactions of uronic acid nucleosides (*N*-uronides) have been considered in a review.[89]

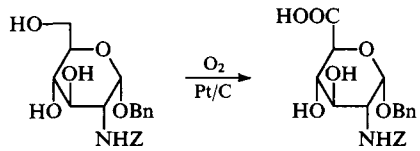
The methods of synthesis of the aminodeoxyuronic acid forming part of the composition of nucleoside antibiotics have been partly described in Suhadolnik's book.[90]

Mild oxidation by oxygen over platinum at pH 7 makes it possible to obtain 2-amino-2-deoxy-D-glucuronic acid **239** from glucosamine **238**.[91]



238 **239**

Since the free amino-group lowers the activity of the platinum catalyst, sugars with protected amino-group and hemiacetal hydroxyl are usually employed for the oxidation. The oxidation of the sugar **240** yields the acid **241**, the hydrolysis of which leads to the aminoacid **239**.[92]



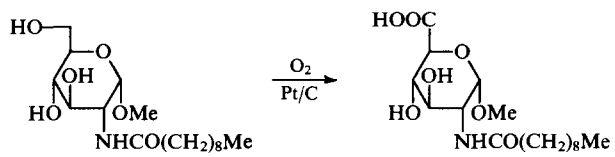
240 241

Z = $C_6H_5CH_2COO$.

It has been shown[93-95] that an increase in the rate of stirring of the solution leads to an appreciable improvement of the yield of the acid synthesised from the sugar **240** and its β-anomer.

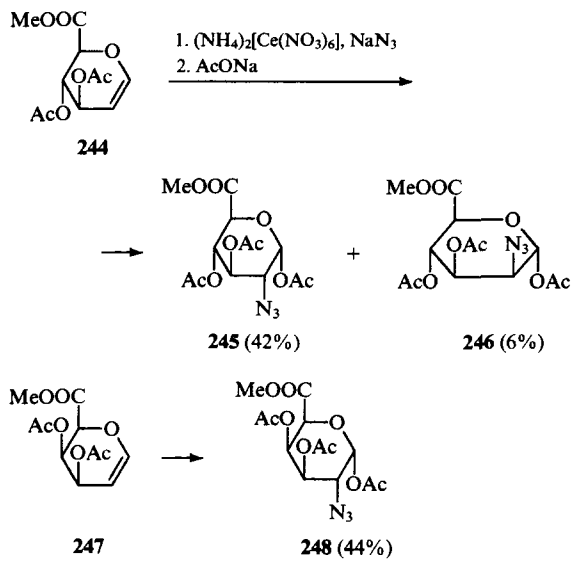
The corresponding aminouronic acids have been obtained similarly from D-galactosamine and D-mannosamine.[96-98]

Oxidation by oxygen over platinum has been used to obtain from the methyl glycoside derived from *N*-decanoyl-D-glucosamine **242** the aminodeoxyuronic acid derivative **243**, which forms part of the composition of the antibiotic aridicin.[99]



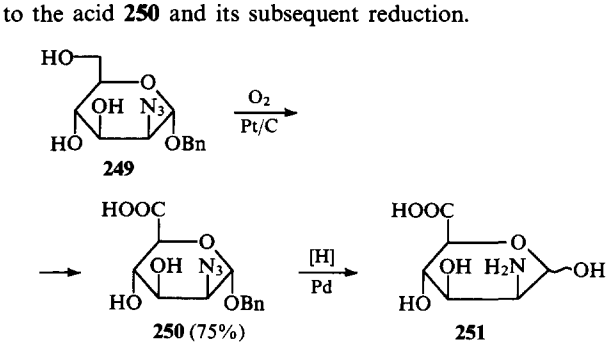
242 243

Another approach to the synthesis of 2-amino-2-deoxyuronic acid has been proposed.[100] It consists in the successive treatment of the glycal **244** with cerium ammonium nitrate and sodium azide and acetate, which results in the formation of the azides **245** and **246**. The azide **248** was obtained from the glycal **247**. The hydrogenolysis of the azides affords high yields of the corresponding amines.



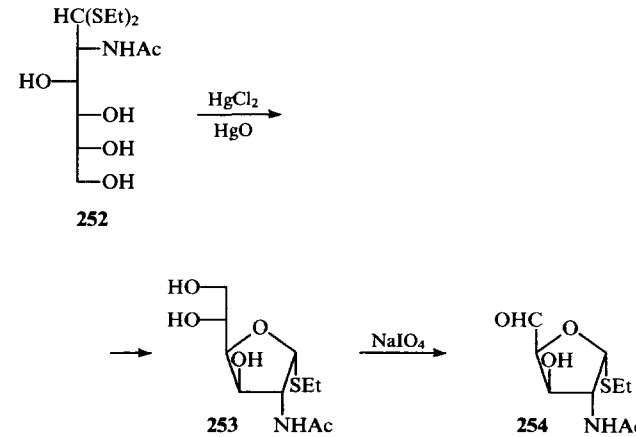
244 245 (42%) 246 (6%) 247 248 (44%)

An alternative scheme for the synthesis has been developed by Paulsen et al.[98] who employed catalytic oxidation of the azide **249** to the acid **250** and its subsequent reduction.



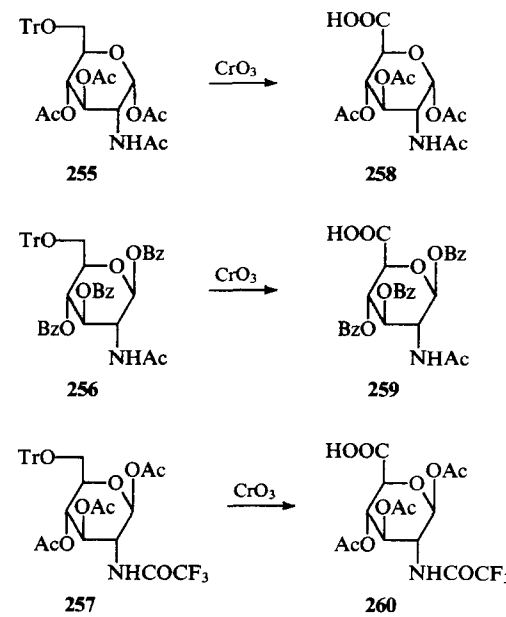
249 250 (75%) 251

The diethyl dithioacetal of 2-acetamido-2-deoxy-D-glucose **252** is a potential source for the synthesis of aminodeoxyuronic acids. The aldehyde **254**, obtained from the furanose **253** by periodate oxidation, may be readily converted into the corresponding acid.[101]



252 253 254

It has been shown[102] that the trityl derivatives **255**, **256**, and **257** of the acylated glucosamine are readily oxidised by the Jones reagent to the corresponding aminodeoxyglucuronic acids **258**–**260**.

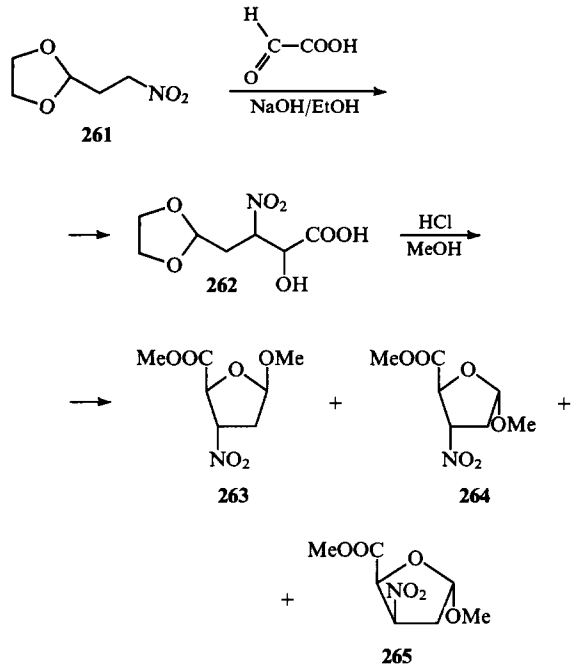


255 258 256 259 257 260

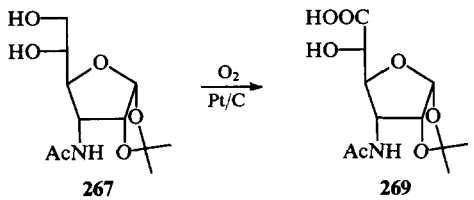
Since the nitro-group in sugars can be readily reduced, nitrodeoxyuronic acids are of definite interest. The synthesis of compounds of this type has been described. The nitroacid **262**, formed from the ethylene acetal of 3-nitropropanal **261** and glyoxylic acid, affords a mixture of the isomeric 2,3-dideoxynitro-D,L-furanuronates **263**, **264**, and **265** in HCl solution in methanol.[103]

The same authors proposed 2,3-*O*-isopropylidene-D-glyceraldehyde as the initial compound for the synthesis of 3-nitrouronic acids of this type.[104]

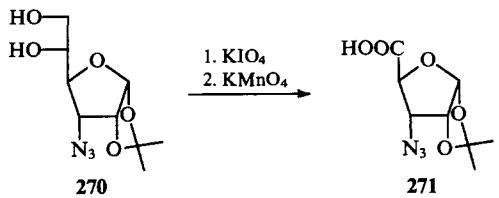
3-Acetamido-3-deoxy-α-D-ribofuranuronic acid **268** has been obtained by oxidising the pentofuranose **266** with $KMnO_4$ and by the successive treatment of the hexofuranose **267** with $NaIO_4$ and Br_2.[105]



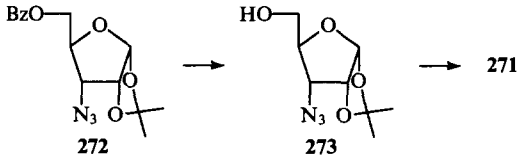
Catalytic oxidation of 3-acetamidoallofuranose **267** leads to the 3-amino-3-deoxy-D-allofuranuronic acid derivative **269**.[106,107]



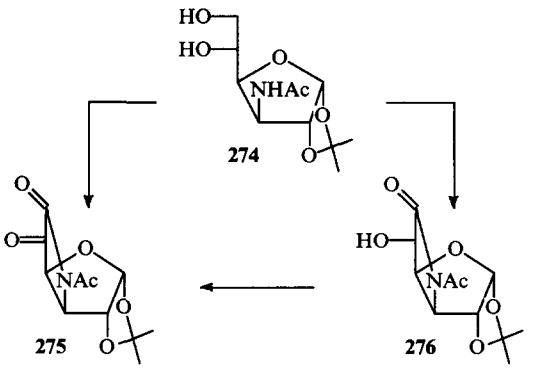
The successive oxidation of the azide **270** with KIO_4 and $KMnO_4$ leads to a satisfactory result in the synthesis of 3-azido-3-deoxyriburonic acid **271**.[108]



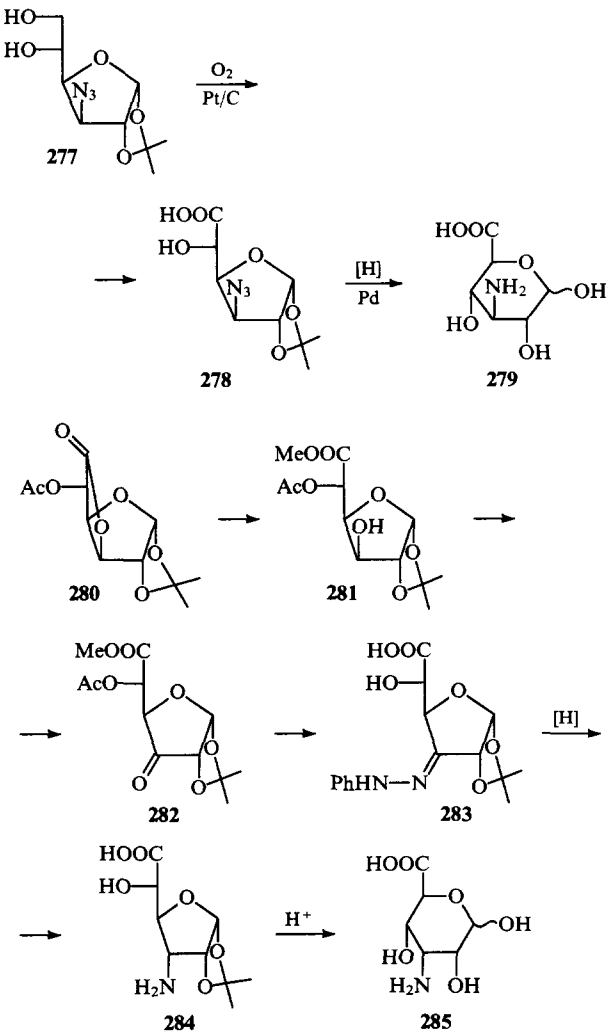
The acid **271** has been obtained by the debenzoylation of the azide **272** and the oxidation of the resulting alcohol **273** with $KMnO_4$.[109]



The oxidation of 3-acetamido-3-deoxyglucofuranose **274** with pyridinium dichromate in DMF leads to the ketolactone **275**, while oxidation with the Jones reagent affords the lactam **276**.[44]

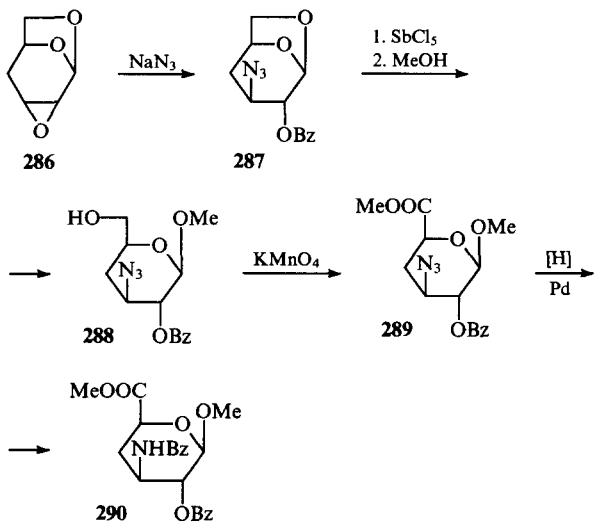


3-Amido-3-deoxyglucuronic acid **279** has been obtained from the azide **277**, which was oxidised by oxygen over platinum to the acid **278** and the product of its spontaneous hydrolysis was reduced over palladium, which led to the isolation of the required aminoacid **279**.[110]



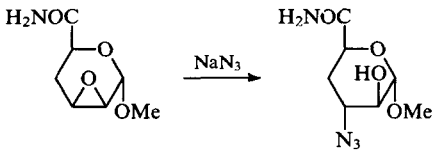
The transesterification of the lactone **280** in methanol, catalysed by an anion-exchange resin, and the oxidation of the resulting alcohol **281** with chromium trioxide in ethyl acetate lead to the ketone **282**. Its phenylhydrazone **283** is reduced by hydrogen over platinum to the aminoacid **284**, the acid hydrolysis of which affords 3-amino-3-deoxy-D-alluronic acid **285**.[111]

The ezoaminuronic acid derivative **290**, which forms part of the composition of the antibiotic ezomycin, has been obtained from the oxirane **286**, which is converted into the azide **287** on heating with sodium azide and acylation. The alcohol **288**, formed as a result of the opening of the 1,6-anhydro-ring by antimony pentachloride, is oxidised with $KMnO_4$, the acid is esterified, the ester **289** is reduced, the amino-group is benzoylated, and 3-benzamido-3,4-dideoxy-D-glucopyranuronide **290** is obtained.[112]



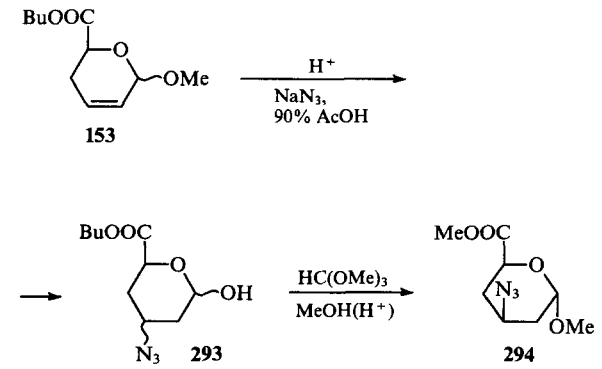
286 287 288 289 290

The 3-azido-3,4-dideoxyuronamide **292** is formed as a result of the interaction of the oxirane **291** with sodium azide.[113]

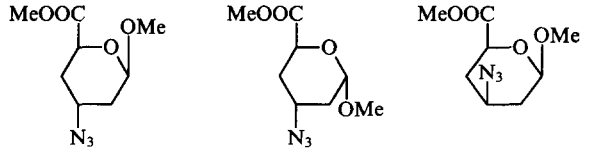


291 292

The unsaturated 4-deoxyuronides **153** interact with sodium azide in 90% acetic acid to form a mixture of the isomeric azides **293**, the treatment of which with orthoformic ester in methanol leads to the isomeric 3-azido-3-deoxypyranuronides **294**–**297**.[114]

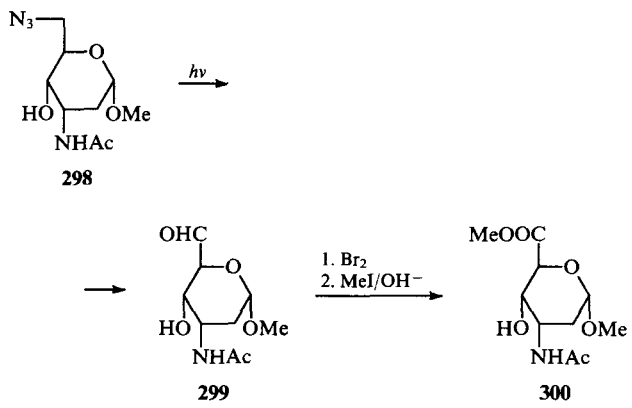


153 293 294



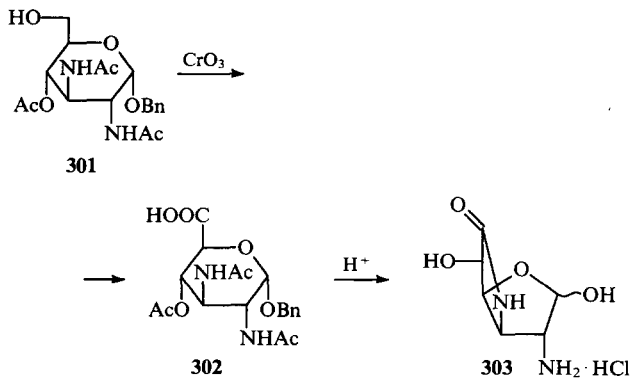
295 296 297

The primary azido-group in sugars is capable of being transformed into an aldehyde as a result of photocleavage. The aldehyde **299**, obtained on UV irradiation of the azide **298**, is oxidised with bromine, esterified, and the ester of the methyl glycoside derived from 3-acetamido-2,3-dideoxy-D-allopyranuronic acid **300** is isolated.[115]



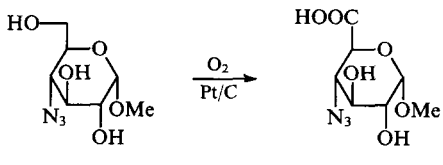
298 299 300

Diaminouronic acids have been detected in certain polysaccharides. The 2,3-diacetoamidouronic acid **302** has been obtained when the α-benzyl glycoside derived from 2,3-diacetamidoglucopyranose **301** was oxidised with the Jones reagent. Hydrolysis of the acid **302** leads to the 2-amino-6,3-lactam **303**.[116]



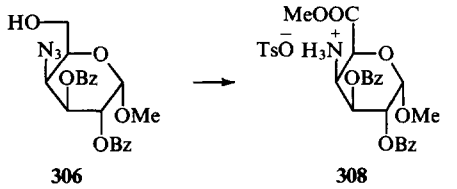
301 302 303

Apart from the methods of synthesis of 4-amino-4-deoxyuronic acids (forming part of the composition of the nucleoside antibiotics gougerotin and blasticidin S) considered in Suhadolnik's review,[90] there are at least two further examples of their synthesis in the literature. It has been shown[108] that the 4-azido-4-deoxy-D-glucopyranoside **304** is smoothly oxidised by oxygen over platinum to the azidoacid **305**.

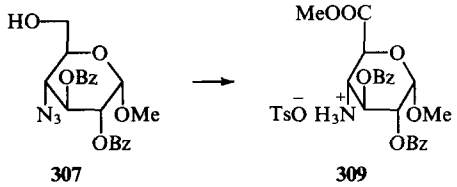


304 305

The oxidation of the 4-azidosugars **306** and **307** with the D-galacto- and D-gluco-configurations by $KMnO_4$ in acetone and acetic acid afforded the corresponding acids, the esterification and hydrogenolysis of which give rise to the aminodeoxyuronic acid esters **308** and **309**.[117]

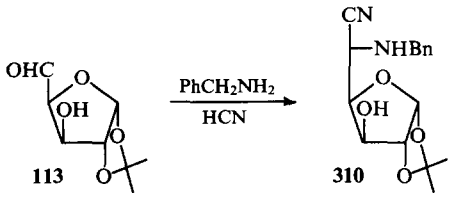


306 **308**



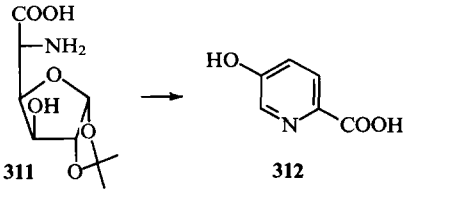
307 **309**

5-Aminodeoxyuronic acids have been detected in polyoxine antibiotics.[90] One of the first syntheses of compounds of this group described involves the addition of benzylamine and hydrocyanic acid to the aldehyde **113** with formation of 5-benzylamino-L-iduruononitrile **310**.[118]

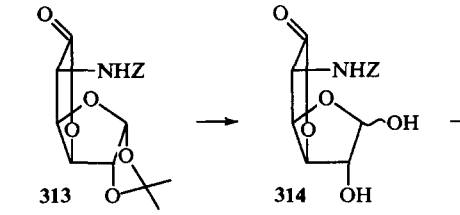


113 **310**

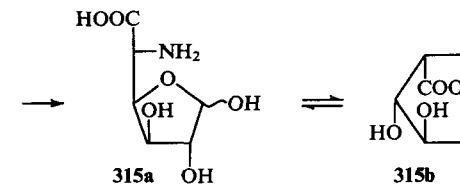
The hydrolysis of the nitrile **310** and the reductive elimination of the *N*-benzyl group over Raney nickel lead to the aminoacid **311**, the acid hydrolysis of which results in the formation of the pyridinecarboxylic acid **312**. 5-Amino-5-deoxy-L-iduronic acid has been obtained as an equilibrium mixture of the isomers **315a** and **315b** after the hydrolysis of the *N*-benzyloxycarbonyl derivative **313** and the removal of the *N*-protecting group from compound **314**.[119]



311 **312**

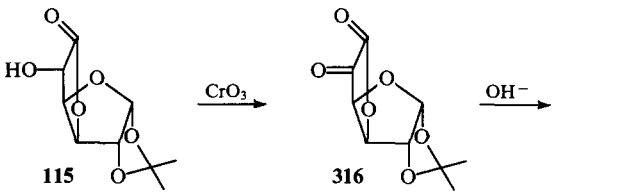


313 **314**

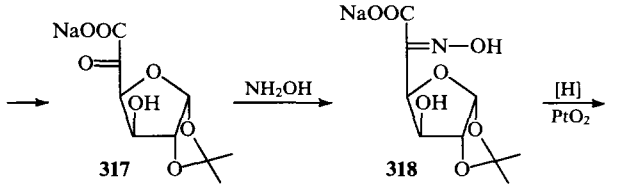


315a **315b**

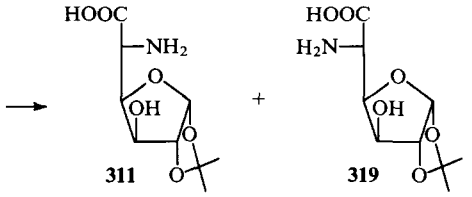
L- and D-5-amino-5-deoxyidoglucofuranuronic acids (compounds **311** and **319**) have been obtained from the glucurone acetal **115** as a result of its oxidation to the ketolactone **316**, the conversion of the salt **317** into an oxime, and the reduction of the oxime **318** by hydrogen over platinum black under pressure.[120]



115 **316**

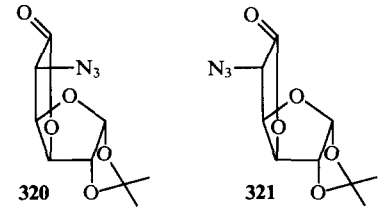


317 **318**



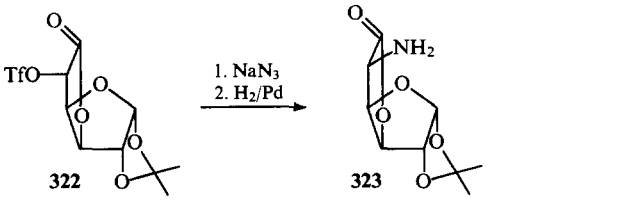
311 **319**

5-Azido-5-deoxyhexofuranuronolactones have found an application in the synthesis of 5-aminodeoxyuronic acids. The interaction of the lactone **115** with hydrazoic acid in the presence of triphenylphosphine and azodicarboxylic acid ester leads to the formation of 5-azidolactones with the L-ido- and D-idogluco-configurations (compounds **320** and **321**) in 45% and 20% yields respectively.[121]

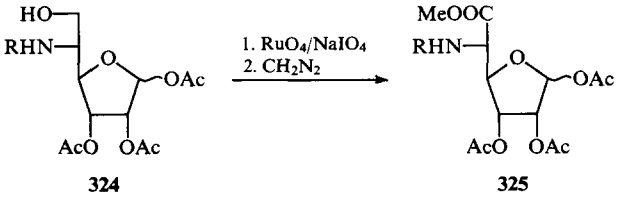


320 **321**

Treatment of the glucurone triflate **322** with sodium azide at −20 °C affords a satisfactory yield of the azide **320**, the reduction of which leads to the aminolactone **323**.[122]



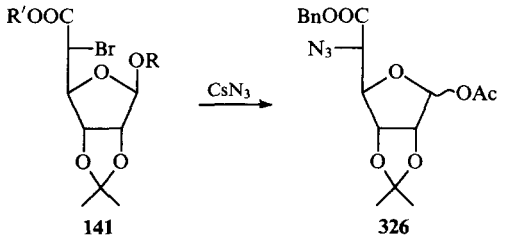
322 **323**



324 **325**

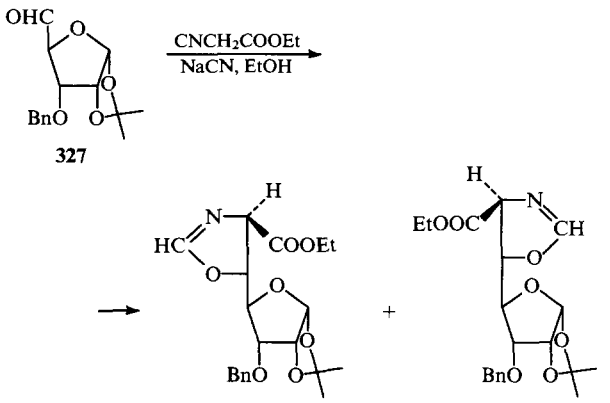
The oxidation of a derivative of the amine **324**, obtained as a result of asymmetric synthesis from the *N*-BOC-*N*,*O*-isopropylidene derivative of D-serinal and the ester of lithioethynecarboxylic acid (BOC = *tert*-butoxycarbonyl), to the aminodeoxyuronate **325** has been described.[123]

5-Azido-5-deoxy-D-allofuranuronate **326** has been obtained by the nucleophilic substitution reaction between the bromoderivative **141** and caesium azide.[58]

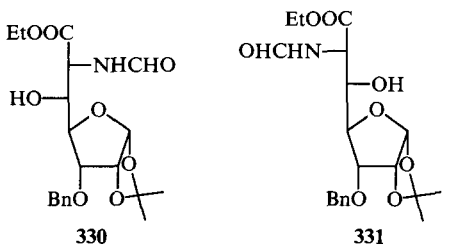


141 **326**

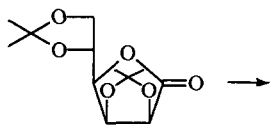
In connection with the problem of the synthesis of the structural fragments of certain antibiotics, methods have been developed for the synthesis of higher and branched aminodeoxyuronic acids. Thus treatment of the aldehyde **327** with ethyl isocyanoacetate and sodium cyanide in ethanol results in the formation of a diastereoisomeric mixture of the oxazolines **328** and **329**, the hydrolysis of which leads to the formation of isomeric 6-formamido-6-deoxyhepturonates **330** and **331**.[124]



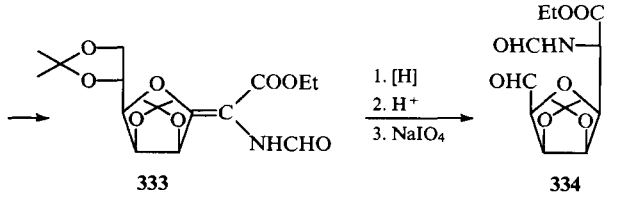
327 **328** **329**



330 **331**



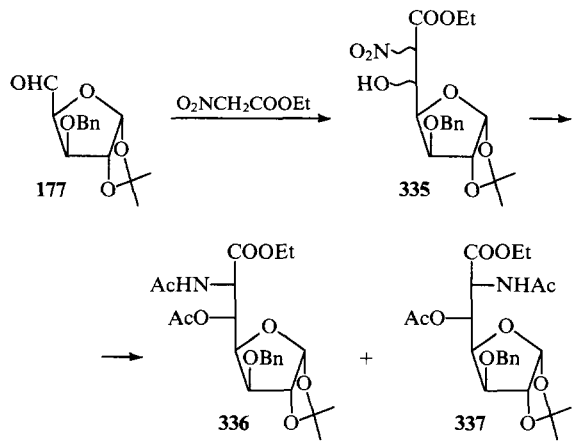
332



333 **334**

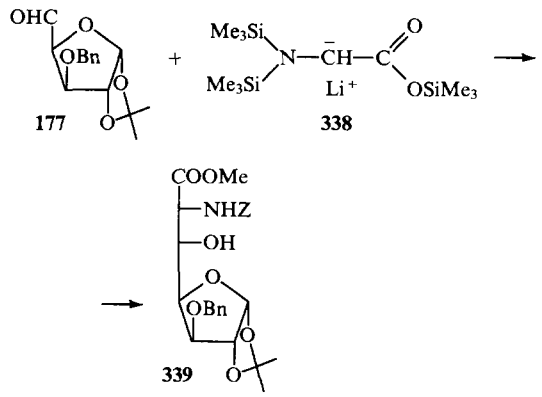
The unsaturated adduct **333**, formed from the lactone **332** and ethyl isocyanoacetate, is transformed into 6-formamido-6-deoxy-L-hepturonate **334** as a result of hydrogenation, the selective removal of one isopropylidene group, and oxidation with sodium metaperiodate.[125]

The nucleophilic addition of ethyl nitroacetate to the aldehyde **177**, the hydrogenation of the nitroester **335**, and subsequent acetylation also lead to the formation of 6-amino-6-deoxyhepturonate derivatives (compounds **336** and **337**).[126]



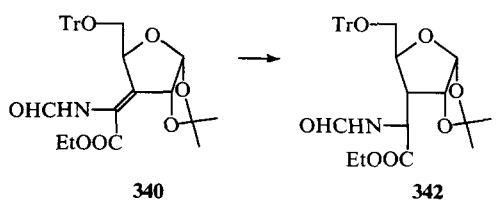
177 **335** **336** **337**

The 6-amino-6-deoxy-L-hepturonate derivative **339** was obtained in the same laboratory by adding the lithium salt of silylated glycine **338** to the aldehyde **177**.[127]

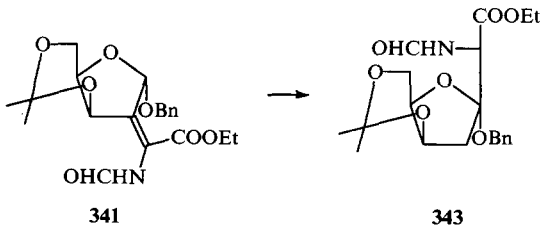


177 **338** **339**

The unsaturated esters **340** and **341**, obtained from the corresponding ketones and ethyl isocyanoacetate, are used for the synthesis of branched aminodeoxyuronic acids. The hydrogenation of compounds **340** and **341** leads to the aminoacid derivatives **342** and **343**.[128,129]

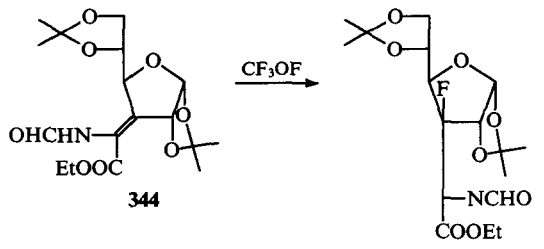


340 **342**



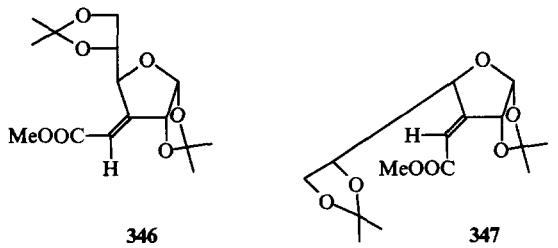
341 **343**

The fluorine-containing aminouronic acid derivative **345** is formed when the adduct **344** interacts with trifluoro-(fluorooxy)methane.[130]

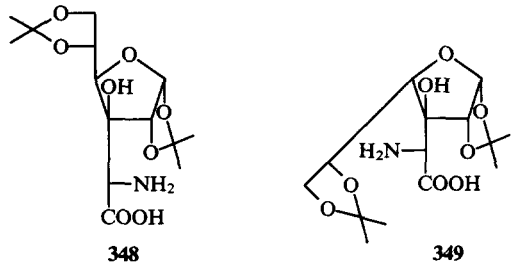


344 **345**

The unsaturated esters **346** amd **347** are converted by hydroxylation with the aid of $KMnO_4$ into branched uronic acids, which are transformed into the aminodeoxyuronic acids **348** and **349** as a result of the substitution of a hydroxyl by an amino-group.[131,132]

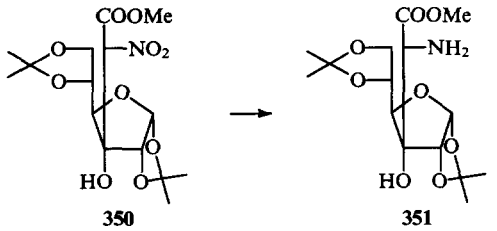


346 **347**



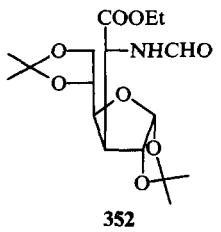
348 **349**

The addition of methyl nitroacetate to the aldehyde **205** with formation of the nitroester **350** is one of the ways of obtaining the branched aminouronate **351**.[133]



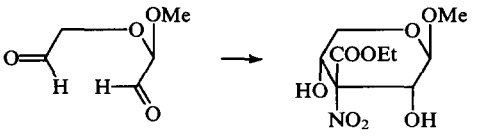
350 **351**

The aminouronate **352**, having a similar structure, has been synthesised by adding ethyl isocyanoacetate to the aldehyde **205**.[134]



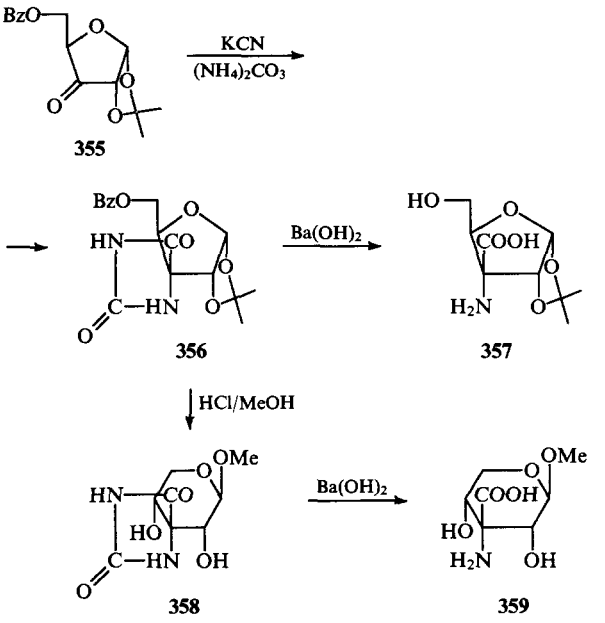
352

The ability of type **353** dialdehydes, synthesised from pyranosides, to interact with ethyl nitroacetate, forming, for example, the nitroester **354**, may serve as yet another way of synthesising branched aminouronic acids.[135]



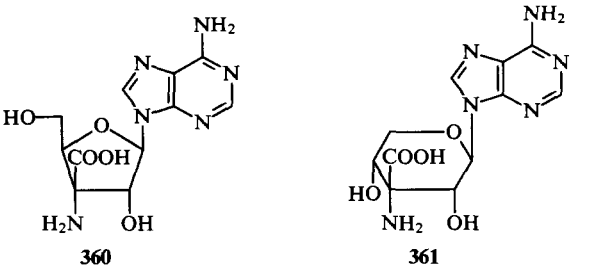
353 **354**

Another scheme for the synthesis of branched aminouronic acids involves the Bucherer conversion of the ketone **355** into the hydantoin **356**, the hydrolysis of which with $Ba(OH)_2$ leads to the aminoacid **357**, while methanolysis affords the hydantoin **358**, which is easily hydrolysed by $Ba(OH)_2$ to the aminoacid **359** with a pyranose ring.[136]



355 **356** **357** **358** **359**

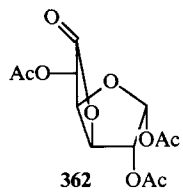
The sugars **358** and **359** obtained have been used to synthesise analogues **360** and **361** of the nucleoside antibiotic puromycin.

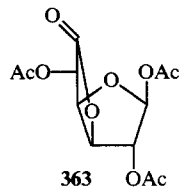


360 **361**

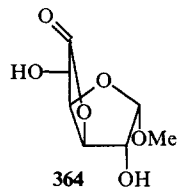
VII. Reactions of uronic acids

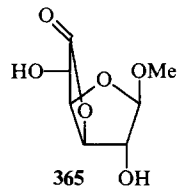
One of the most typical reactions of uronic acids is the formation of lactones. Lactones with different positions and sizes of the lactone rings are in their turn widely used for the synthesis of sugars with the necessary set of protecting groups. D-Gluco-furanurono-6,3-lactone (glucurone) **24** is formed when an aqueous solution of D-glucuronic acid is evaporated. The acetates **362** and **363** with the α- and β-anomeric configurations are synthesised by acetylating glucurone with acetic anhydride in the presence of pyridine or $ZnCl_2$.[137] Brief treatment of glucurone with boron trifluoride etherate in acetic anhydride gives the acetate **363** in 90% yield.[28]


362

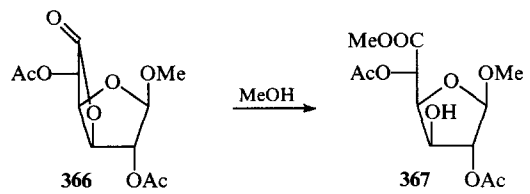

363

A convenient method of synthesis of 1,2-*O*-isopropylidene-glucurone **115** involves the refluxing of glucurone in acetone over a cation-exchange resin.[138] Treatment of glucurone with methanol and the cation-exchange resin leads to a mixture of the α- and β-D-glucofuranuronides **364** and **365**.[139]

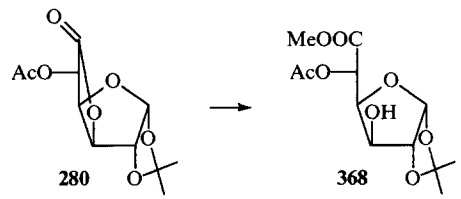

364


365

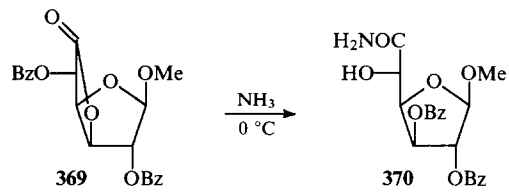
It has been shown that under controlled conditions the lactone **366** is deacetylated (with retention of the lactone ring) by ammonia to the lactone **365**, while refluxing in methanol converted it into the methyl ester **367**.[140]


366 → 367

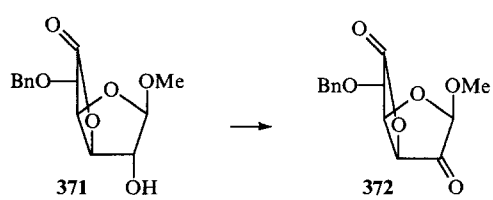
The opening of the lactone rings in the lactone **280** with formation of the ester **368** is readily achieved with the aid of triethylamine or an anion-exchange resin.[141,142]


280 → 368

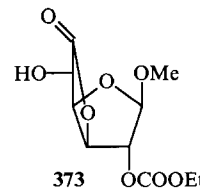
On treatment of the lactone **369** with ammonia in chloroform, the benzoyl group is found to migrate from the 5-position to the 3-position with formation of the amide **370**.[143]

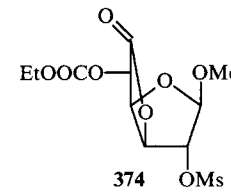

369 → 370

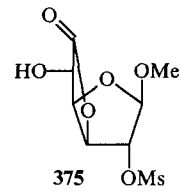
The ketolactones **100** and **372** have been obtained from the lactones **115** and **371** by treatment with DMSO and acetic anhydride as well as RuO_4.[144,145]

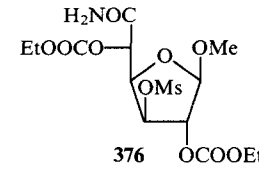

371 → 372

A difference between the reactivities of glucurone and its derivatives has been demonstrated.[146] Conditions were selected under which it is possible to obtain the sugars **373**–**376** protected in different ways.[146]


373

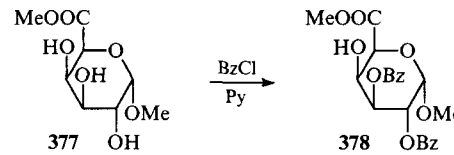

374


375

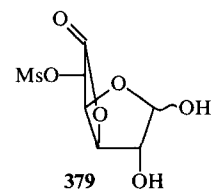

376

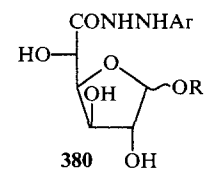
Selective acylation of glucurone and its derivatives by pivaloyl chloride in pyridine affords reaction products with different numbers of pivaloyl groups. The relative reactivities of the hydroxy-groups [OH(5) > OH(2) > OH(1)] depend to a large extent on the reaction conditions.[147]

The dibenzoate **378** can be obtained by the selective benzoylation of the galacturonide **377**.[148]

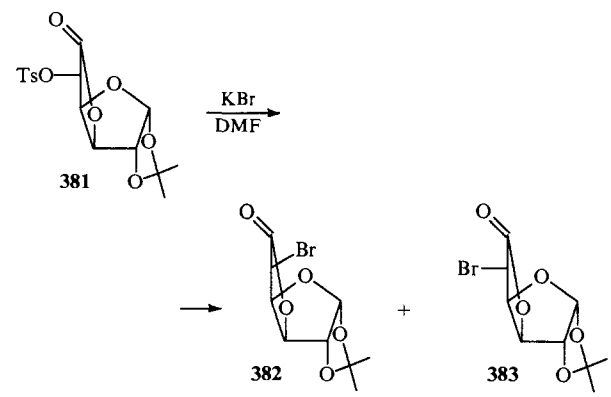

377 → 378

The methods of synthesis of various amides and *N*-aryl-glucuronides from D-glucurone, ammonia, and aromatic amines have been described.[149] The methanesulfonate **379** was found to possess an antitumour activity,[150] while the hydrazides having the general formula **380** were found to offer protection against hepatitis.[151]


379

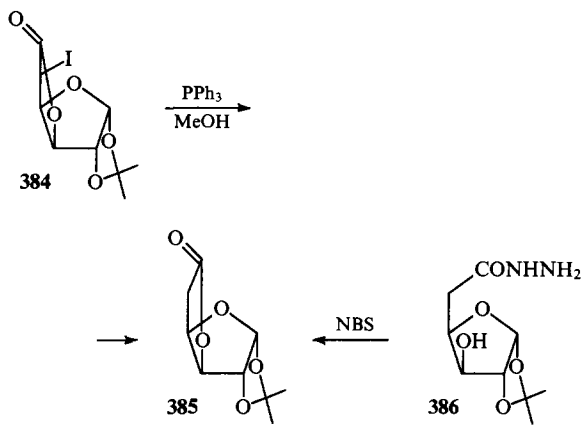

380

A characteristic property of glucurone derivatives is their extensive decomposition with formation of conjugated polyenes as a result of β-elimination, which competes with nucleophilic substitution at the C(5) carbon atom. Examples of reactions of this kind have been reviewed.[152]


381 → 382 + 383

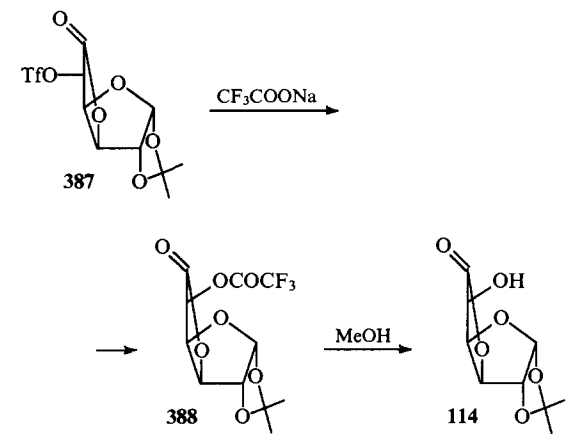
Nucleophilic substitution of the tosyl group can be achieved only with the aid of nucleophiles having a low basicity. Thus a mixture of the isomeric bromo-derivatives **382** and **383** is obtained when the tosylate **381** is heated with KBr in DMF.[153]

The interaction of the lactone **115** with triphenylphosphine iodide leads to the iodo-derivative **384** (with inversion of configuration), which is converted into 5-deoxylactone **385** on treatment with triphenylphosphine in methanol.[154]

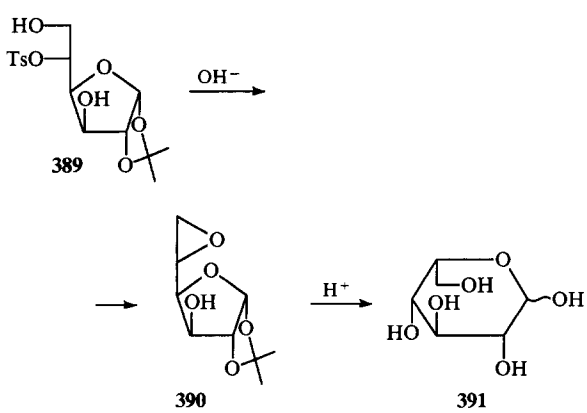


It has been observed that the tosylate **381** is readily converted into the 5-deoxysugar **386** as a result of its reaction with hydrazine.[105] Treatment of the hydrazide **386** with *N*-bromosuccinimide (NBS) leads to the 5-deoxylactone **385**.[154]

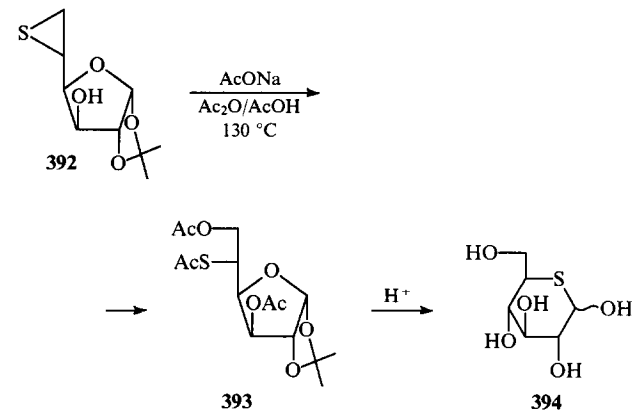
The triflate **387** is transformed under very mild conditions into the trifluoroacetate **388**, the methanolysis of which results in transition to the L-iduronolactone **114**.[155]



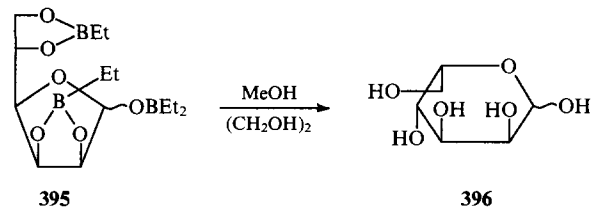
The lactone **381** is smoothly reduced by $NaBH_4$ to the alcohol **389**, from which the oxirane **390**, transformed further to L-idose **391**, is obtained on treatment with a base.[156]



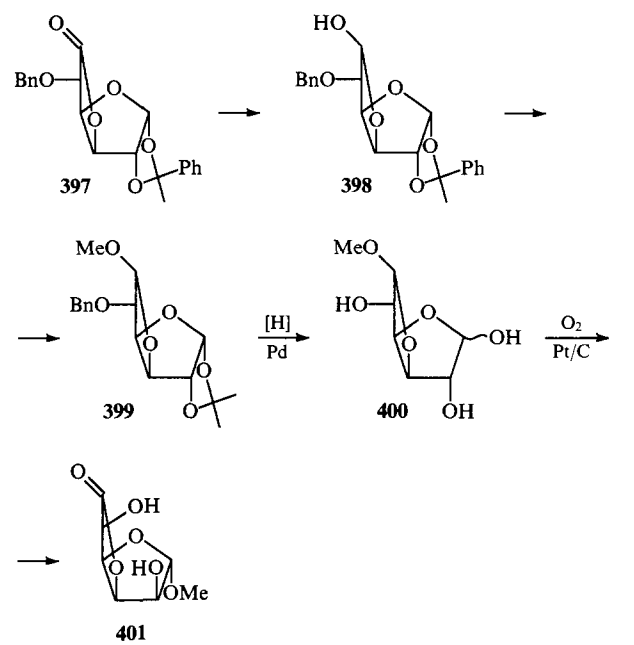
The oxirane **390** interacts with thiourea to form the thiirane **392**. Its treatment with sodium acetate in an acetate anhydride–acetic acid mixture leads to the triacetate **393** and to 5-thio-D-glucose **394** after the removal of the protecting groups.[157]



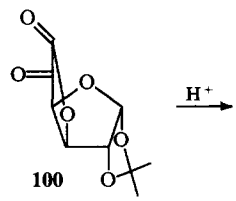
The reduction of glucurone by diethylborane takes place with formation of the borate **395**, which is readily hydrolysed to L-gulose **396**.[158]



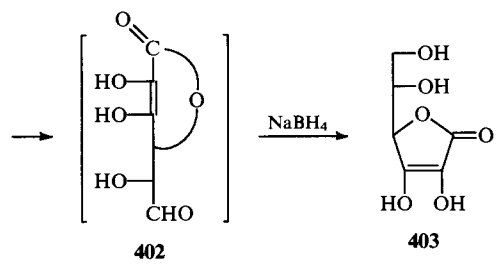
Yet another example of the transformation of the lactones into sugars which are otherwise difficult to obtain is the reduction of the D-glucuronolactone derivative **397** to the hexodialdofuranose **398**, the formation of the methyl glycoside **399**, its hydrogenolysis to the sugar **400**, and the catalytic oxidation of the latter to L-gulofuranourono-6,3-lactone **401**.[159]



Hydrolysis of the ketolactone **100** gives the aldehyde **402**, the reduction of which with $NaBH_4$ leads to L-ascorbic acid **403**.[160,161]

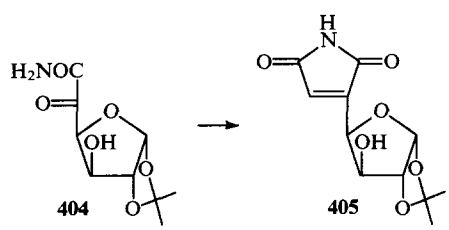


100



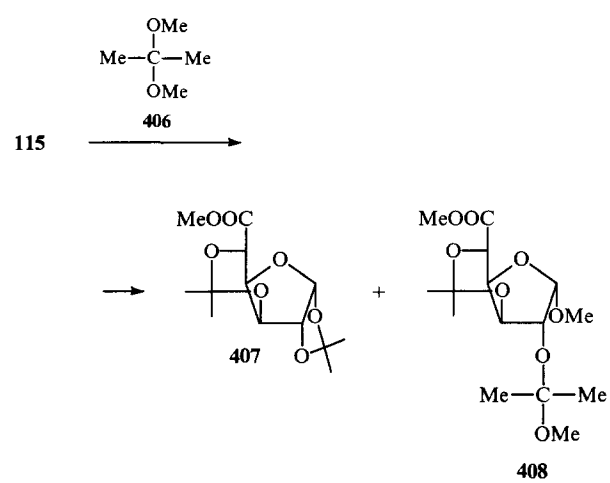
402 403

The ketoamide **404**, obtained from the lactone **100**, reacts with ethoxycarbonylmethylenetriphenylphosphorane to form the analogue of the antibiotic showdomycin **405**.[162]



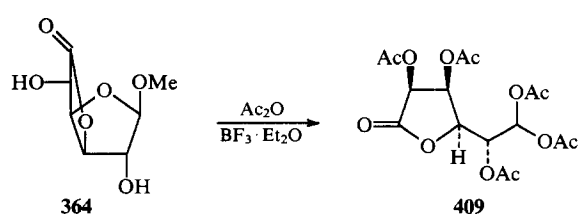
404 405

Prolonged refluxing of the lactone **115** with dimethoxypropane **406** and *p*-toluenesulfonic acid in acetone results in the formation of the diacetal **407** and the uronide **408**.[163]



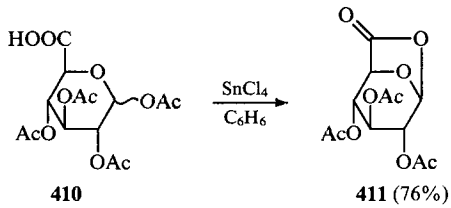
115 406 407 408

Acetolysis of the lactone **364** gives rise to the acylal **409**.[164]



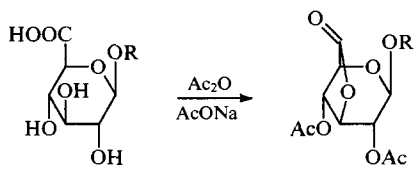
364 409

Acetylation of the sodium salt of D-glucuronic acid by acetic anhydride and *p*-toluenesulfonic acid makes it possible to obtain an anomeric mixture of the tetraacetates **410**. Its refluxing with $SnCl_4$ in benzene leads to the 6,1-lactone **411**.[165]

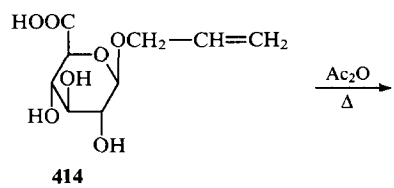


410 411 (76%)

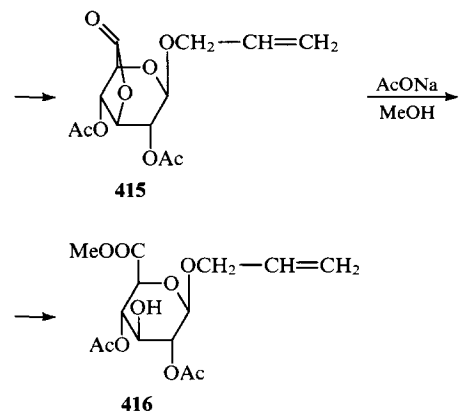
D-Glucopyranurono-6,3-lactone **413** has been obtained by treating the glucuronide **412** with sodium acetate in acetic anhydride at room temperature.[166] Brief heating of the glucuronide **414** in acetic anhydride with subsequent addition of pyridine also makes it possible to obtain the 6,3-lactone **415**, which is converted on treatment with sodium acetate in methanol into the uronate **416** with a free hydroxy-group.[167]



412 413

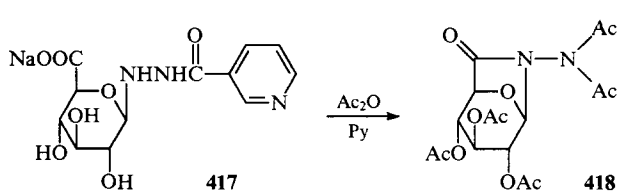


414



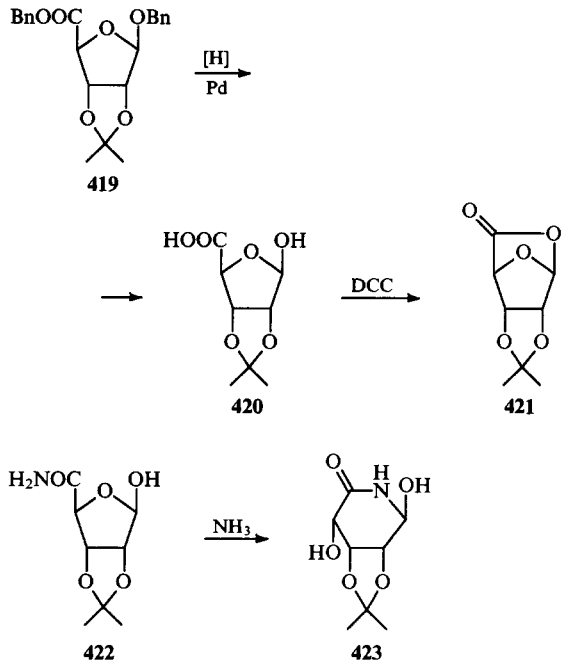
415 416

The formation of the lactam **418** has been detected after prolonged treatment of the hydrazide **417** with acetic anhydride and pyridine.[168]

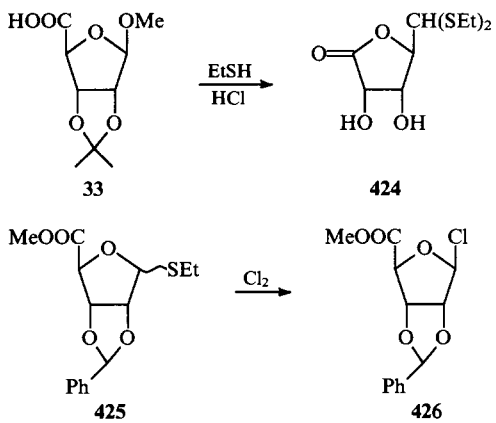


417 418

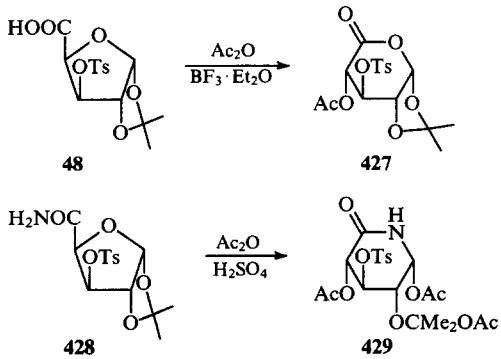
The formation of the lactones and lactams having different structures is characteristic also of penturonic acids. Thus the acid **420**, formed as a result of the hydrogenolysis of the D-riburonate **419**, can be cyclised to the 5,1-lactone **421** with the aid of dicyclohexylcarbodiimide (DCC) in ether. On treatment with ammonia, the amide **422** is converted into the lactam **423**.[169]



The acid **33** reacts with ethanethiol and concentrated HCl to form the lactone **424**. Chlorination of the ribouronate **425** obtained from compound **424** led to the synthesis of the glycosyl chloride **426** and some of its analogues.[170]

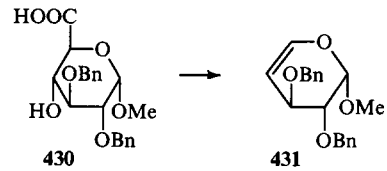


On treatment with acetic anhydride and boron trifluoride etherate, the acid **49** rearranges to the lactone **427**. Under acetolysis conditions, the amide **428** is transformed into the lactam **429**.[171,172]

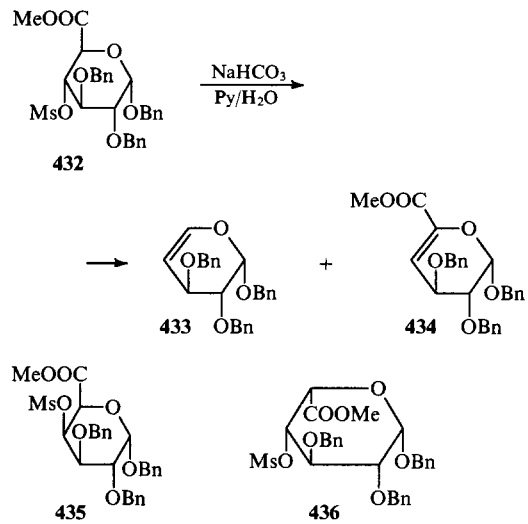


A characteristic feature of uronic acids is their ability to be converted by bases, as a result of β-elimination reactions, into unsaturated compounds, which are used in their turn in the synthesis of diverse derivatives of uronic acids. The principal characteristics and a large number of examples of β-elimination reactions have been described in a review.[173]

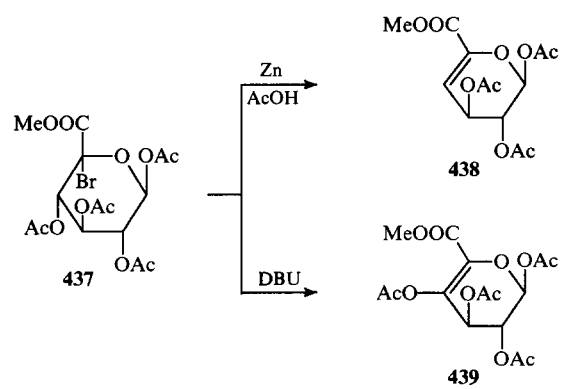
The β-elimination reaction coupled with decarboxylation merits special attention. Thus heating of the glucuronide **430** with the dineopentyl acetal of dimethylformamide leads to the formation of the unsaturated sugar **431**.[174]



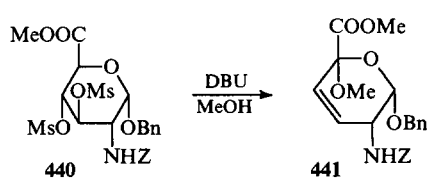
Treatment of the glucuronate **432** with sodium bicarbonate in aqueous pyridine leads to the formation of the decarboxylated sugar **433** and the eneuronate **434**. The galacturonate **435** is not decarboxylated under these conditions, giving rise only to the uronate **434**. The L-iduronate **436** is converted into the uronate **434** and a small amount of the sugar **433**.[175]



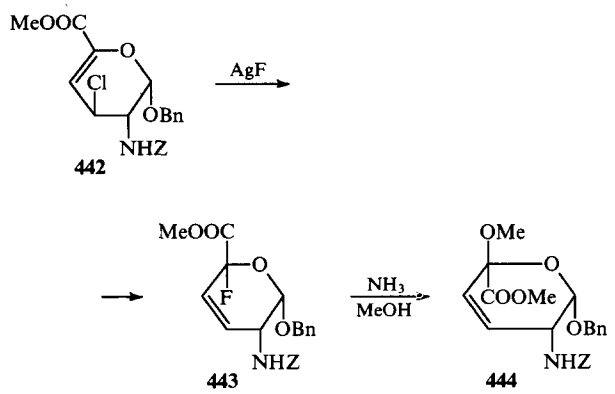
The 5-bromouronate **437** interacts with zinc in acetic acid to form the 4,5-unsaturated uronate **438**, whilst its reaction with DBU leads to its 4-acetoxy-analogue **439**.[176]



Treatment of the di(methanesulfonate) **440** with DBU in methanol led to the formation of the 3,4-unsaturated 4-methoxyuronate **441**.[177]

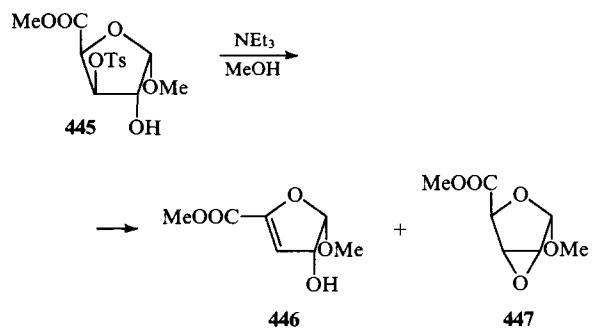


The unsaturated 3-chlorouronate **442** interacts with AgF, affording the 5-fluorouronate **443**, which is converted on treatment with ammonia in methanol into the uronate **441** and its isomer **444**.[178]



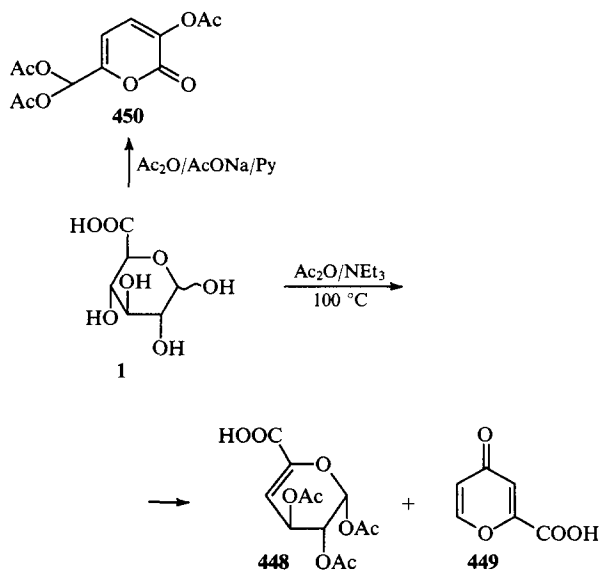
442 **443** **444**

The xyluronate **445** exhibits a dual reactivity.[179,180] Its refluxing with triethylamine in methanol gives rise to the 3,4-unsaturated uronate **446** and the oxirane **447**.[21]



445 **446** **447**

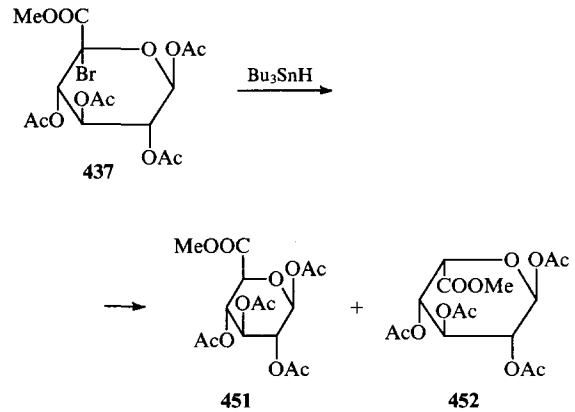
The formation of β-elimination products is observed in the interaction of free uronic acids with weak bases in acetic anhydride. When D-glucuronic acid **1** is heated with triethylamine in acetic anhydride, the 4,5-unsaturated acid **448** and coumanic acid **449** are formed. Heating of the acid **1** with pyridine in a mixture of acetic acid and its anhydride leads to the acylal of the unsaturated lactone **450**.[181]



450 **1** **448** **449**

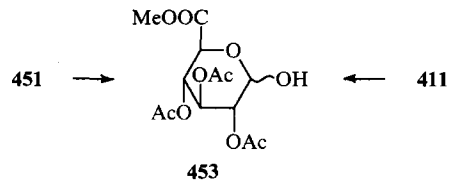
Coumanic acid **449** is formed in a satisfactory yield on heating the peracetate of D-glucuronic acid **410** with pyridine in acetic anhydride.[182]

On interaction with tributyltin hydride, the 5-bromouronate **437** already mentioned is converted into a mixture of the D-glucuronate **451** and the L-iduronate **452**.[183,184]



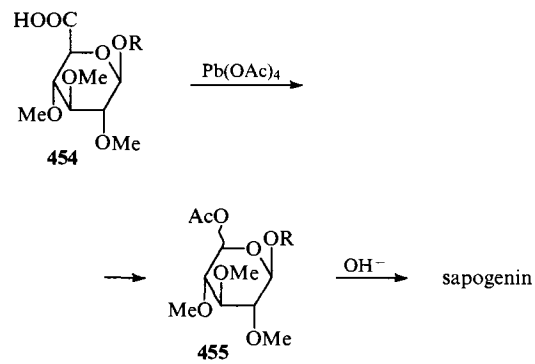
437 **451** **452**

The acetate of D-glucuronic acid **453** with a hemiacetal hydroxy-group, which is of definite interest, may be obtained in two ways: by heating the peracetate **451** with Bu_3SnOMe in toluene and by treating the lactone **411** with methanol in the presence of pyridine.[165]



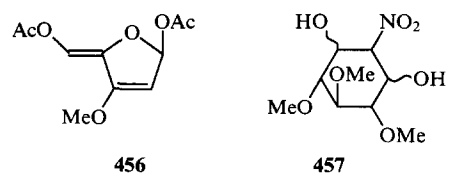
453

The methylated glycosides of uronic acids are decarboxylated by refluxing them with lead tetraacetate in benzene. The acetate **455** formed from the acid **454** as a result of the decarboxylation decomposes on treatment with alkali, liberating the aglycone and a product the acylation of which leads to the diene **456**.[185,186]



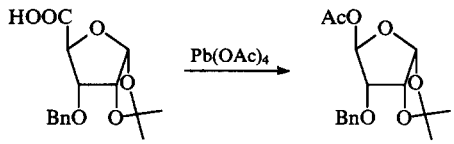
454 **455**

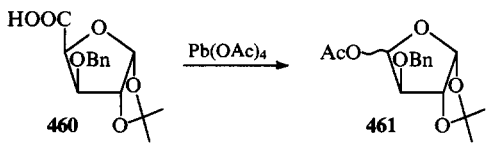
The condensation of the acetate **455** with nitromethane has found an application in the synthesis of the nitrocyclitols **457**.[187]



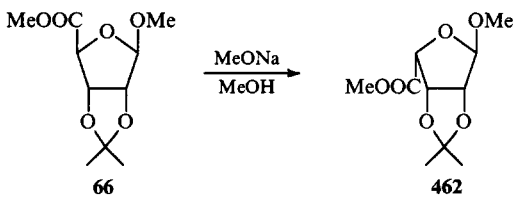
456 **457**

The interaction of protected riburonic and xyluronic acids (compounds **458** and **460**) with $Pb(OAc)_4$ results in the formation of the corresponding acetates **459** and **461**.[188]

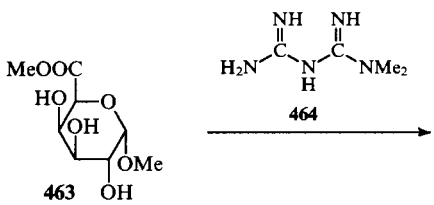


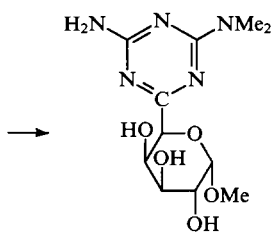


The D-riburonic acid ester **66** can be converted into the L-lyxuronic acid ester **462** by simple treatment with sodium methoxide in methanol.[11,189]

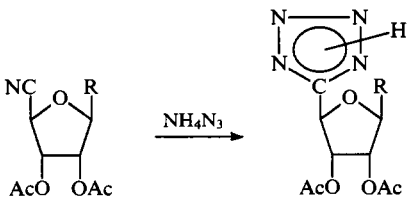


Reactions characteristic of the carboxy-group and its derivatives constitute yet another means for the modification of uronic acids. On treatment with dimethylbiguanidine **464**, the galacturonate **463** is transformed into the 5-triazine derivative of the β-L-arabinopyranoside **465**.[190]

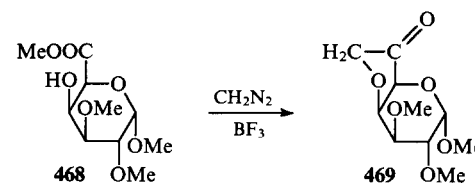




On treatment with ammonium azide, the nitrile **466** is converted into the tetrazole derivative **467**.[191]

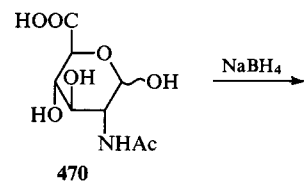


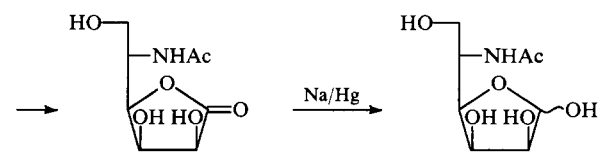
An unusual result has been obtained on treating the galacturonate **468** with diazomethane in the presence of BF_3. Together with the expected methylation product, the formation of the ketone **469** was observed.[192]

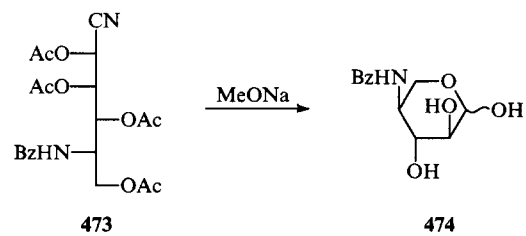


Uronic acids serve as a source of glyconolactones. L-Gulono- and L-galactono-lactones are obtained by reducing D-glucuronic and D-galacturonic acids with $NaBH_4$.[193]

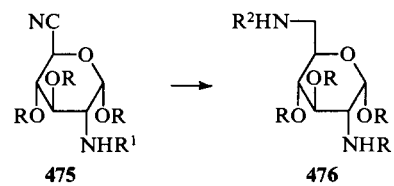
The possibility of using aminodeoxyuronic acids for the synthesis of aminosugars which are difficult to obtain has been demonstrated.[194] The lactone **471** has been obtained by reducing 2-acetamidoglucuronic acid **470**. Its reduction with sodium amalgam affords 5-acetamido-L-gulofuranose **472**. The nitrile **473**, obtained from the *N*-benzoylated lactone, is converted into 4-benzamido-L-xylopyranose **474** on treatment with sodium methoxide.







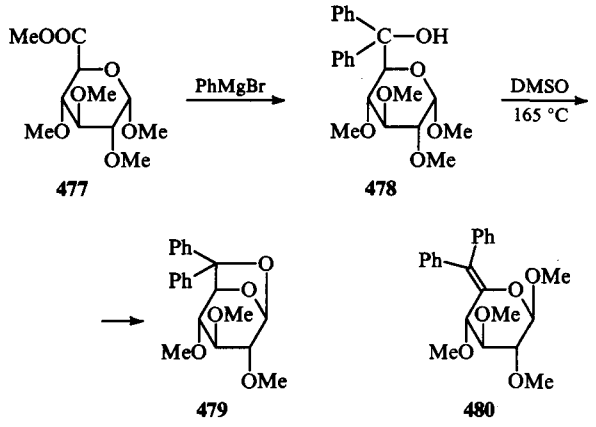
The reduction of the nitrile **475** makes it possible to synthesise the diaminosugar **476**.[195]



Treatment of the permethylated methyl α-D-glucuronide **477** with phenylmagnesium bromide gives the tertiary alcohol **478**, which is converted into the anhydrosugar **479** on heating in DMSO, whereas the corresponding β-glycoside preferentially forms the 5-enylpyranoside **480** under the same conditions.[196]

Numerous examples of the synthesis of glycuronides have been described systematically in a review.[197]

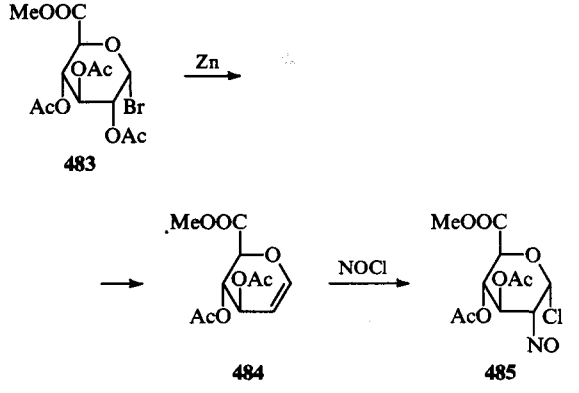
The presence of an alkoxycarbonyl group in the molecule exerts a significant influence on the stereochemical result of the reactions involving glycosylation by uronic acids, which depends in many respects on the selected reaction conditions (solvent, condensing agent, temperature). Halogenoses



[haloakylhalides? Ed.] are the most active glycosylating agents. The formation of the halo-derivatives of uronic acids is achieved with the aid of dihalomethyl methyl ether together with the employment of the traditional method. The $ZnCl_2$-catalysed reaction of the galacturonide **481** with dichloromethyl methyl ether affords the chlorosugar **482** in a satisfactory yield.[198]

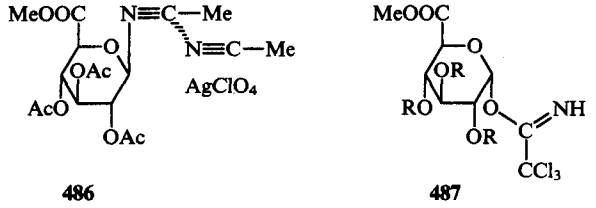


The addition of nitrosyl chloride to the glycal **484**, synthesised from the bromo-derivative **483**, leads to the chlorosugar **485** containing a nitroso-group, which is capable of being transformed further into an aminosugar.[199]

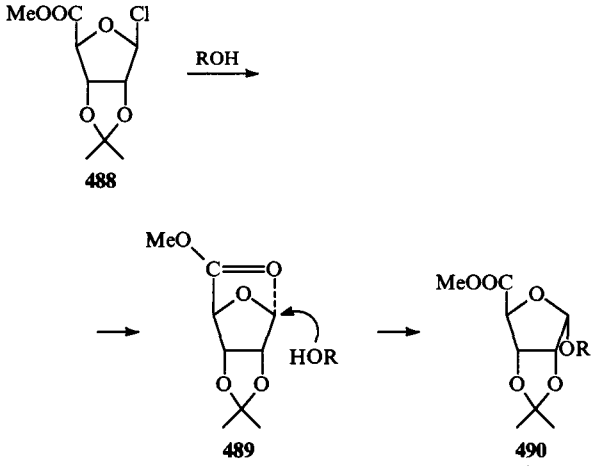


Alcohols are glycosylated by the peracetate **451** in the presence of $SnCl_4$ in dichloroethane in satisfactory yields, both α- and β-anomers being formed under these conditions.[200]

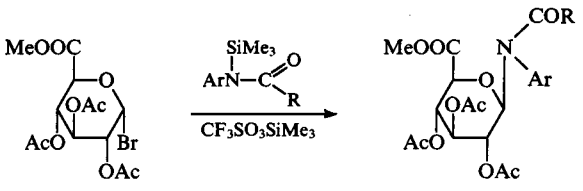
It has been shown[201] that the stereochemical specificity of the glycosylation of alcohols by the bromo-derivative **483** in acetonitrile in the presence of $AgClO_4$ is controlled by the presence in solution of type **486** conjugated compounds, which results in the preferential formation of the α-anomers. It has been suggested that trichloroacetimidates, for example compound **487**, be employed as active glycosylating agents.[202,203]



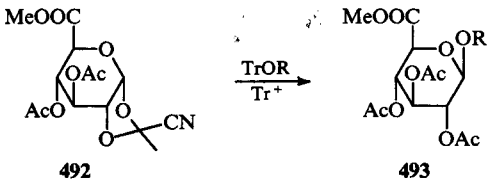
The synthesis of mainly the α-riburonide **490** from the chlorosugar **488** has been explained by the formation of the intermediate **489**, which can undergo nucleophilic attack only in the α-region.[204]



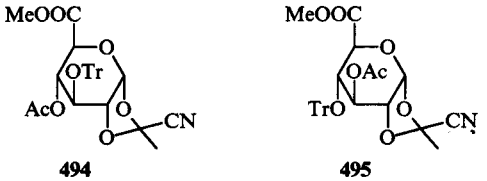
Trimethylsilyl triflate is a very effective condensing agent for the synthesis of uronides. The condensation of the bromo-derivative **483** with alcohols in its presence makes it possible to obtain glucuronides in satisfactory yields.[205] The condensation of the bromo-derivatives **483** with secondary arylamides to the *N*-glycuronides **491** has been carried out with its aid.[206]



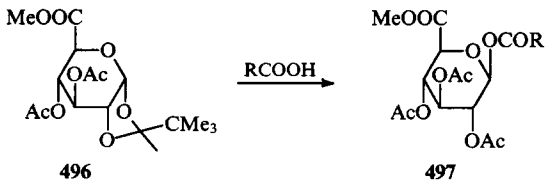
An effective method has been developed for the synthesis of the β-D-glycuronides **493**, which consists in the condensation of the cyanoethylidene derivative **492** with tritylated alcohol in the presence of a triphenylmethylium salt.[207]



In order to obtain disaccharides by this method, the cyanoethylidene derivatives of glucuronic acids **494** and **495** with the trityl group in different positions were synthesised.[208]

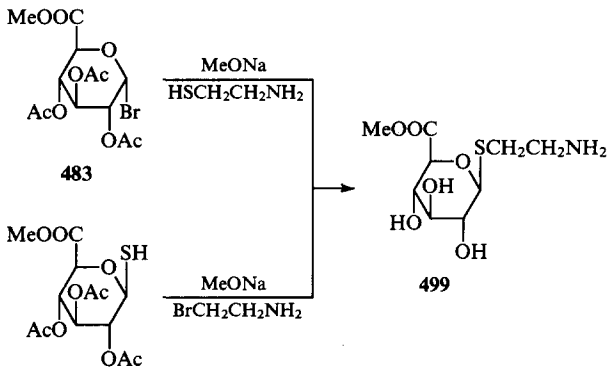


The *tert*-butoxyethylidene D-glucuronate derivative **496** is converted into the 1-*O*-acylates **497** on treatment with carboxylic acids.[209]



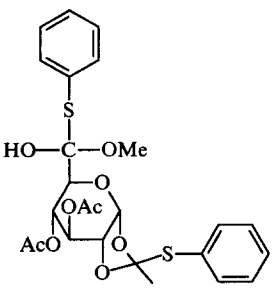
496 497

The β-*S*-alkylglucuronide **499** has been obtained by condensing the bromo-derivatives **483** with cystamine or the mercaptan **498** with 2-bromoethylamine.[210]



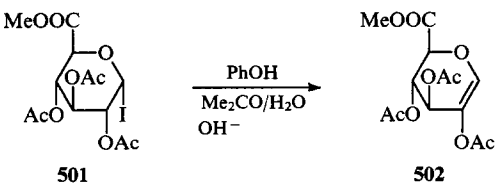
483 498 499

The glycosylation of thiophenol by D-glucopyranose pentaacetate in dichloroethane in the presence of $SnCl_4$ affords the tetraacetate of phenylthio-β-D-glucopyranoside. The 1-[2-phenylthio]orthoacetate of 3,4-di-*O*-acetyl-6-methoxy-6-phenylthio-α-D-glucopyranose **500** is formed from the acetate **451** under the same conditions.[211]



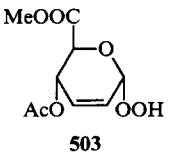
500

Instead of the expected *O*-phenylglucuronide, the glycosylation of phenol by the iodo-derivative **501** in aqueous acetone in the presence of base led to the isolation of the 2-acetoxyglycal **502** as the main reaction product.[212]



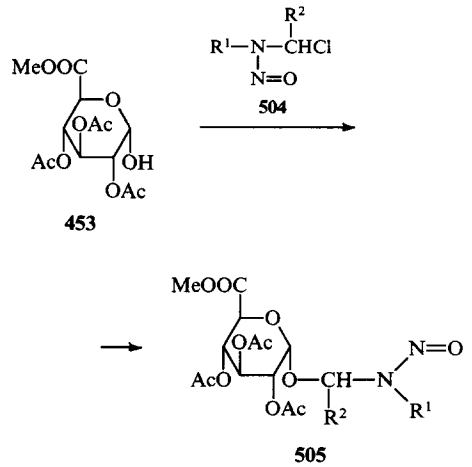
501 502

On treatment with 85% H_2O_2, the glycal **484** is converted into the hydroperoxide **503**.[213]



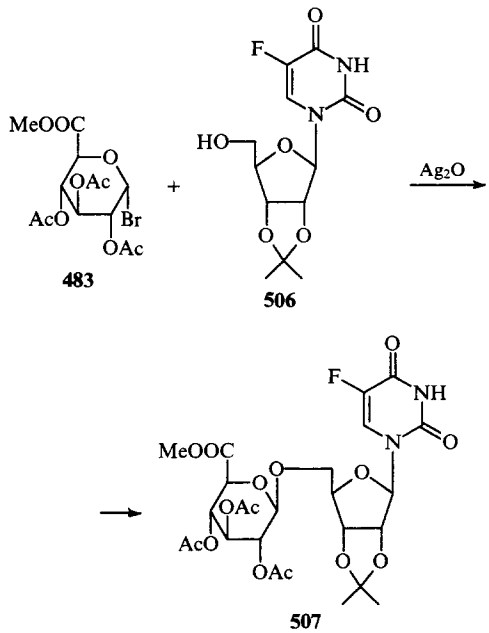
503

The glucuronate **453** condenses in pyridine with the chloroderivative of the *N*-nitrosodialkylamine **504** to the glucuronide **505**, which models the conjugates of D-glucuronic acid with nitrosoaminoalcohols formed in the organism.[214]



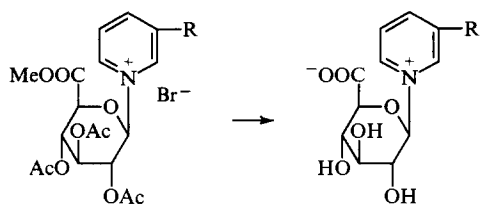
453 505

In order to synthesise the conjugate of D-glucuronic acid with 5-fluorouridine (a cytostatic agent), the bromo-derivative **483** was condensed with the 5-fluorouridine acetal **506** in the presence of Ag_2O, which led to the formation of the glucuronide **507**.[215]



483 506 507

The bromo-derivative **483** interacts with pyridines, affording the *N*-glycuronides **508**, which hydrolyse to analogues of nicotinamidoriboside **509** on treatment with bases.[216,217]



508 509

R = H, Me, $CONH_2$.

VIII. Conclusion

The data presented in the review make it possible to establish a general idea about the possibilities in the synthesis of uronic acids with a specified structure, in particular the methods for the oxidation or the conditions governing the transformation of monosaccharide derivatives.

The unique combination of functional groups in uronic acids and especially aminodeoxyuronic acids is the reason for the diversity of their chemical properties. The numerous examples of the nontrivial reactions of uronic acids described in this review should be borne in mind in planning new synthetic approaches to the preparation of chiral natural products which are difficult to obtain on a preparative scale. The broad spectrum nucleoside antibiotics, the composition of which incorporates uronic and aminodeoxyuronic acids, may serve as an example of a class of such substances which are important from the practical standpoint.[89] The syntheses of the natural representatives of this class and their structural analogues, based on the chemical reactions of uronic acids, are very important for the development of ideas concerning the biological role of uronic acid residues in the molecules of these compounds.

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Photochemical reactions of complexes of aromatic amines with polyhalomethanes

M F Budyka, M V Alfimov

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Abstract. Data concerning the chemical processes occurring under light irradiation of complexes of aromatic amines with polyhalomethanes are critically reviewed. It is shown that electron transfer from an amine to a halomethane is the main photochemical reaction of the complexes. The properties and reactions of primary radical-ion species and secondary inter-mediates formed are discussed. The mechanisms of photo-induced formation of triphenylmethane dyes and acridine derivatives are considered in detail. The bibliography includes 234 references.

I. Introduction

Charge transfer complexes (CTC) are rather labile self-organising systems consisting of at least two components, an electron donor and an electron acceptor. The formation of a CTC manifests itself most clearly in the appearance of a new absorption band, the charge transfer (CT) band, in the electronic spectra of the mixtures of components. Electron transfer (ET) is the most typical reaction of such complexes. Depending on the properties of the donor and acceptor and on the external conditions, ET can occur either thermally or under light irradiation. Therefore, CTC provide a convenient model for studying the ET process.[1–6] In recent years, the attention of investigators has been attracted to molecular-bonded donor-acceptor systems.[7–13]

Of particular interest is the chemical aspect of ET, since this process is the primary step in many chemical transformations.[14–19] One can vary the rate of initiation of chemical reactions over a wide range and make them follow a required path by varying the properties of CTC components. This allows one to study reaction mechanisms, detect intermediate compounds, and determine their structures.

M F Budyka Institute of Chemical Physics in Chernogolovka, Russian Academy of Sciences, Chernogolovka, 142432 Moscow Region, Russian Federation. Fax (7–096) 515 35 88
M V Alfimov Semenov Institute of Chemical Physics, Russian Academy of Sciences, ul. Kosygina 4, 117977 Moscow, Russian Federation. Fax (7–095) 938 21 56

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In the present review we consider the photochemical reactions of complexes formed from aromatic amines (Am) with polyhalomethanes (PHM). The amine complexes have been known for a long time, but the use of PHM, particularly the chloro-substituted ones, in complexation reactions started only in the 1960s, when it was found that they could act as acceptors in complexes with comparatively strong donors, such as Am.[20] Since PHM correspond to 'sacrificial' acceptors (which decompose irreversibly when they capture an electron), irradiation of an Am + PHM mixture inevitably results in the initiation of chemical transformations. For this reason, studies of the photochemical properties of PHM started shortly after the discovery of their complexation ability.[21–26]

Two main aspects can be distinguished in the photochemical studies of Am – PHM systems: (1) the study of primary reactions and properties of primary photogenerated species; (2) the isolation of end products (dyes) formed under the irradiation of solutions simultaneously containing an Am and a PHM, and the determination of their structures and mechanisms of formation. Although the viewpoints of scientists on the first aspect are well founded and common, the data on the structures of dyes and the mechanisms of their formation are contradictory. The subject of the present review is analysis of these data, and we shall hardly deal at all with the rather broad and important aspect relating to study of the possibility of practical use of Am · PHM complexes, in particular in systems for information recording. These problems have been thoroughly discussed in works by Vannikov and Grishina.[27–30]

Prior to discussing the photochemical reaction of CTC we should also mention the complexation reaction itself, which occurs before light irradiation of the system is started. A detailed analysis of this reaction is a subject for special consideration. We shall note only the particular features of the donor – acceptor interaction of amines with PHM which affect considerably the photochemical properties of the complexes.

An important photochemical parameter is the action spectrum, i.e. the spectral region in which the irradiation results in light absorption and initiation of a chemical reaction. The action spectrum of Am · PHM complexes is generally located in the near UV region, e.g., in the 330–380 nm region for the CTC of diphenylamine (DPA) with CBr_4.[21,31] It has traditionally been accepted that CBr_4 forms 1:1 complexes with amines.[31–33] However, it was shown recently that DPA derivatives can form higher complexes, the so-called polycomplexes,

whose absorption spectra are shifted bathochromically relative to that of the 1:1 CTC.[34,35] Owing to the formation of such complexes, whose absolute content in an equilibrium mixture increases with increasing concentrations of the components, the action spectrum of the CTC of diphenylamine (and its derivatives) with CBr_4 expands significantly into the visible region up to 500–550 nm.[27,34] On the other hand, the relative content of polycomplexes in the mixture is small in comparison with that of the free amine, and hence they do not affect the kinetics of secondary chemical reactions initiated by light absorption.[36]

II. Primary photochemical processes during irradiation of amine–polyhalomethane systems

To date, it has been established unambiguously that the transfer of an electron from an amine to a halohydrocarbon (HC) is the primary photochemical act during the irradiation of mixtures of amines with PHM or, more widely, with HC. Depending on the structure of the donor and acceptor components, three routes for the photoinitiation of ET exist: excitation of CTC, selective excitation of Am, and selective excitation of HC. All three ways do not necessarily actually occur for any arbitrary Am–HC pair, since this would require that the absorption bands of Am, HC and CTC are sufficiently different.

Relatively strong donors (alkylarylamines, di- and triarylamines, diamines) and/or acceptors (polybromohydrocarbons, nitrohalo-derivatives, halocarbonyl compounds) form complexes whose absorption spectra are shifted bathochromically relative to the spectra of the components, since selective excitation of their complexes in the CT bands is possible.[27,37–39] In this case, ET occurs within the complex and, in essence, corresponds to an intramolecular process[40] (static quenching of Am luminescence,[41] or innersphere ET, according to the terminology accepted in the literatire[1,42]).

$$Am + RX \rightleftharpoons (Am \cdot RX) \xrightarrow{h\nu} (Am^{+\cdot} RX^{-\cdot}) \qquad (1)$$

Chlorohydrocarbons form weak complexes with amines (with stability constants $< 0.1\ l\ mol^{-1}$), whose concentrations are much less than those of the starting components and whose absorption spectra almost coincide with those of the amines. When such mixtures are irradiated, an Am reacts with a HC to give a radical cation (RC) of the amine[43–48] (dynamic quenching of Am luminescence, outersphere ET).

$$Am \xrightarrow{h\nu} (Am)^* \xrightleftharpoons{RX} \rightleftharpoons [(Am)^* \cdot RX] \longrightarrow (Am^{+\cdot} RX^{-\cdot}) \qquad (2)$$

Although it is assumed that reaction (2) occurs via quasistable intermediates, exciplexes,[44,45,49,50] their formation in the reactions of amines with alkyl halides has not been proved, unlike e.g. photochemical reactions of amines with carbonyl[51,52] or aromatic compounds,[53–57] including aryl halides.[58–62]

Selective excitation of a HC results in homolytic cleavage of a C–X bond (see Ref. 63)

$$RX \xrightarrow{h\nu} R^{\cdot} + X^{\cdot}, \qquad (3)$$

(heterolytic cleavage with formation of a carbonium ion is also possible for branched R).[64] Several authors assume that reaction (3) occurs when mixtures of aromatic amines with CX_4 (X = Cl, Br) are irradiated.[21,65,66] Probably, photoinitiation of Am + RX reactions by excitation of RX in their own absorption bands to a noticeable extent is possible only for aryl halides,[67–69] whose absorption spectra are shifted relative to those of the amines. Since the absorption spectra of alkylated HC overlap considerably with those of amines, selective excitation of the former in Am–HC mixtures is unlikely.

In some cases, it was possible to determine the nature of the excited state involved in the ET process. It was shown by the chemically induced nuclear polarisation (CINP) method for the $Et_3N \cdot CCl_4$ complex that ET occurs by reaction (1) in a excited singlet state.[70,71] The reactions of arylamines with chloro-containing HC also occur by the singlet mechanism.[59,72–75]

A study of the photochemical properties of the system *N*, *N*, *N'*, *N'*-tetramethyl-*p*-phenylenediamine–carbon tetrachloride showed that the reaction in a benzene solution occurs via an excited triplet state,[76] while in pure CCl_4 it probably occurs in a singlet state.[77] In both cases, the quantum yield of the contact ion pair $Am^{+\cdot}/Cl^-$ is close to unity and decreases somewhat when tetramethylbenzidine is used as the electron donor.[78]

It was found in a study of photo-ET from excited *N*,*N*-dimethylaniline (DMA) to chlorobenzene that both the singlet and the triplet states of DMA are reactive.[79,80] It was assumed that photodebromination of bromoanthracene by amines also occurs by the triplet pathway,[81] but recent studies by nanosecond laser photolysis has shown that an excited singlet state is reactive and that an intermediate anion radical ($RX^{-\cdot}$) is formed.[68]

A triplet mechanism was proposed[82–86] for the photochemical reaction of arylamines with CBr_4 in a polymer matrix. A reaction scheme was considered which involved transfer of triplet energy from the excited CTC to the free amine followed by the formation of a triplet exciplex, which gives the final dye.[82]

$$\begin{aligned} &Am \cdot CBr_4 \xrightarrow{h\nu} (Am \cdot CBr_4)^1 \longrightarrow (Am \cdot CBr_4)^3, \\ &(Am \cdot CBr_4)^3 + Am \xrightarrow{k_4} Am \cdot CBr_4 + (Am)^3, \\ &(Am)^3 + CBr_4 \longrightarrow (Am)^3 \cdot CBr_4 \longrightarrow Dye. \end{aligned} \qquad (4)$$

The authors assume that an additional reaction occurs in the presence of naphthol (NP)

$$(Am \cdot CBr_4)^3 + NP \xrightarrow{k_5} Am \cdot CBr_4 + (NP)^3, \qquad (5)$$

It was noted that $k_5[NP] \gg k_4[Am]$.[83] Such a relation of reaction rates is reasonable as the energies of the triplet levels are ~ 3.5 eV (CTC) and 2.5 eV (NP), respectively, i.e. NP is an effective triplet 'trap'. In this case, the formation of a dye should be suppressed completely at high NP concentrations, which contradicts the experimental data: at $[NP] \sim [Am] \sim 1\ mol\ l^{-1}$, the quantum yield of the reaction (~ 0.1) is almost the same as that in the absence of NP.[83]

In the case when triplet energy is transferred from an excited CTC to the amine, the nature of this excited state and the reasons for its stability in comparison with the triplet exciplex remain unclear. Excitation of a weak CTC leads to the transfer of an electron from the donor to the acceptor, and formation of a radical-anion of the latter. Since the radical-anion of CBr_4 is unstable, excitation of an Am – CBr_4 CTC results in irreversible decomposition of the complex with formation of an amine radical-cation, a tribromomethyl radical and a bromide ion (see below).

Obviously, studies on the dependence of the quantum yield of photo-ET processes on the presence in solution of various admixtures, energy acceptors of various types, would throw light on the problem of the stability of excited CTC. But, although many studies on the primary processes in Am – PHM systems have been reported, unfortunately no data on the quantum yields φ_i of primary photochemical reactions are available for diarylamines.

If chain processes are absent in the system, φ_i cannot be lower than the sum of the quantum yields of all products of the photoinitiated reaction. Bearing in mind the wide variety of pathways in the transformation of primary photogenerated species, the fact that the quantum yield of dye formation exceeds 0.1,[27] and

that the quantum yield of acridines reaches 0.2,[87] one can assume that the quantum yield of the primary process involved in photo-ET during the excitation of Am–PHM complexes is close to unity, which is consistent with the dissociative nature of this process.

III. Reactions of radical-anions of halohydrocarbons

The properties of radical-anions of HC ($RX^{-\bullet}$) and the fact of their existence as separate species have been considered in a number of reports.[88–92] It was believed that when ET occurs to HC with R = Alk, the latter 'instantly' decompose releasing X^- (see Refs. 93, 94) ($HC^{-\bullet}$ exist only for a few vibration periods[95]). Therefore, the whole process was named (photo)dissociative transfer (capture) of an electron. When $RX^{-\bullet}$ is generated in frozen matrices (4–77 K), the problem discussed was: to what extent can we distinguish between a σ* ion ($RX^{-\bullet}$)[95] and a $R^{\bullet}\cdot X^-$ complex (see Ref. 96), which appears in a matrix 'cage' due to cleavage of a C–X bond.

To date, several anion radicals have been detected experimentally. The $CCl_4^{-\bullet}$ radical-anion absorbs at 354 nm (4.2 K)[97] or 365 nm (77 K).[98] According to the EPR spectrum and ab initio calculations, the unpaired electron in $CCl_4^{-\bullet}$ is located at the antibonding σ* orbital of a C–Cl bond.[99] At room temperature, $CCl_4^{-\bullet}$ decomposes in $\tau < 18$ ps.[100] The $C(NO_2)_4^{-\bullet}$ radical-anion, whose properties are similar, decomposes in less than 10 ps.[101] Recently the $CBr_4^{-\bullet}$ radical-anion was detected by mass spectroscopy of positive ions.[102] Perhaps femtosecond laser techniques would also make it possible to observe these species in the photoexcited state. In a solid matrix (77 K), absorption at 365 nm was ascribed to $CBr_4^{-\bullet}$.[103]

The location of negative charge in products of decomposition of a HC radical-anion can be estimated by comparing the electron affinities (EA) of the fragments. For example, the values of EA (eV) of radicals formed owing to decomposition of $CX_4^{-\bullet}$ are: Cl$^{\bullet}$ 3.61; Br$^{\bullet}$ 3.36 (see Ref. 104), $CCl_3^{\bullet}$ 1.88, $CBr_3^{\bullet}$ 0.57 (see Ref. 105), i.e. the formation of a halide anion is much more favourable energetically than the formation of a trihalomethyl anion. It should be noted that considerably different EA values are available in the literature for the starting CCl_4 and CBr_4: from 0.15 and 1.2 (see Ref. 106) to 2.12 and 2.06 eV.[107] Obviously, the data in Ref. 106 are more suitable for a consideration of the complexation properties of these compounds, since they have been obtained under similar conditions from the energies of excited complexes of CCl_4 and CBr_4 with tetramethylbenzene. According to the data in Ref. 107, the electron-accepting properties of CCl_4 and CBr_4 should almost coincide, which contradicts numerous experimental data on the properties of CTC of these PHM.

In quantum-chemical calculations, various authors considered, in essence, four different pathways of decomposition of PHM radicals.

$$RCH_nX_{3-n}^{-\bullet} \longrightarrow \begin{cases} RCH_nX_{2-n}^{\bullet} + X^- & (6) \\ RCH_nX_{2-n}^{-} + X^{\bullet} & (7) \\ RCH_nX_{3-n} + e^- & \\ RCH_{n-1}X_{3-n}^{-} + H^{\bullet} & (8) \end{cases}$$

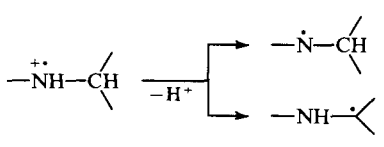
According to the data in Ref. 108, the most frequently occurring pathway (6) leading to a halide anion is characterised by the minimum energy. The formation of a halogen radical, pathway (7), is possible only through decomposition of iodine derivatives, since iodine has the lowest EA among halogens;[109] moreover, it is important that the remaining radical should contain strong electron-accepting substituents stabilising the anion. It has been shown by MNDO and AM1 methods for chloro- and bromomethanes[110] that for $n = 1, 2$, ET directly results in decomposition of the C–X bond by pathway (6). Decreasing n and the polarity of the medium favours stabilisation of the primary radical-anion as a kinetically independent species, which subsequently also decomposes by pathway (6). Fragmentation by pathway (8) is energetically unfavourable. According to the opinion of the authors,[110] it can occur by the mechanism of dissociative electron capture only in the presence of additional factors facilitating this reaction.

Aromatic radical-anions $RX^{-\bullet}$ are much more stable than aliphatic ones. For example, the rate constant for dissociative capture of a solvated electron measured for R = Ph ($l\ mol^{-1}\ s^{-1}$) increased in the series: Cl (5×10^8) < Br (4×10^9) < I (1.2×10^{10}).[111]

IV. Reactions of radical-cations of amines

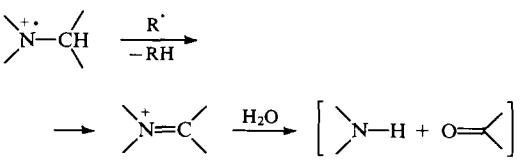
Unlike radical-anions of HC, the radical-cations of aromatic amines formed owing to ET during a chemical reaction have been reliably detected by many authors from their typical absorption spectra.[43,91,112–119] The radical-cations of monoarylamines, $(ArNRR')^{+\bullet}$, display absorption bands in the short-wave spectral region at 400–500 nm.[119–122] The radical-cations of diarylamines $Ar_2NR^{+\bullet}$ and triarylamines $Ar_3N^{+\bullet}$ absorb in the long-wave region at 600–800 nm.[123–126] In comparison with the $Ar_2NHm^{+\bullet}$ radical-cation, the spectra of the corresponding neutral radicals $Ar_2N^{\bullet}$ are shifted bathochromically and have lower intensities:[127,128] e.g., λ_{max} (nm) and ε_{max} (litre $mol^{-1}\ cm^{-1}$) are 670 and 1.8×10^4, for $Ph_2NH^{+\bullet}$ (see Ref. 128) and 770 and 3.9×10^3 for $Ph_2N^{\bullet}$ respectively (see Ref. 129).

As is evident from the previous section, the reverse electron transfer from decomposition products of an HC radical-anion to an amine radical-cation is unlikely, since the latter cannot oxidise a halide anion or a $RCH_nX_{2-n}^{\bullet}$ radical. The amine radical-cation therefore undergoes various chemical reactions. The simplest one is deprotonation,[130] which, in the general case, can occur via two pathways.

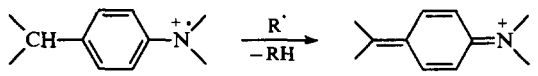


The acidity of the NH group does indeed increase considerably when an Am is oxidised into the radical-cation. For example, pK_a = 30.6 for $PhNH_2$ and 6.5 for $PhNH_2^{+\bullet}$ (see Ref. 131); 24.9 for Ph_2NH and 4.2 for $Ph_2NH^{+\bullet}$ (see Ref. 128). In both cases the acidity increases by more than 20 orders of magnitude. Values of the same order were obtained for the α-CH group in DMA: pK_a(DMA) is ~ 34, whereas pK_a($DMA^{+\bullet}$) is ~ 9 (Ref. 132). However, Nelsen and Ippoliti[133] consider that the acidity of the α-CH group in the radical-cation is usually unduly overestimated: for example, they obtained pK_a ~ 15 for the radical-cations of trialkylamines.

Not only heterolytic cleavage of the α-C–H bond is possible but also homolytic cleavage resulting in an iminium cation.

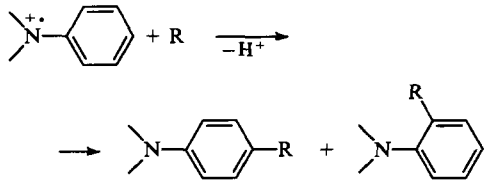


This is probably one of the pathways of dealkylation of radical-cations followed by hydrolysis.[140–142] Homolytic cleavage of a benzyl C–H bond with the formation of quinonoid compounds is known for radical-cations of amines that are toluidine derivatives.



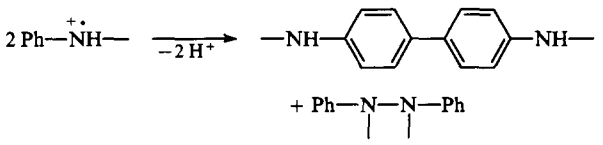
This class of reactions includes photooxidation of leuco-dyes with diverse structures in the presence of HC into the corresponding dyes.[46,143–146] It is suggested that the reaction may occur in two consecutive steps, first with abstraction of a proton and then of an electron, rather than by abstraction of a hydrogen atom.[147]

One of the typical and practically important reactions of radical-cations of aromatic amines is recombination, which occurs predominantly at the *ortho* and/or *para* positions of the benzene ring.



The ratio of reaction products is determined by the nature of the substituents on the nitrogen atom and on the aromatic ring and by the properties of radical R.[58,61,113,140,148–151]

The typical mode of recombination of radical-cations of aromatic amines with one another is C–C-dimerisation into benzidine derivatives (for radical-cations of amines having a free *para* position) and N–N-dimerisation into hydrazines (for radical-cations of primary and secondary amines).[125,152–157]

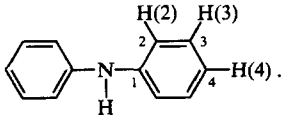


In addition to this, radical-cations of certain diarylamines dimerise into phenazines.[125,154,156]

It should be noted that C–C-dimerisation precedes deprotonation,[158] whereas N–N-dimerisation is likely to occur after deprotonation, i.e. it involves neutral radicals.[159] For example, it has been shown that protonation of the $Ar_2N^{\bullet}$ radical blocks the interaction at the reaction centre, the nitrogen atom.[160] In addition to C–C- and N–N-dimerisation, C–N-dimerisation is also observed for diarylnitrogen radicals.[161,162] According to quantum-chemical calculations and in agreement with the experiment, the labile N–N dimer is formed quickly and reversibly in one step, whereas stable C–N- and C–C-dimers are formed slowly and in two steps, the final step being irreversible.[163]

As to the electronic structure of the $Ar_2NH^{+\bullet}$ radical-cation and the neutral $Ar_2N^{\bullet}$ radical, the density distributions of the unpaired electrons in both radical species virtually coincide, judging from the coupling constants in the ESR spectra (Table 1). About 1/3 of the spin density is located on the nitrogen atom, while ~ 2/3 is located on the benzene rings at the *ortho* and *para* positions. Depending on the method, quantum-chemical calculations give somewhat differing results, but the preference for the *ortho* and *para* positions in delocalisation over the benzene rings is maintained. On the whole, one can conclude that the calculated data agree with the above main pathways in the interactions of these reactive species: the attack on the N, C(2) and C(4) atoms.

Table 1. EPR spectra (A) and data of quantum-chemical calculations (B) for radicals formed from DPA

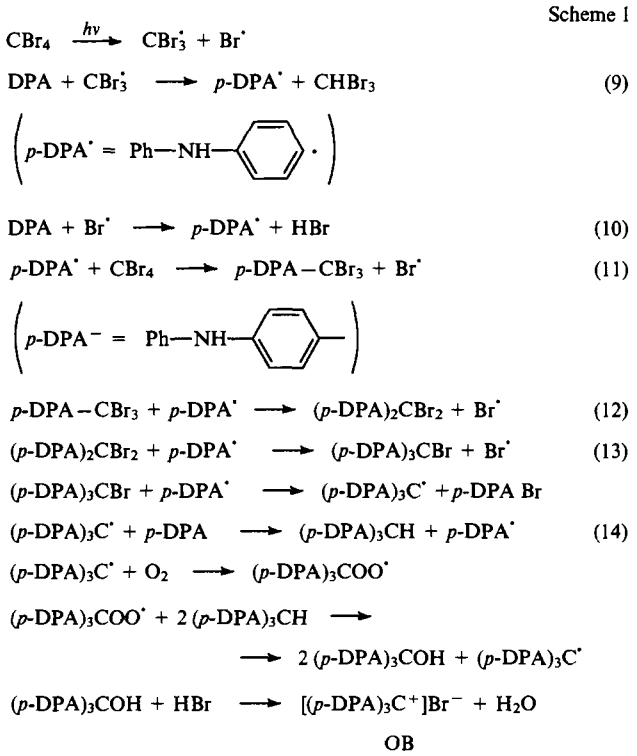


Radical	N	H(N)	H(2)	H(3)	H(4)	Ref.
A. Coupling constants (a_i, G)						
$Ph_2N^{\bullet}$	8.9	–	3.7	1.49	4.34	134
$Ph_2NH^{+\bullet}$	9.17	11.14	3.51	1.36	4.88	135
B. Spin densities (ρ_i)						
		C(1)	C(2)	C(3)	C(4)	
$Ph_2N^{\bullet}$	0.307	0.005	0.110	0.002	0.114	136
$Ph_2NH^{+\bullet}$	−0.29	0.25	0.22	−0.14	−0.48	158
	−0.801	0.096	−0.125	0.073	−0.115	137, 138
	0.501	0.006	0.080	0.002	0.079	139

V. Photoinduced chain radical reactions

It has been suggested that several types of chain radical processes can be involved in photoinduced reactions of amines with PHM, but the existence of some of them has not been proven. For example, a scheme for the formation of a triphenylmethane dye (TPMD), Opal Blue (OB), in a photochemical reaction of DPA with CBr_4 has been proposed. The scheme involves the following radical-chain reactions (Scheme 1).[21]

Scheme 1



This scheme has been accepted by many authors (see, for example, the relevant reviews[164–167]), but the feasibility of these reactions is doubtful. Reactions (9), (10) and (14) are assumed to occur by the abstraction of a hydrogen atom from the aromatic ring, which is an unlikely process. In the case of reaction (14), this is a highly improbable process, since the stable triphenylmethane radical with a delocalised electron is transformed into an energy-rich unstable radical with an electron localised on an sp^2 orbital. For example, when benzophenone was used as acceptor instead of CBr_4 in the reaction with amines, it was found that the H atom was abstracted only from the α-carbon of the alkyl substituent, giving stable radicals of the type $PhN(R)C^{\bullet}HR'$ (see Ref. 168) or from the

N atom in Am, giving radicals of the $Ph_2N^{\bullet}$ type.[169,170] It was shown that similar radicals are formed in the reaction of DPA with $CCl_3^{\bullet}$ (see Ref. 43) and with fullerene.[171] However, the abstraction of an H atom from the aromatic ring has never been observed in these reactions.

Reactions (11) – (13), which involve radical substitution of a halogen radical at a saturated carbon atom, also look improbable (no reactions of this type have been reported in the literature).[172,173] If they occurred in the system under consideration, chain transfer (10) → (11) → (10) etc. would appear, and the quantum yield (φ) of the dye would exceed 1. It will be shown below that reactions of amines with HC can sometimes involve a chain process with $\varphi > 1$, but this is related to another reaction pathway, and the φ values for TPMD are always less than one.

A radical scheme for the formation of Opal Blue has been adopted in studies[43,44,50,114,115] dealing with reactions of Am with HC. Since the authors[114] have observed experimentally the formation of the $Ph_2N^{\bullet}$ radical, they tried to reconcile this result with the participation of the *p*-DPA$^{\bullet}$ radical, formed due to the inversion $Ph_2N^{\bullet} \rightarrow p$-DPA$^{\bullet}$, in the above reaction scheme. However, it was shown later that photochemical generation of the $Ph_2N^{\bullet}$ radicals resulted in their transformation into carbazole in a good preparative yield.[174] The reaction did not occur if methyldiphenylamine (MDPA) was used instead of DPA, also supporting the view that the formation of carbazole occurs via the $Ph_2N^{\bullet}$ radical. It is known that direct excitation of both DPA and MDPA results in carbazole by cyclisation directly in the excited state without the participation of radicals.[175]

However, the reactions of completely *N*-substituted amines with PMH also led to the isolation of TPMD, which confirms that *N*-radicals, whose generation from these amines occurs with difficulty, do not play a predominant role in TPMD formation.[43,176] It follows from the data in Ref. 177 that a dye results from the reaction of a $CX_3^{\bullet}$ radical with a radical-cation $Am^{+\bullet}$ (a dye does not form when $CX_3^{\bullet}$ is generated in the presence of neutral Am).

In the next section we present a scheme for the synthesis of TPMD, including OB, through a series of reactions of electrophilic aromatic substitution involving Am and intermediate dyes, together with experimental evidence for this scheme.

In the context of the discussion of chain radical reactions, it is of interest to consider a series of works by Latovskii et al.,[141,176,178–181] the purpose of which was to study the characteristics of the photochemical behaviour of the system of bonds Ph–N–Me in reactions with polychloromethanes. DMA and MDPA were used as reagents.

The reaction of DMA with CCl_4, as with many other compounds, gave a TPMD, Crystal Violet (CV). The quantum yields of many compounds were measured. The focus of attention of the authors was drawn to reactions related to the formation and transformations of an α-methylene radical $>N-CH_2^{\bullet}$, and they tried to explain the formation of all of the photoproducts on the basis of this radical. Although the quantum yield of the formation of CV did not exceed unity, the authors proposed a scheme of chain radical reactions,[141] which, although it differs from Scheme 1, is also rather unlikely.[182]

During the studies of simpler systems of DMA with CH_2Cl_2 (Ref. 179) and $CHCl_3$ (Ref. 180), results were obtained suggesting that interaction of $Cl_nH_{3-n}C^{\bullet}$ type radicals with the benzene ring of the DMA radical-cation, rather than with the α-methylene radical, is important (these results are considered in more detail in the following section).

However, chain reactions still occur in the DMA–CCl_4 system, which is evident from the experimentally found high quantum yields for the formation of HCl and the disappearance of DMA, $\varphi(HCl) \approx \varphi(DMA) > 10$. This fact was explained[183] by reactions involving an α-radical, a CTC, and an amine.

$$Ph(Me)NCH_2^{\bullet} + PhNMe_2 \cdot CCl_4 \longrightarrow$$
$$\longrightarrow Ph(Me)NCH_2C_6H_4NMe_2\text{-}p + HCl + CCl_3^{\bullet}$$

$$CCl_3^{\bullet} + PhNMe_2 \longrightarrow Ph(Me)NCH_2^{\bullet} + HCCl_3$$

However, this scheme seems doubtful. First, it is more likely that a radical would attack a free amine rather than a CTC, since the concentration of the former is much higher, [DMA] ≫ [CTC]. Second, it is unlikely that a CCl_4 molecule can accept an H atom giving the $CCl_3^{\bullet}$ radical; more probably, the latter captures H to give chloroform. Third, if the assumption in Ref. 183 is valid, the DMA·CCl_4 complex is the chain carrier. In this case, increasing DMA concentration should lead to elongation of the chain. But, the authors observed a reverse dependence: when the concentration of DMA in CCl_4 increased, the quantum yield decreased,[183] and conversely, when the reaction was carried out in dioxane, the quantum yield increased with increasing CCl_4 concentration.[178] It follows from these data that a CCl_4 molecule is the chain carrier.

$$Ph(Me)NCH_2^{\bullet} + CCl_4 \longrightarrow Ph(Me)NCH_2Cl + CCl_3^{\bullet}$$

$$CCl_3^{\bullet} + PhNMe_2 \longrightarrow Ph(Me)NCH_2^{\bullet} + HCCl_3$$

A similar sequence of transformations occurs in reactions of CX_4 with alkylamines, which do not contain an aromatic ring but contain an H atom in the α-position relative to the nitrogen atom; the quantum yields of these reactions can be as high as 100.[184–186]

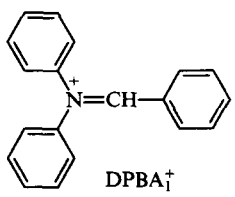
It should be emphasised once more that a $\varphi > 1$ in reactions of DMA and isomeric toluidines with CCl_4 is observed only for HCl formation and results from a different reaction, which is a side reaction with respect to CV formation. The φ value for the latter, like the values for the formation of other dyes from amines, is always less than one.

VI. Formation reactions of triphenylmethane dyes

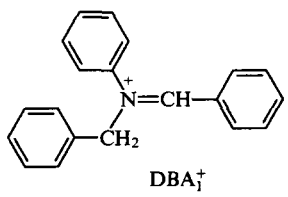
To date, the formation of two types of dyes during the photolysis of complexes of aromatic amines with PHM has been proved reliably. These include triphenylmethane dyes, which absorb light at 600–700 nm, and acridine dyes absorbing light at 450–550 nm and possessing luminescent properties. Studies on the mechanisms of their formation revealed a number of common features. Of the primary reactions, we should mention the formation of radical-cations or, in some instances (for secondary amines), neutral amine radicals on irradiation of CTC and the recombination of these radicals with halomethyl radicals. Their participation in the electrophilic alkylation of the free amine (which is present in excess in the reaction mixture) is a general feature. As noted in the Introduction, different viewpoints exist concerning the structure of the intermediates and the mechanism of their transformation into the final dyes, as well as for the structure of the dyes absorbing in the region of 600–700 nm. Below we present these viewpoints and make a reasoned choice of one of them.

The extensive experimental data concerning the photochemical reactions of Am with CBr_4 and $CBr_3SO_2CBr_3$ in solution and in polymer layers are presented in studies by Vannikov and Grishina et al.[27,82,83,187–196] DPA, diphenylbenzylamine (DPBA), and dibenzylaniline (DBA) were used mainly as the amines. It was found that irradiation of all three amines with CBr_4 first gave dyes with $\lambda_{max} \sim 665$ nm, which were given a general conventional designation D665, and which were then thermally ('in the dark') transformed into dyes with $\lambda_{max} \sim 605$ nm (D605). The activation energy for the D665 → D605 transformation for DPA was found to be half of that for DPBA (43 and 86 kJ mol^{-1}, respectively), whereas the activation energies for the sensitised formation of D665 were the same for all three amines (24 kJ mol^{-1}).[189]

The quantum yields for the formation of dyes D665 measured during direct photolysis of the complexes were $\varphi = 0.14$ (DPBA) and $\varphi = 0.07$ (DBA).[27] As shown above, the D605 formed from DPA is Opal Blue. The structures of D605 dyes obtained in the reactions with DPBA and DBA, and the D665 obtained from DPA, are not reported in the works cited. The authors [27] propose diarylmethyleneiminium structures (Am_I^+) for the D665 formed from DPBA and DBA. Diarylmethyleneimines are formed due to abstraction of H atoms from the benzyl groups of the amine radical-cations.



$DPBA_I^+$



DBA_I^+

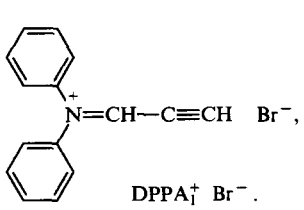
To substantiate the structures of the Am_I^+ type, the authors drew an analogy with photochemical reactions of amines with CBr_4 and with the Methylene Blue dye (MB^+). It was found that MB^+ was reduced on illumination by various benzylamines through the transfer of an H atom from the CH_2 group.[197,198]

$$MB^+ + \mathbf{Am} \xrightarrow{h\nu} MB^{\cdot} + Am^{+\cdot} \longrightarrow MBH + Am_I^+$$

The reactivity of the amines in this reaction increases with increasing number of benzyl groups, i.e., DPBA is less reactive than DBA. However, judging from the quantum yields of D665 formation, a reverse order of reactivity is observed in the reaction with CBr_4: DPBA > DBA, in agreement with the number of phenyl groups, which are obviously involved in formation of the dyes.

In addition, it is clear that an Am_I^+ structure is not feasible for DPA, although its photochemical properties coincide with those of DPBA and DBA. Probably the structures of all three dyes (based on DPA, DPBA, and DBA) should be similar, hence the Am_I^+ structure is inappropriate for them.

To confirm the Am_I^+ type structure for D665, the authors of a book (Ref. 27) cite the previously published data (Ref. 199), where a dye with $\lambda_{max} = 670$ nm, obtained from diphenylpropargylamine and CBr_4, is assigned the following structure:



$DPPA_I^+ \ Br^-$.

Let us consider the arguments presented in Ref. 199 in order to confirm this structure: (1) the retention of phenyl groups and an acetylene group, according to IR and ^1H NMR spectral data; (2) instead of the signal of two methylene group protons, the appearance of a new broadened signal around 5.2 ppm, which disappeared in a deuteriated solvent; (3) the presence of bromine, according to mass spectrometric data. Strictly speaking, the first argument does not confirm the structure $DPPA_I^+$ but merely does not contradict it, as well as many other possible structures. The second argument is qualitatively consistent with the structure $DPPA_I^+$; however, it follows from various known data [200–202] for the chemical shifts of the methine proton in the iminium moiety that the value of 5.2 ppm is too low for such a structure, since the normal signal for this proton is found at 9–9.5 ppm. The third argument in the form presented is inconsistent with the structure of $DPPA_I^+$, since the presence of bromine in the molecular ion implies that the bromine atom is covalently bonded to the skeleton of the molecule. However, $DPPA_I^+$ does not incorporate the bromide ion, and the latter is merely the counterion of the dye cation. Unfortunately, the authors do not report the m/z value measured experimentally.

It is known that phenyliminium salts have absorption bands in the middle UV region,[203–205] spectra considerably different from the postulated spectrum of Am_I^+. Diphenylmethyleneaniline $Ph_2C{=}NPh$ and triphenylethene $Ph_2C{=}CHPh$, whose molecules are isoelectronic with DPBA, also absorb in the UV region: $\lambda_{max} = 346$ and 298 nm, respectively.[206] Thus, the validity of the structure $DPPA_I^+Br^-$ for the dye with $\lambda_{max} = 670$ nm obtained in Ref. 199 and the structure Am_I^+ for D665 described in Vannikov and Grishina's book [27] is doubtful.

The Am_I^+ type structure for D665 also contradicts flash photolysis data.[119] The formation of Am_I^+ should involve abstraction of an H atom from an $Am^{+\cdot}$ radical-cation, hence the accumulation of Am_I^+ should occur in parallel with the disappearance of $Am^{+\cdot}$ and over the same time interval. Such a reaction occurs during photooxidation of leuco-dyes in the presence of HCs. The final dye is formed in <100 μs, which is comparable with its lifetime.[207] When a D665 is formed in the system $Am \cdot CBr_4$, the lifetime of $Am^{+\cdot}$ also does not exceed 100 μs, but the appearance and increase of D665 absorption occurs over seconds,[119] and even more slowly (over minutes) at low concentrations of the amine.[36] The time difference between the two processes is several orders of magnitude. Obviously, the transformation of $Am^{+\cdot}$ into D665 is a more complex reaction (or a sequence of reactions) than simple removal of a hydrogen atom from the benzyl group.

In order to determine the structural moiety of amines involved in the formation of D665 and D605, photochemical reactions of CBr_4 with several groups of amines, differing in the presence of an unsubstituted benzene ring and an *N*-benzyl group in their molecules, were studied.[208] It was found that dyes are formed only from amines whose molecules contain a benzene ring unsubstituted at the *para*-position and linked to the amine nitrogen atom (an 'aniline' ring). If the *para*-position is blocked, dyes are not formed, irrespective of the presence of a *N*-benzyl group. For example, irradiation of the complex of CBr_4 with MDPA, which does not contain an *N*-benzyl substituent, resulted in the formation of a dye. However, the reaction of *N*-benzyl-di(*p*-tolyl)amine under the same conditions did not give products absorbing in the visible region, although a benzyl group was present.

Based on an analysis of experimental data on primary reactions, reactions in solutions and in polymer layers, and taking into account analogies with photochemical and thermal reactions of Am with PHM, we proposed a general scheme for the photochemical synthesis of dyes (Scheme 2; for simplicity, the positive charge is shown as localised at one of nitrogen atoms),[182] which was then confirmed experimentally [209] for all of the above aromatic amines whose reactions gave D665 and D605 (the latter are di- and triphenylmethane dyes, respectively).

Scheme 2 shows reaction initiation by excitation of a CTC, which is easily performed for X = Br by irradiation of the reaction mixture by light with $\lambda > 350$ nm. The free components virtually do not absorb in this region, hence selective excitation of the CTC occurs, since the absorption spectra of the $Am \cdot CBr_4$ complexes are shifted bathochromically relative to the spectra of the components. Then the first steps of the process (15) – (17) correspond to the sequence of the static quenching [reaction (1)] and dissociation [reaction (6)] reactions discussed above. During amine photoexcitation ($\lambda < 300$ nm), which is the more probable in the case of X = Cl, the ET changes somewhat in nature and occurs by the dynamic quenching pathway (2).

For any initiation pathway, the primary reactive species are an amine radical-cation $Am^{+\cdot}$, a $CX_3^{\cdot}$ radical, and an X^- anion. Subsequently, reaction (18) involves recombination of radicals into a *p*-amino-substituted trihalotoluene, which undergoes ionization giving a *p*-quinonoid ('monophenylmethane') dye

Scheme 1

$$PhNR'R'' + CX_4 \rightleftharpoons PhNR'R'' \cdot CX_4 \quad (15)$$

$$PhNR'R'' \cdot CX_4 \xrightarrow{h\nu} (PhNR'R'' \cdot CX_4)^* \quad (16)$$

$$(PhNR'R'' \cdot CX_4)^* \longrightarrow (PhNR'R'')^{+\cdot}\,{}^{\cdot}CX_3^-, X^- \quad (17)$$

$$(PhNR'R'')^{+\cdot} + CX_3^{\cdot} \xrightarrow[-H^+]{} R'R''N\text{-}C_6H_4\text{-}CX_3 \longrightarrow R'R''\overset{+}{N}{=}C_6H_4{=}CX_2, X^- \quad (18)$$

ICI DI

$$DI + Am \xrightarrow[-HX]{} R'R''N\text{-}C_6H_4\text{-}CX_2\text{-}C_6H_4\text{-}NR'R'' \longrightarrow R'R''N\text{-}C_6H_4\text{-}CX{=}C_6H_4{=}\overset{+}{N}R'R'', X^- \quad (19)$$

ICII DII

$$DII + Am \xrightarrow[-HX]{} [R'R''N\text{-}C_6H_4]_3CX \longrightarrow [R'R''N\text{-}C_6H_4]_2C{=}C_6H_4{=}\overset{+}{N}R'R'', X^- \quad (20)$$

ICIII DIII

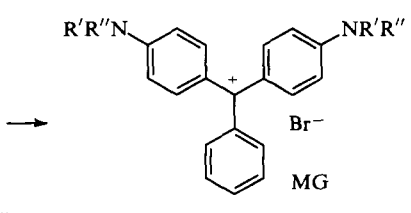
X = Cl, Br; R', R'' = H, Alk, Ar.

DI; ionisation is facilitated by the strong mesomeric effect of the nitrogen atom and the thermodynamic stability of the halide ion. It was noted in studies by flash photolysis [50,65,114,115] dealing with the primary steps of the reactions of Am with CBr_4 that the destruction of $Am^{+\cdot}$ obeys second-order kinetics, which corresponds to a recombination of the two radical species present in solution in equal concentrations.

After that, the amine present in excess acts as a nucleophile with respect to DI [reaction (19)]. In turn, this is an electrophilic aromatic substitution (alkylation) reaction with respect to the amine, in which DI is the alkylating agent. This results in diphenylmethane dye DII (named as D665 owing to its spectral properties [27]). Subsequently, DII reacts as an electrophile with respect to a new Am molecule in reaction (20), which is similar to reaction (12), giving the final TPMD — DIII, i.e. D605.

The lability of compounds such as DI and DII and the ease of their reaction with Am were described in Ref. 210, where a TPMD was obtained in the cold simply by mixing an amine with the corresponding halo-derivative. The reaction of Am with tribromotoluene, which is, in essence, the simplest model of intermediate compound (IC) I without an amino group in the *para*-position, also occurs readily to give dyes like Malachite Green (MG). The reaction can occur both thermally and under light irradiation. [36]

$$PhNR'R'' + PhCBr_3 \xrightarrow{\Delta\ (\text{or } h\nu)}$$



R' = R'' = Me.

Thermal synthesis of di- and triphenyl dyes directly from Am and PHM is carried out under pressure at an elevated temperature in the presence of metal salts. [211,212] The reaction occurs as a Friedel–Crafts alkylation of Am. [213] The amino group, which is a type I substituent, directs the attack predominantly to the *ortho*- and *para*-positions. The behaviour of aromatic amines in thermal reactions of arylamines with PHM, as in photochemical reactions, is exactly the same, irrespective of the presence or absence of the *N*-benzyl group in their molecules.

The spectral properties of arylmethane dyes are characterised by a clear relation between the positions of the absorption band maxima and the number of donor (amine) groups in the benzene rings for related mono- (λ_I), di- (λ_{II}) and triphenylmethane dyes (λ_{III}): introduction of the second substituent into the molecule results in a marked red shift of the colour — the maximum shifts considerably towards longer wavelengths, whereas introduction of the third substituent causes a slight blue shift of the colour, and the maximum slightly shifts towards shorter wavelengths, i.e. $(\lambda_I) < (\lambda_{III}) < (\lambda_{II})$. [212,214,215] For example, for Crystal Violet and its analogues (Scheme 2, R' = R'' = Me), the values of λ_I, λ_{II}, and λ_{III} are ~ 415, ~ 610, and ~ 590 nm, respectively. [182]

According to Scheme 2, when the number of halogen atoms in an HC molecule is gradually decreased from 4 to 1, the reaction can be terminated at any of steps (18)–(20), since the absence of a halogen atom in the corresponding intermediate makes the latter unable to participate in subsequent substitution reactions with Am. All of the six possible compounds, ICI–ICIII and DI–DIII, have been obtained in the case of DMA in the above studies by Latovskii et al. Along with the *para*-substituted derivatives shown in Scheme 2, similar *ortho* isomers were also obtained, in agreement with the directing effect of the amino group in aromatic electrophilic substitution reactions. When the free amine is present in deficit, the reaction stops at the recombination step (18), since subsequent reactions of electrophilic alkylation become impossible under these conditions. [112,182]

The process presented in Scheme 2 can be controlled by varying the temperature and by using matrix effects. For example, if the reaction is carried out at 77 K in frozen solutions, irradiation leads only to ET and generation of an amine radical-cation, [43,115,119] which is stable under these conditions. When the reaction is carried out at −15 °C in a polystyrene matrix, recombination (18) already occurs giving DI; however, further reaction is impossible owing to limited diffusion of the reagents. [209] When polystyrene layers containing a CTC of Am with CBr_4 are irradiated at room temperature, reaction (19) occurs in several minutes, and DII is detected immediately. A longer time or heating are required for reaction (20) to occur. [189,209]

Obviously the difference in the rates of reactions (19) and (20) involving the same amine is explained by the different alkylating power of DI and DII. The reactivity of these compounds depends on the positive charge on the reaction centre, the exocyclic carbon atom. The conjugation chain in DII, which stabilises the charge, is twice as long as that in DI, which results in a decrease in the charge on DII in comparison with DI and manifests itself by reaction (20) being slower than reaction (19).

The difference between the alkylating activities of DI and DII was used for determining the rate constants for reactions (19) and (20) during the formation of Opal Blue in a toluene solution.[216] Since the process was carried out with a great excess of DPA, pseudounimolecular constants were measured which were directly proportional to amine concentration. Relatively low activation energies (16.8 and 40 kJ mol^{-1}) and high negative entropies of activation (−187 and −155 J mol^{-1} K^{-1}), typical of bimolecular processes, were found for reactions (19) and (20), respectively.

Interesting results were obtained by comparing the rates of formation of DII and DIII during the photoionisation of DPA and DPBA with CBr_4 in polystyrene.[36] It was found that the rate constants for reaction (19) are ca. 10^{-2} for both amines, and those for reaction (20) are ca. 10^{-4} l mol^{-1} s^{-1}. For reactions (19) and (20), the ratio of the reaction rate constants for the two amines is $k_i(DPA)/k_i(DPBA) \approx 3$, and the ratio of the rate constants for both reactions is $k_{19}/k_{20} \approx 90$ for both amines. Obviously such a coincidence of kinetic parameters indicates the similarity of the reactions of formation of D665 and D605 from these amines.

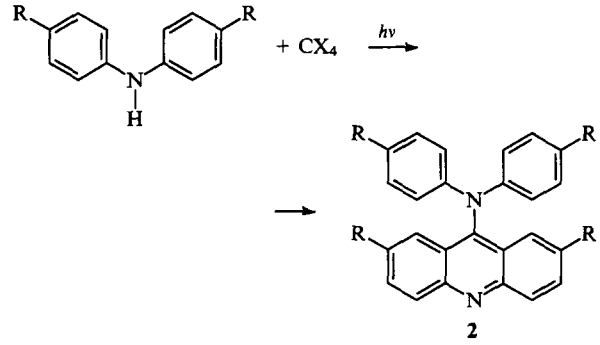
Although an analogy exists between aromatic amines with respect to the formation of TPMD, this reaction, as shown in the previous section, is not the only possible process during the photochemical irradiation of amine – CBr_4 complexes. Therefore, the experimentally observed difference in, say photochemical behaviour and photographic properties of DPA·HC and DPBA·HC complexes,[217] can be explained by various side processes in these systems, which occur in parallel with the formation of dyes but are not related to them. For example, in the case of DPBA these can be reactions involving the α-aminyl radical, which is readily formed from DPBA but not from DPA, whereas in the case of DPA these are reactions involving the amine hydrogen atom, which is absent in DPBA. The side processes result in sets of products possessing different properties and specific to different amines. However, it should be emphasised once more that these features refer to side processes, whereas, as shown experimentally, the formation of TPMD from all amines studied, whose molecules contain a benzene ring unsubstituted in the *para*-position and linked to an amine nitrogen atom ('aniline' ring), react via a common mechanism giving D665 and D605, i.e. DII and DIII (Scheme 2), respectively.[208,218]

VII. Formation reactions of acridine compounds

The formation of acridine compounds upon irradiation of DPA·CX_4 complexes was found in the early 1980s independently by two scientific groups.[219,220] In both studies, the authors reported that 9-diphenylaminoacridine (DPAA) was isolated as one of the reaction products, and the possible pathways for its formation were considered. Scheme 3 shows the sequence of reactions suggested in Ref. 219. This sequence involves recombination of primary radicals into intermediate **1** of *o*-quinonoid structure, which undergoes cyclisation directly into 9-bromoacridine. The latter reacts with a second amine molecule to give DPAA, which (like bromoacridine) exists in the reaction medium as a hydrobromide.

As already noted, direct irradiation of DPA results in carbazole through unimolecular photocyclisation.[221] Unlike this reaction, the formation of the acridine ring involves at least two molecules, an Am and a PHM, and several consecutive reactions result in photoinduced bimolecular cyclisation.

A study of the preparative possibilities of this reaction showed that DPAA analogues, the corresponding 9-diarylaminoacridines **2**, can be obtained in up to 40% yield and in up to 0.08 quantum yield from DPA derivatives substituted in the *para*-position.[36,222]

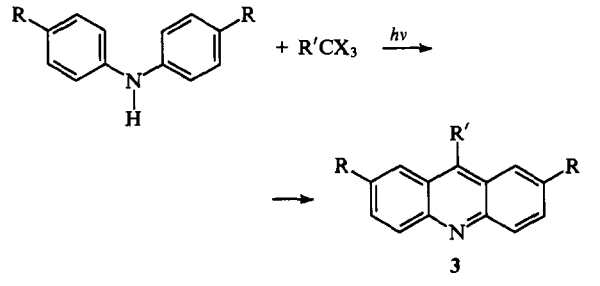


2

R = Me, $PhCMe_2$; X = Cl, Br.

The use of *para*-substituted derivatives instead of DPA increases the yields of cyclisation products considerably, since in this case the above TPMD formation reaction, which is a side process with respect to cyclisation, is blocked.[223]

A similar effect, i.e. an increase in the yield of acridine to 50% and above with R ≠ H, has been observed in reactions of diarylamines with trihalomethanes.[224] In this case acridines **3** containing no amino-substituent in position 9 are the end products. Thus, as in the case of the formation of TPMD, a decrease in the number of halogen atoms in a PHM molecule results in a decrease in the number of steps in the chain of consecutive photoinduced reactions, and the whole process ends at the ring closure step due to the absence of a halogen atom in the acridine molecule after cyclisation.

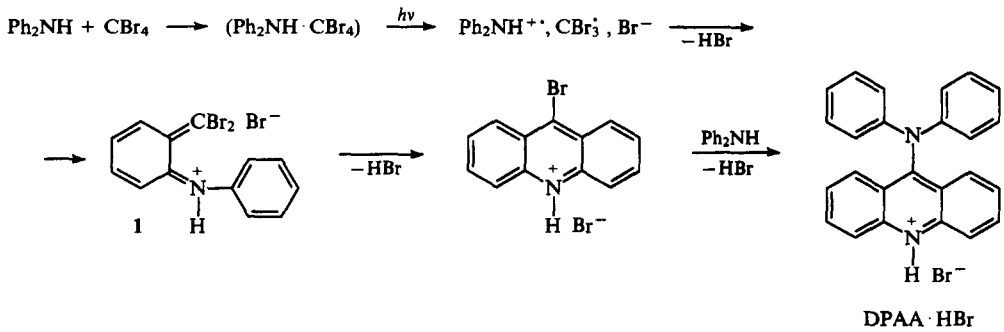


3

R = H, Me, Br; R′ = H, Ph; X = Cl, Br.

The reaction of amines with tribromotoluene occurs not only photochemically but also thermally to give the corresponding 9-phenylacridines (R′ = Ph).[225]

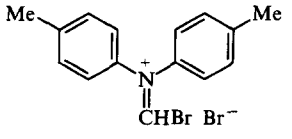
Scheme 2



DPAA·HBr

Although the experimental data considered above were consistent with Scheme 3 and even seemed to confirm it, data were accumulated during studies of photoinduced bimolecular cyclisation that could not be completely explained within the process described. According to Scheme 3, the last step of the reaction is nucleophilic substitution of a halogen atom by an amine molecule. Modelling this step by examples of reactions of 9-bromo- or 9-chloroacridine with various aromatic amines showed that only primary amines undergo the reaction at room temperature.[225] Thermal reaction involving diarylamines occurred only at high temperatures (>100 °C), which differed from the conditions of the photoinduced reaction (< 25 °C). In addition, according to Scheme 3, *N*-methylated amines should give *N*-methylated acridines, but the latter were not found in the reaction mixture.[226] Thus, both the structures of the intermediates and the overall mechanism of the formation of aminoacridines proved to be doubtful.

A study of photochemical reactions of complexes of di-*p*-tolylamine (DTA) with tetra- and tribromomethane by pulse methods showed that in both cases an amine radical-cation absorbing around 700 nm was formed as the primary product.[227,228] As a subsequent intermediate in the reaction with bromoform, a product was detected which absorbed at 540 nm. It was formed by a pseudo-first-order reaction with a rate constant proportional to the amine concentration and was then transformed into acridine by a unimolecular reaction.[228] A comparison of spectral and kinetic properties of the intermediates detected and the time scales of the transformations of compounds into each other led to the conclusion that one more intermediate, which does not absorb in the visible region, exists on the coordinate of the photoinduced reaction of DTA with $CHBr_3$. This intermediate was assigned the bromomethyleneiminium structure **4**.[87]



4

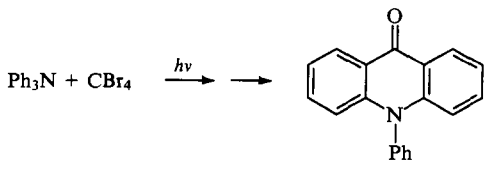
This compound is formed by recombination of primary radicals with participation of the nitrogen atom in $Am^{+\cdot}$ rather than of the *ortho*-positions of the benzene ring, as was assumed according to Scheme 3. Since methyleneimine salts possess pronounced electrophilic properties,[229] compound **4** readily reacts with a new amine molecule to give the next intermediate, which was detected by spectral methods.

Attempts were made to detect a similar intermediate in the reaction of DTA with CBr_4, but only data on the kinetics of the formation of aminoacridine **2** (R = Me) were obtained in this case.[230,231] However, analysis of the kinetic curves of spectral changes in various wavelength ranges confirmed the assumption of the absence of a haloacridine as an intermediate compound during the formation of aminoacridine.

The results of the works cited can be generalised as Scheme 4, where (for DTA as an example) the sequence of photoinduced reactions that occur during the interaction of diarylamines with tri- or tetrahalomethanes to give acridine compounds is shown. The scheme shows: first, that the incident light can be absorbed both by the complex and by the free amine (this is determined by the spectral range of the incident light), and second, that the methyleneiminium intermediate can really be formed owing to recombination involving not the nitrogen atom of the amine radical-cation but a neutral diarylnitrogen radical formed after deprotonation of the radical-cation (see Section IV). Since the data available are insufficient for making an unambiguous choice, both possible recombination pathways are shown.

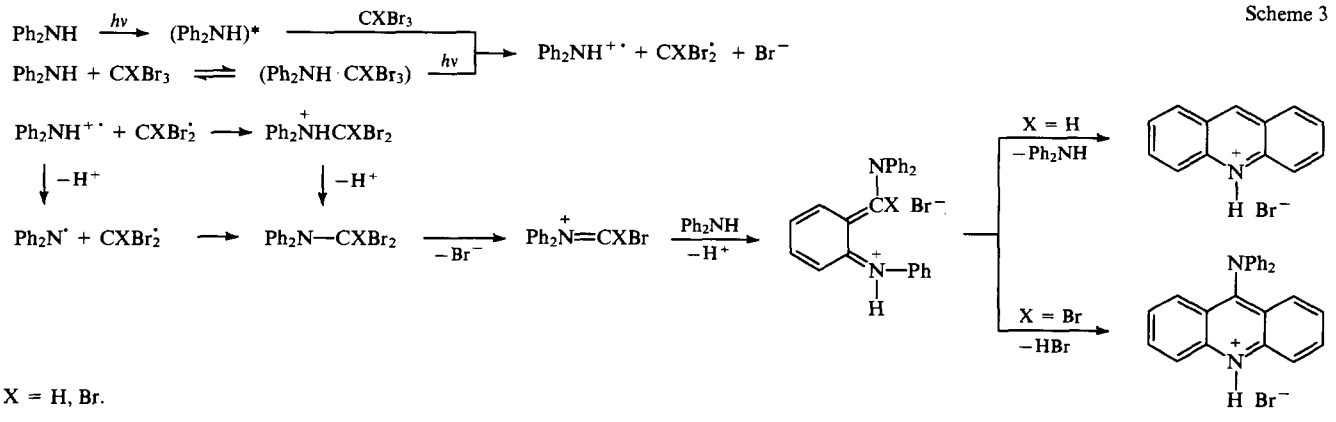
It should be noted that Scheme 4 reflects the main but not the only pathway for the formation of acridine compounds in photochemical reactions of amines with PHM. As shown above (see Table 1), in agreement with quantum-chemical calculations and in conformity with EPR spectra, the maximum density of the unpaired electron in radicals of the type $Ph_2NH^{+\cdot}$ and $Ph_2N^{\cdot}$ is located at the central nitrogen atom, which serves as the main reaction centre for the recombination of primary radicals. The recombination involving the carbon atoms of benzene rings also occurs, although with a lower probability. But, if the nitrogen atom is blocked by a third substituent, this becomes the main reaction pathway, e.g. as in the formation of TPMD.

Obviously recombination in the *ortho*-position of the benzene ring is also the only pathway in the photochemical reaction of triphenylamine with CBr_4, which results in *N*-phenylacridone (from the intermediate *N*-phenylbromoacridinium after treatment of the reaction mixture with water).[33]



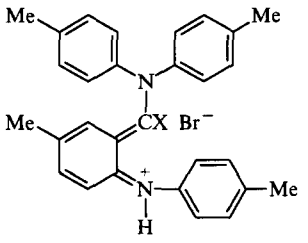
Interesting data were obtained by comparing the rates of the formation of intermediate compounds **5a,b** in reactions of DTA with $CHBr_3$ (**5a**, X = H) and CBr_4 (**5b**, X = Br). These compounds are formed by alkylating DTA with type **4** methyleneiminium salts. It was found that the rate constant for the formation of compound **5a** is more than an order of magnitude higher than the constant for compound **5b**; these constants were 10.8 and 0.32 l mol^{-1} s^{-1} (toluene, 20 °C), respectively.[232] The activation enthalpies (kJ mol^{-1}) and entropies (J mol^{-1} K^{-1}) for the formation of compounds **5a** and **5b** were found to be 36.3 and −101 (**5a**) and 24.6 and −169 (**5b**), respectively. It follows from these data that the entropy factor makes the greatest contribution to

Scheme 3



X = H, Br.

the retardation of the reaction for compound **5b** compared with compound **5a**, and the entropy decreases so much that the simultaneous decrease in the activation enthalpy does not compensate for the former effect.



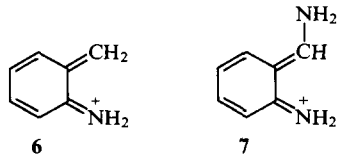
5

X = H (**a**), Br (**b**).

In comparison with the alkylation reaction, the intramolecular cyclisation of compound **5a** into 2,7-dimethylacridine is characterised by a higher activation energy (68 kJ mol^{-1}) but a lower magnitude of entropy of activation (−58 J mol^{-1} K^{-1}).

As mentioned above, the efficiency of the processes shown in Scheme 3 (formation of *N*-substituted diarylamines) is lower than that of the reactions shown in Scheme 4 (for Ar_2NH diarylamines). A comparison of Schemes 3 and 4 shows that, in both cases, *ortho*-quinonoid compounds are the key structures in the cyclisation process. An analysis of the structures of these compounds and a comparison of this process with similar processes of thermal intramolecular cyclisation[233,234] leads to the conclusion that cyclisation is possible only in *cis*-isomers, whereas compounds **5a** and **5b** obviously exist at room temperature in the *trans*-forms, which are thermodynamically more stable. Thus, the general sequence of reactions should include a step involving the isomerisation of the C=N double bond, omitted in Schemes 3 and 4.

The potential barrier to rotation about the C=N bond was calculated for model compounds **6** and **7** by the MNDO method. It was found that the activation energy for isomerisation is twice as high for compound **6** as that for compound **7**: 77.5 and 44.4 kJ mol^{-1}, respectively.[232]



6 **7**

This effect is related to a decrease in the multiplicity of the C=N bond in compound **7** in comparison with compound **6** due to delocalisation of the positive charge onto the second nitrogen atom. It should be noted here that isomerisation of compounds of type **1** and **5** can occur not only by rotation around the C=N double bond, but also by inversion of the sp^2-orbital of the nitrogen atom in the neutral compound after deprotonation. As a result, the energy barrier to isomerisation decreases. The isomerisation of *N*-substituted diarylamines can result only in type **1** *o*-quinonoid compounds, in which, owing to the impossibility of deprotonation, the only isomerisation pathway is rotation in which a high potential barrier is overcome. This makes it possible to explain the low effectiveness of *N*-substituted diarylamines in the photoinduced bimolecular cyclisation.

VIII. Conclusion

The review of the available data on the photochemical reactions of complexes of aromatic amines with halohydrocarbons shows that these systems attract the attention of researchers because of two factors. First, they are convenient systems for studying the process of electron transfer, the main primary chemical reaction occurring upon the irradiation of complexes. Second, they provide a broad range of compounds, including triphenylmethane dyes (reactions of photoinduced consecutive aromatic substitution), acridine derivatives (photoinitiated bimolecular cyclisation), carbazoles (intramolecular cyclisation of diarylamines on their direct excitation), benzidines (photooxidation of amines), etc. The ratio of reaction products is primarily determined by the structures of the amine and the halohydrocarbon, and also by the spectral range of the incident light (excitation of the complex, local excitation of the amine or the acceptor) and by the ratio of reagent concentrations.

In many cases, the nature of the excited state (singlet or triplet) involved in the reaction and the structures of the reacting primary species (radical-cation or neutral amine radical) remain unclear. The mechanism of secondary thermal reactions occurring after irradiation of the complexes has been studied in more detail. Reaction schemes have been proposed that are confirmed by direct observation of the corresponding intermediates, their spectral and kinetic properties, and by modelling separate steps in the general sequence of photoinitiated reactions.

We may note that the photoinitiated formation reactions of triphenylmethane dyes and acridine compounds involve common photochemical and some thermal stages. In both cases, the reactions start as photo-transfer of an electron due to excitation of a charge transfer complex or a free amine. One of the intermediate stages involves electrophilic alkylation of the amine by cations of dyes or by iminium salts. The alkylation reactions are characterised by relatively low activation energies (no higher than 40 kJ mol^{-1}) and high negative entropies of activation (up to −190 J mol^{-1} K^{-1}) typical of bimolecular reactions of this class.

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Complex oxides with coherent intergrowth structures

A M Abakumov, E V Antipov, L M Kovba, E M Kopnin, S N Putilin, R V Shpanchenko

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Abstract. The review deals with the characteristic features of the formation of certain complex perovskite-like oxides. In the crystal structures of these compounds, it is possible to differentiate fragments with different structures, which alternate along the three-fold or four-fold axis of the perovskite sublattice. This approach has been applied successfully to the synthesis of a large number of new complex transition metal oxides, in particular those belonging to the family of Hg-containing high-temperature superconductors with the highest transition temperatures for superconduction. The bibliography includes 79 references.

I. Introduction

Fragments with different structures, for example blocks of the perovskite ($CaTiO_3$), sodium chloride (NaCl), and fluorite (CaF_2) types or individual layers alternating along the large period of the unit cell may be conventionally differentiated in the structures of many complex oxides. In many instances, the differentiation of such fragments is conventional [for example, the differentiation of the (TiO_2) layers in the perovskite structure]. However, in the structures of the superconducting complex copper oxides, which will be considered in the second section of the present review, the differentiation of the (CuO_2) layers is justified, since the Cu – O distance in these layers is much shorter than the distances between the atoms of the neighbouring layers. A necessary condition for the formation of structures consisting of alternating blocks is the geometrical compatibility of fragments with different structures, for example in the *ab* plane. The cubic unit cell parameters a of oxides with structures of the NaCl and CaF_2 types are in the range from 5.4 to 5.7 Å. The cation–cation distance in these structures is close to the corresponding distances in perovskite-type structures — 3.8 – 4.2 Å ($a_{NaCl} \approx a_{fl} \approx \sqrt{2}a_{per}$). The face-centred unit cells of the NaCl and fluorite types can be transformed into tetragonal body-centred cells with the parameter a close to a_{per}. We may note that the motif in the arrangement of the cations in the perovskite structure and in the transformed cells of the fluorite and NaCl types is the same, but the coordinates of the oxygen atoms are different (Fig. 1).

A M Abakumov, E V Antipov, L M Kovba, E M Kopnin, S N Putilin, R V Shpanchenko Faculty of Chemistry, Lomonosov Moscow State University, Vorob'evy gory, 119899 Moscow, Russian Federation. Fax (7-095) 939 09 98

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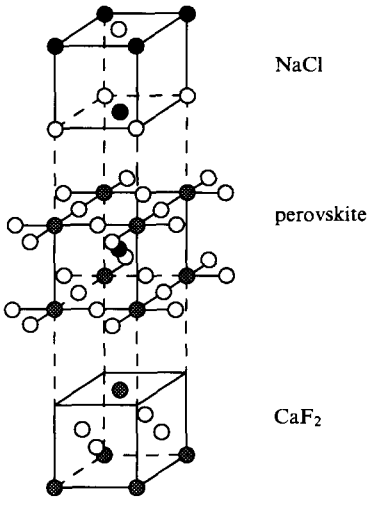


Figure 1. Schematic illustration of the formation of intergrowth structures for the alternation of NaCl- or fluorite-type blocks and (CuO_2) layers along the fourfold axis.

The third section of the review deals with compounds in the structures of which the common elements of the fragments are close-packed layers. In this case, the coalesceing fragments are oriented at right angles to the threefold axis of the perovskite sublattice. An obligatory condition for the formation of coherent intergrowth structures is also the chemical compatibility of the ions entering into their composition (for example, the situation where powerful oxidants and reductants are not present simultaneously) and the electrical neutrality of the unit cell. One should also note that the consideration of structures in inorganic chemistry as sequences of simpler structures arranged in a definite order is to some extent analogous to the description of homologous series of organic compounds. The difference consists in the fact that the alternating elements in the latter case are isolated groups of atoms, whereas in inorganic compounds these are layers or blocks of infinite extent in two directions.

The use of such a treatment of the structures makes it possible to predict the feasibility of synthesising new compounds having the necessary structural fragments giving rise to unique physical properties. For example, we have used this to synthesise new superconducting complex copper oxides.

II. Structures with alternation of fragments with different structures along the fourfold axis

1. Complex copper oxides having the general formula A_2BO_4

The simplest coherent intergrowth structure is that of K_2NiF_4. Numerous complex lanthanide and transition element oxides crystallise in this structural type.[1,2] The structure contains fragments of the perovskite and NaCl types (Fig. 2). The structure of K_2NiF_4 can be represented schematically as the following arrangement of layers along the threefold axis:

$$\cdots(NiF_2)-(KF)-(FK)-(F_2Ni)-(FK)-(KF)-(NiF_2)\cdots$$
$$\longleftarrow\!\!\!

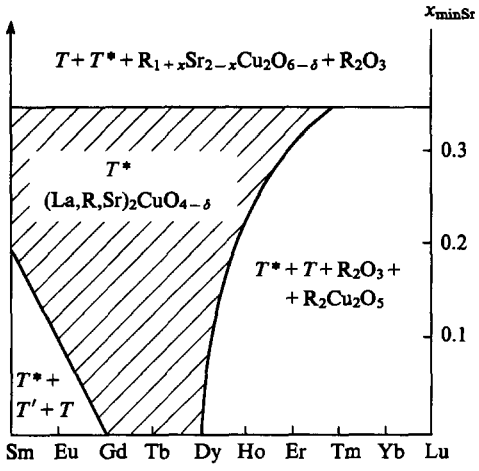


Figure 5. Dependence of the minimum concentration of strontium on the nature of the lanthanide for solid solutions with the structure of the T^*-phases.

cations Sr^{2+} or Ba^{2+} makes it possible to obtain the T^*-phases also with other lanthanide elements. Such phases have been obtained in systems with R = Sm – Lu and Y (Fig. 5).[13–16]

It is noteworthy that the X-ray diffraction patterns of the T-, T'- and T^*-phases are very similar. This is due to the fact that the cations in the structures of the phases populate the same positions. However, the unit cell of the T^*-phases is primitive, in contrast to the body-centred cells of the T- and T'-phases. Furthermore, the ratios of the unit cell parameters of the above phases differ significantly: the ratio $c/3a$ is ~ 1.15 for the T-phases, $\sim 1.06 - 1.08$ for the T^*-phases, and ~ 1.02 for the T'-phases.

It has been suggested on the basis of the analysis of the tolerance factors $t(t = d_{A-O}/\sqrt{2}d_{B-O})$ for a large number of the compounds A_2BO_4 that the structures of phases with a given composition can be predicted from the value of t.[17] The authors established that $0.87 \leqslant t \leqslant 0.99$ for the T-phases and $0.83 \leqslant t \leqslant 0.855$ for the T'-phases, while the T^*-phases exist (if they are formed in the given system) within the very narrow range $0.855 \leqslant t \leqslant 0.87$. Naturally, in the latter case at least two A-type cations are needed for the ordered population of two different positions.

Undoubtedly the employment of the tolerance factor is useful and in many cases makes it possible to predict correctly the structures of the compounds. However, the limitations and disadvantages of this method must be noted. Firstly, the above model presupposes the purely ionic character of the A–O and B–O bonds, which is not quite correct when B is a transition element, since in this case the B–O bond is to a large extent covalent. Secondly, the model ignores the electronic structure of the B cations. It is well known that the T'-phases are formed only for $B = Cu^{2+}$, whereas the square coordination is characteristic also of other cations (Ni^{2+}, Pt^{2+}, etc.). However, the compound Gd_2NiO_4, for example, which should have the structure of a T'-phase in terms of the value of t, has in fact the structure of a T-phase.[18] Thirdly, with the aid of this model it is impossible to explain why a compound with the same cationic composition subjected to different heat treatment conditions has different structures. For example, the compound $La_{1.2}Dy_{0.7}Ce_{0.1}CuO_{4+\delta}$, synthesised at $p_{O_2} = 1$ bar, has the structure of a T^*-phase, whereas after annealing under a nitrogen atmosphere a T'-phase is formed.[19]

In our view, apart from the purely geometrical criteria, it is also necessary to take into account electronic structure factors. For example, Ni-containing compounds with the structure of a T'-phase are not formed, apparently because the pairing energy of the e_g electrons is higher for the Ni^{2+} cation with the $3d^8$ electronic configuration than the energy gain in the subsequent removal of degeneracy when the environment of Ni^{2+} is altered to the square form. Furthermore, the geometrical dimensions of the (CuO_2) layer also depend on the electronic factors. We shall consider this in greater detail.

The size of the perovskite block in the *ab* plane is to a large extent determined by the length of the Cu – O bonds in the (CuO_2) layer. The length of these bonds is determined by the degree of filling of the σ^*-zone, formed mainly as a result of the overlap of the $3d_{x^2-y^2}$ orbitals of copper and the $2p_{x,y}$ orbitals of oxygen. An increase in the degree of filling of the σ^*-zone (an increase in the height of the Fermi level), which corresponds to a decrease in the formal oxidation state of copper, leads to an increase in the length of the Cu–O bonds in the (CuO_2) layer. When electrons are removed from the σ^*-zone (this corresponds to an increase in the formal oxidation state of copper), the lengths of these bonds diminish. The degree of filling of the above zone can therefore determine to a large extent whether the perovskite and other structural fragments have common dimensions. It can be altered by the heterovalent substitution of the cations in the structure and by varying the heat treatment atmosphere.

In the La–R–Cu–O systems, T^*-phases are formed only for R = Gd – Dy. The lanthanide atoms in the structure of the T^*-phase populate in an ordered manner two different crystallographic sites. For the lanthanides at the beginning of the series with ionic radii similar to that of lanthanum, such ordering does not occur. Instead, the formation of extended regions of solid solutions with T'-phase structures is energetically more favourable. When R = Ho – Lu and Y, an appreciable decrease in the effective radius of the cation in the fluorite fragment leads to the disappearance of common dimensions between this fragment and the (CuO_2) layer. As a result, the corresponding T^*-phases are not formed.

However, the partial substitution of La^{3+} by Sr^{2+} or Ba^{2+} in the NaCl-type fragment leads to the stabilisation of the T^*-phase structure. It has been established in relation to the solid solutions $La_{1.2-x}Dy_{0.8}M_xCuO_{4-\delta}$ (M = Sr or Ba) that such substitution leads to an increase in the average formal oxidation states of copper.[16] The Cu–O distance then diminishes in the (CuO_2) layer, which is reflected by a decrease in the unit cell parameter a with increase in the concentration of the alkaline earth metal cations despite the fact that their ionic radii are greater than that of La^{3+}.

With decrease in the R^{3+} radius in the series of lanthanides, there is an increase in the oxygen nonstoichiometry indices of the compounds obtained (Table 1). This results in an increase in the concentration of electrons in the antibonding σ^*-zone (or in the 'reduction' of copper), which should be accompanied by an increase in the Cu–O distance in the (CuO_2) layer. Thus, the decrease in the size of the fluorite fragment owing to the decrease in the ionic radius of the lanthanide is accompanied by an increase in the linear dimensions of the (CuO_2) layer and the T^*-phase is not formed as a result. However, the addition of an alkaline earth element, accompanied by a decrease in the equatorial Cu–O distance as a consequence of the 'oxidation' of the (CuO_2) layer, makes it possible to stabilise the T^*-phase structure also in systems with R = Ho – Lu and Y. It is noteworthy that the minimum Sr concentration required in the given series of lanthanides increases steadily with decrease in the ionic radii of the latter (Fig. 5).

Table 1. The unit cell parameters (a), the oxygen nonstoichiometry indices (δ), and the formal oxidation states of copper (V_{Cu}) for the T^*-phases $LaR_{0.8}Sr_{0.2}CuO_{4-\delta}$ (R = Sm, Gd, or Ho).

Compound	a/Å	δ	V_{Cu}
$LaSm_{0.8}Sr_{0.2}CuO_{4-\delta}$	3.8710(4)	0.06	2.08
$LaGd_{0.8}Sr_{0.2}CuO_{4-\delta}$	3.8583(2)	0.08	2.04
$LaHo_{0.8}Sr_{0.2}CuO_{4-\delta}$	3.8375(4)	0.11	1.98

In the systems with R = Sm and Eu, the addition of strontium or barium also leads to a decrease in the Cu–O distance in the (CuO_2) layer, whereupon the resulting 'contraction' of the structure in the *ab* plane leads to a decrease in the M–O interatomic distances for the cations in the fluorite fragment. The filling of the cationic sites in the latter by lanthanum atoms becomes energetically unfavourable. This results in the formation of a T^*-phase structure in which the La and Sr atoms populate statistically the cationic sites in a NaCl-type block, while the Sm and La atoms populate the sites in the fluorite fragment.

As noted above, the degree of filling of the σ*-zone depends on the oxygen pressure employed in the synthesis. For example, after synthesis at 950 °C in a stream of oxygen, $La_{1.5}Nd_{0.5}CuO_{4-\delta}$ has a T-phase structure ($\delta = -0.01$), whereas heat treatment under less oxidising conditions (1050 °C, air) leads to a phase transformation with formation of a T'-phase ($\delta = +0.02$).[19] The decrease in the Cu–O distance in the (CuO_2) layer and the stablisation of the phase with a smaller unit cell parameter a during synthesis under an oxidising atmosphere are a consequence in this case of the increase in the formal oxidation state of copper.

2. Compounds of the 223 and 1222 types

Another example of compounds in the structures of which it is possible to differentiate fragments with different structures are the 223 phases. The first representatives of this family of phases having the composition $(R_{1-x}Ba_x)_2(R'_{1-y}Ce_y)_2Cu_3O_{8+\delta}$ (R = R′ = Nd, Sm, or Eu, $x = 0.67$, $y = 0.33$) have been obtained by Japanese investigators.[20] The structure of these phases (Fig. 6) is derived from the tetragonal modification of the 123 phases ($RBa_2Cu_3O_{7-\delta}$), but the $(R'_2O_2)^{n+}$ fluorite fragment is located between the (CuO_2) layers instead of the $(R\square)^{3+}$ layer. This results in the doubling of the unit cell parameters c, since in the (R′)(O_2)(R′) fluorite block the (R′) layers are displaced relative to one another by the $\frac{1}{2}(\vec{a}+\vec{b})$ translation. The 223 phases have superconducting properties, but the transition temperatures for superconduction in these phases are lower than for the 123 phases ($T_c^{max} = 59$ K).[21] The 223 phases have a tetragonal body-centred cell ($a \approx a_{per}$, $c \approx 7a_{per}$). The model of their structure can be described as of the 14-layer type in which the layers are arranged in the following manner along the c axis:

$$\cdots(CuO_2\square_{2-\delta})-(RO)-(R'_2O_2)-(O_2Cu)-(OR)-(\square_{2-\delta}O_\delta Cu)\cdots$$
$$\longleftarrow\!\!\!

formed only in systems with R = La or Pr.[22] The effective radius of the cation in the perovskite fragment of Th-containing compounds must increase compared with the Ce-containing phases. This can be achieved not only by replacing Nd^{3+} by La^{3+} in the perovskite fragment but also by increasing the Ba^{2+} concentration in the cationic sites of the perovskite block.

The 223 phases $(R,M)_2(R',Th)_2Cu_3O_{8+\delta}$ are not formed for M = Sr, whereas in the Ba-containing system such compounds have been obtained for R′ = La – Gd. However, when the sites in the fluorite block are populated statistically by the Ce^{4+} and R^{3+} cations, the size of the cationic vacancies diminishes significantly, as a result of which the formation of Sr-containing 223 phases becomes possible in systems with R = Pr – Gd.[25] We may note that the phases with R = Sm and Eu possess superconducting properties, whereas the large Cu – O distance in the (CuO_2) layer in the Th-containing compounds is responsible for the localization of the electronic states. On further contraction of the fluorite fragment for R = Dy – Yb and Y, Ba-containing phases were not obtained, while in the case where M = Sr the 1222 phases, differing from the 223 phases in composition and structure, were produced. The partial or complete substitution of the copper cation in the $(CuO_\delta\square_{2-\delta})$ layer by another cation takes place in the structure of the 1222 phases. The filling of the oxygen sites in this layer is determined by the crystal chemistry of the given cation. Such change in the structure leads to a marked deformation of the CuO_2 layers and to the loss of superconducting properties. On the basis of experiments of this kind, one may conclude that the synthesis of superconducting complex copper oxides with a fluorite fragment requires the presence of Ce^{4+} and $Nd^{3+} - Gd^{3+}$ in the latter, since this leads to the optimum Cu – O distances for the manifestation of superconductivity.

The 1222 phase was first obtained in the Pb – Pr – Sr – Cu – O system.[26] Instead of the $(CuO_\delta\square_{2-\delta})$ layer, its structure contains the $(Pb_{0.5}Cu_{0.5}O_\delta)$ layer in which the anions populate statistically both the sites at the centre of the square $(\frac{1}{2}, \frac{1}{2}, 0)$ and the perovskite sites $(0, \frac{1}{2}, 0)$. The $TlSr_2(Nd,Ce)_2Cu_2O_{8+\delta}$ phase is close to those described above, but the $(CuO_\delta\square_{2-\delta})$ layer in its structure is fully replaced by the (TlO_δ) layer.[27] The compounds $(R_{1.5}Ce_{0.5})Sr_2Cu_2Nb(Ta)O_{10}$ (R = Pr – Eu), the structures of which contain the (NbO_2) or TaO_2 layers instead of the $(CuO_\delta\square_{2-\delta})$ layer, have also been described.[28,29]

There is a possibility also of a further increase in the complexity of the structures of the 223- and 1222-phases as a result of the incorporation in the fluorite fragment of additional (R′) and (O_2) layers. In this case, the fluorite block has the composition (R'_3O_4). The 233-phases $Sr_2(R,Ce)_3Cu_3O_{10+\delta}$ [30] and the 1232-phases $(Pb,Cu)Sr_2(R,Ce)_3Cu_2O_{11+\delta}$, as well as $(Tl,Cu)Sr_2.(R,Ce)_3Cu_2O_{11+\delta}$ [31] are derivatives of the 223- and 1222-phases with 'doubled' fluorite fragments.

3. The superconducting mercury-containing family of layered cuprates: $HgBa_2Ca_{n-1}Cu_nO_{2n+2+\delta}$ ($n = 1-4$)

The structures of the Bi-, Tl-, and Pb-containing high-temperature superconductors (HTSC) can be regarded as intergrowth structures of the perovskite and sodium chloride blocks, the Bi^{3+}, Tl^{3+}, and Pb^{2+} cations being located in the NaCl-type fragment. It is noteworthy that the ideal equatorial M – O distance for these cations is to a large extent determined by the Cu – O distance in the CuO_2 layer: $d_{M-O} \approx \sqrt{2}d_{Cu-O}$. However, the calculated values significantly exceed the characteristic values d_{M-O}. As a consequence of this, marked displacements of these cations and oxygen atoms from the ideal positions take place in the (MO) layers in order to diminish the corresponding interatomic distances and the CN of the cations M. The presence of the lone pair in the Bi^{3+} and Pb^{2+} cations also causes their appreciable displacements, required for the formation of an asymmetric coordination environment.

It is possible to synthesise layered cuprates with structures of this kind by employing Hg^{2+} cations, a characteristic feature of which is the dumbbell-like coordination of the oxygen atoms. In this case, the oxygen sites in the layers with mercury atoms may be partly filled or even remain vacant, since the Hg – O bond in this layer must be very weak. Under these conditions, there should be no incompatibility between the dimensions of the structural NaCl and perovskite fragments.

The new layered oxides $HgBa_2CuO_{4+\delta}$ [32], $HgBa_2CaCu_2.O_{6+\delta}$ [33], $HgBa_2Ca_2Cu_3O_{8+\delta}$, and $HgBa_2Ca_3Cu_4O_{10+\delta}$ [34] (the Hg-1201, Hg-1212, Hg-1223, and Hg-1234 phases respectively) have been obtained. These compounds belong to the homologous series of layered cuprates with the general formula $HgBa_2Ca_{n-1}Cu_nO_{2n+2+\delta}$, in which $n = 1 - 4$ (Fig. 7). In the structures of the Hg-1212, Hg-1223, and Hg-1234 phases, two, three, and four (CuO_2) layers, separated by $(Ca\square)^{2+}$, respectively are located in the perovskite block. The NaCl-type fragment has a similar construction in these structures and is characterised by the sequence of layers $(BaO)(HgO_\delta)(BaO)$. The unit cell parameter c in these compounds is determined by the following relation: $c(Å) \approx 9.5 + 3.2\,(n-1)$.

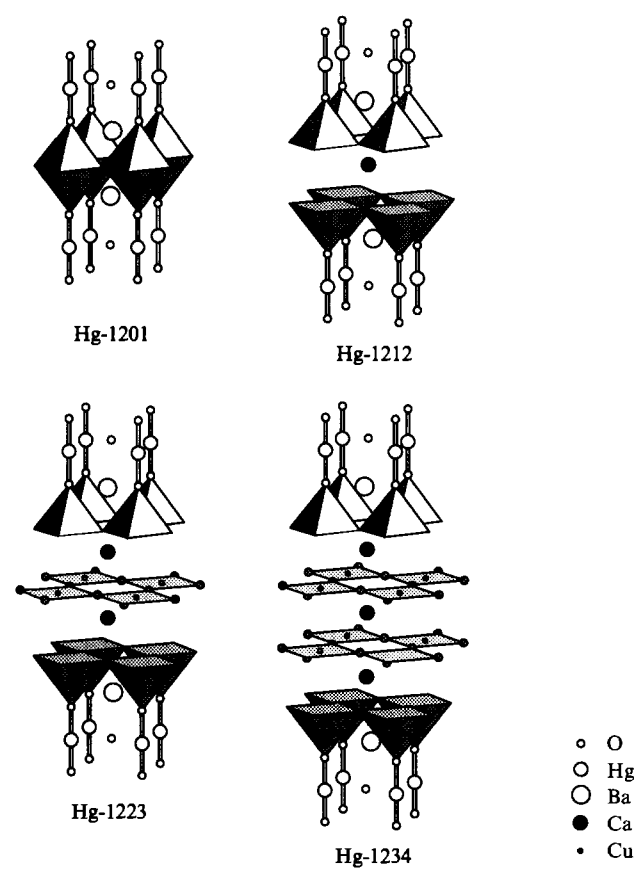


Figure 7. The crystal structures of $HgBa_2Ca_{n-1}Cu_{2n}O_{2+\delta}$ ($n = 1 - 4$).

The results of resistance and magnetic measurements have shown that the Hg-1201, Hg-1212, Hg-1223, and Hg-1234 phases are superconductors with maximum transition temperatures for superconduction of 94, 126, 134, and 126 K respectively.[32,34] The transition temperatures of these compounds can be significantly raised (to 157 K at 235 kbar for Hg-1223) at ultrahigh hydrostatic pressures.[35] The temperature of ~160 K is nowadays the highest at which superconductivity has been recorded. Unfortunately, when the external pressure is removed, the transition temperature falls to the values usual for these compounds.

Neutron and X-ray powder diffraction made it possible to locate the positions of the superstoichiometric oxygen in the Hg-1201 and Hg-1212 structures.[32,33,36,37] It was established that

such oxygen is present in a single layer with mercury atoms and that its content is appreciably less than unity, in contrast to the Tl-containing analogues. Annealing of such phases at different temperatures and partial oxygen pressures leads to a change in the degree of population of this site and hence to an alteration of the concentration of holes in the conduction band and of the transition temperature for superconduction.[32,37]

The family of Hg-containing phases obtained is a promising subject for the investigation of the nature of high-temperature superconductivity in the series of layered cuprates, since high values of T_c are characteristic of these compounds (they are higher than for the Tl-containing phases having a similar cationic composition), this being combined with a fairly simple crystal structure, which is reflected by the absence of modulations and statistical displacements of the atoms and by the high cell symmetry.

III. Intergrowth structures with alternation of fragments along the threefold axis of the perovskite subcell

The structure of the ideal cubic perovskite ABX_3 can be regarded as the spherical close packing of AX_3 layers alternating along the threefold axis. The shift of part of this layer leads to the formation of different types of close packing as regards the layered structure and symmetry, which are also referred to as hexagonal analogues of the perovskite structure. In certain structures of complex perovskite-like oxides with highly layered types of close packing, it is possible to distinguish blocks alternating in an ordered fashion along the c axis (which coincides with the threefold axis of the perovskite subcell), their composition and structures corresponding to those of simpler compounds with less layered packing. Formally, this justifies their consideration as intergrowth structures with alternation of perovskite-like blocks along the threefold axis.

The main geometrical criterion of the possibility of the formation of intergrowth structures is the common dimensions of the initial fragments, i.e. the correspondence of their dimensions in the *ab* plane. In the presence of the same skeleton, formed by close-packed AX_3 layers, the difference between the values of the parameter a is determined by the size of the cations occupying the octahedral vacancies in the close-packed structure.

We shall henceforth consider mainly only compounds in which the close-packed structure is made up of MO_3 (or $MO_{3-\delta}$) layers, where M = Ba, Sr, Ca, or La.

The formation of intergrowth structures is facilitated by the presence of stable structural fragments, the formation of which in the majority of cases is due to the presence of groups of face-linked octahedra arising when part of the layers are displaced by the vector $\frac{1}{3}$, $\frac{2}{3}$, 0 [under these conditions, the 'cubic' (c) layers are transformed into 'hexagonal' layers (h)]. As a result of the presence of common faces in the neighbouring octahedra forming an h-type layer, the distance between the metal cations in these octahedra should correspond to the average thickness of the close-packing layer (for the packing of BaO_3 layers, this range may be 2.2–2.6 Å). This leads to an appreciable electrostatic repulsion of the B cations in the face-linked octahedra. It is useful to discuss the factors stabilising such structural fragments. The electrostatic repulsion of the highly charged B cations may be diminished by the partial population of the B sites by cations with smaller formal charges. This occurs in structures of compounds such as $Ba_4M_3LiO_{12}$ [M = Ta, Nb; 8-layer $(hccc)_2$ packing] and $Ba_5W_3Li_2O_{15}$ [10 layer $(hcccc)_2$ packing].[38–40] In the compound $Ba_5W_3Li_2O_{15}$, chains of vertex-linked octahedra are alternately populated by lithium and tungsten atoms, while pairs of face-linked octahedra are populated statistically: 45% Li + 55% W. A similar motif in the arrangement of the cations is observed also in the structures of the compounds $Ba_4M_3LiO_{12}$. This arrangement of cations leads to minimum repulsion between the highly charged cations M^{6+} or M^{5+}, which is expressed by shortened metal–metal distances (for example, the Ta/Li – Ta/Li distance is 2.258 Å, while the W/Li – W/Li distance is 2.196 Å).

On the other hand, the compounds $Ba_4Ru_3Mo_{12}$ (M = Na, Li) have a different type of distribution of the B cations among the octahedral sites.[41] In the case of the compound $Ba_4Ru_3NaO_{12}$ [8-layer $(hccc)_2$ packing], and $Ba_4Ru_3LiO_{12}$ [6-layer $(hcc)_2$ packing], the face-linked octahedra are populated predominantly by ruthenium, which can be explained by the formation of Ru–Ru bonds.

If the average formal charge of the cations in the B sublattice of the close-packed $A^{2+}O_3$ layers is greater than 4, then, in accordance with the requirement for electroneutrality, cationic vacancies should arise. In the hexagonal analogues of perovskite with cationic vacancies in the B sublattice, the vacancies are located in the blocks of face-linked octahedra. If two types of layers adjoin one another, then there are groups of three face-linked octahedra. When a metal–metal bond cannot be formed owing to electrostatic repulsion forces between cations with a high formal charge, the filling of the middle octahedron is unfavourable and it remains empty. This leads to the formation of phases having the composition $A_nB_{n-1}O_{3n}$, where n is the number of close-packed layers or (for rhombohedral symmetry) the number of layers in one-third of a period. Examples of compounds with such structural organisation are $Ba_5Ta_4O_{15}$ [(hccch) packing][42,43] and $Ba_3Re_2O_9$[$(hch)_3$ packing][44] (Fig. 8), where each octahedron between two type-h layers remains unoccupied by the metal atoms. Members of this homologous series with types of close packing containing 5, 9, 12, 18, and 21 layers are known, all types of packing being trigonal and (apart from the five-layer packing) R-centred.[45–58]

The stability of the chhc fragment justifies the hypothesis that a hexagonal analogue of perovskite exists in which fragments of the $Ba_5Ta_4O_{15}$ and $MZrO_3$ structures (M = Ba, Sr) alternate in

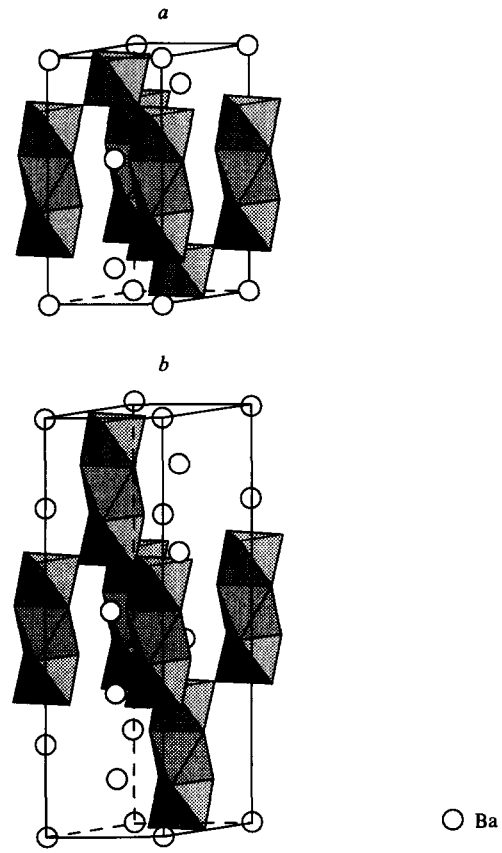


Figure 8. Crystal structures: (*a*) $Ba_5Ta_4O_{15}$; (*b*) $Ba_3Re_2O_9$.

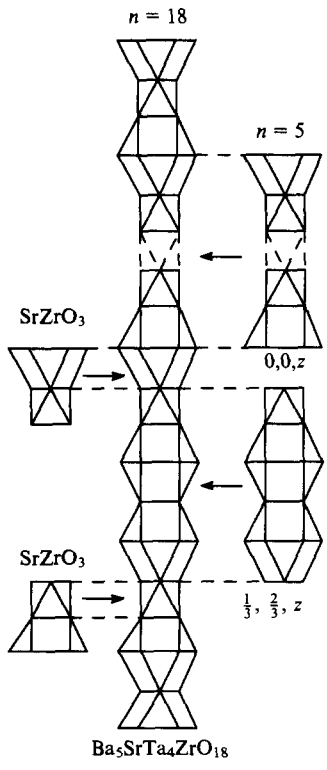


Figure 9. The structure of the compound $Ba_5SrTa_4ZrO_{18}$ resulting from the intergrowth of the $Ba_5Ta_4O_{15}$ and $SrZrO_3$ fragments.

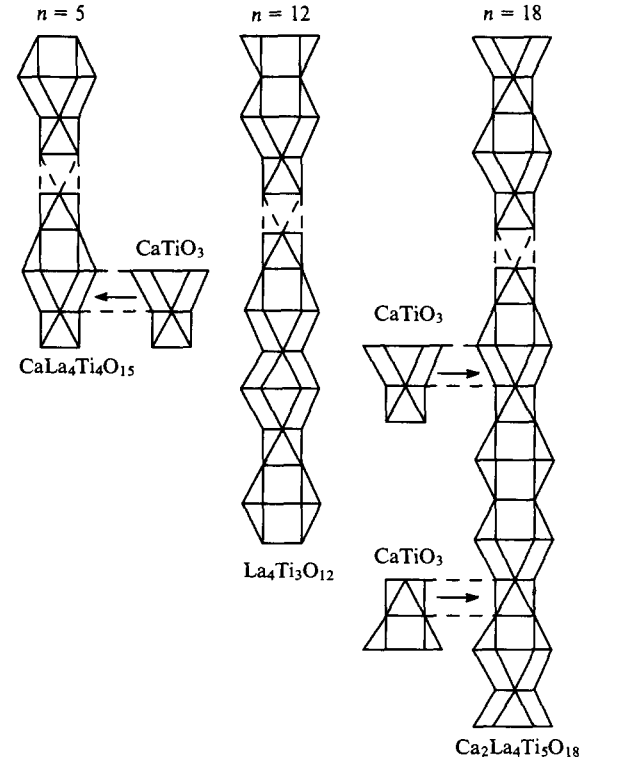


Figure 10. The structures of compounds of the $A_nB_{n-1}O_{3n}$ homologous series resulting from the intergrowth of fragments of the $CaTiO_3$ and $La_4Ti_3O_{12}$ structures.

an ordered fashion along the unit cell *c* axis (Fig. 9). The common dimensions of the fragments in the compound $Ba_5SrTa_4ZrO_{18}$ [(hcccch)$_3$ packing] are attained as a result of the statistical population of the A sites jointly by barium and strontium and of the B sites jointly by tantalum and zirconium, the statistical population of the sites by atoms of two kinds occurring at the block boundaries. Within the $Ba_5Ta_4O_{15}$ blocks, the A sites are occupied only by barium, while the B sites are occupied only by tantalum.

When Ti^{4+} cations are used instead of Zr^{4+}, compounds with structures resulting from the coherent intergrowth of the $Ba_5Ta_4O_{15}$ and $BaTiO_3$ fragments are not formed since the appre-ciably smaller ionic radius of Ti^{4+} (0.605 Å) compared with Zr^{4+} (0.72 Å) gives rise to a lack of common dimensions of the initial structural fragments. Compounds with such structures are formed when barium is replaced by A cations of smaller radius (La, Ca) and when only titanium cations are located in the B sublattice. Obstacles associated with the lack of common dimensions of the fragments do not arise under these conditions and several members of the homologous series are formed — $La_4Ti_3O_{12}$, $CaLa_4Ti_4O_{15}$, and $Ca_2La_4Ti_5O_{18}$.[59] If the 12-layer (hcch)$_3$ packing of the compound $La_4Ti_3O_{12}$ is regarded as a matrix, the subsequent members of the series can be represented as a result of the incorporation in this fragment of a c-type layer corresponding to a fragment of the $CaTiO_3$ perovskite subcell. Structures of this series can be regarded as resulting from intergrowth along the *c* axis of fragments of the $La_4Ti_3O_{12}$ and $CaTiO_3$ packing (Fig. 10). When a single c-type layer is incorporated in the hcch fragment of the initial 12-layer packing of $La_4Ti_3O_{12}$, the compound $CaLa_4Ti_4O_{15}$ with a cell having a P-type symmetry is formed, since the formation of an R-centred cell is impossible in the resulting hccch packing. When two c-type layers are incorporated in the initial fragment, the next member of the homologous series is formed — $Ca_2La_4Ti_5O_{18}$, in the structure of which an 18-layer (hcccch)$_3$ packing is achieved and the symmetry is restored to $R\bar{3}m$. In the case of compounds belonging to this homologous series, an additional factor ensuring the common dimensions of the fragments of the initial types of packing is the joint population of the A sites by lanthanum and calcium atoms. A similar homologous series is formed when the $LaFeO_3$ perovskite fragment is incorporated in the $La_4Ti_3O_{12}$ matrix, two members of this series being known — $La_5FeTi_3O_{15}$ and $La_6Fe_2Ti_3O_{18}$.[60] By using the fact that quadrupole splitting of the Mössbauer signal for Fe(III) in a high-spin state depends only on the degree of distortion of the coordination environment, which is much greater for the octahedra located between the h and c layers owing to the presence of a cationic vacancy, it is possible to show that the iron ions are located predominantly in the octahedral vacancies within the perovskite blocks. Such distribution of the cations among the B sites agrees well with the intergrowth structures model.

Apart from the structures of compounds which are formed as a result of an increase in the number of type $LaTiO_3$ blocks, a series of phases with different ratios of structural blocks exist along the $La_4Ti_3O_{12} - LaTiO_3$ section.[61] The simplest example of such phases is the oxide $La_9Ti_7O_{27}$. The structure of this compound can be represented as a result of the intergrowth of $2 \times La_4Ti_3O_{12} + LaTiO_3$ blocks. Formally, this structure can be more conveniently considered as a result of the intergrowth of higher homologues ($n \leqslant 6$): $La_4Ti_3O_{12} + La_5Ti_4O_{15}$ (or ...4545..., in terms of the number of blocks). The results of detailed microscopic studies of the phases formed along the $La_4Ti_3O_{12} - LaTiO_3$ section have been published.[62] The authors demonstrated the existence of a large number of ordered polytypes — $La_{11}Ti_9O_{33}$: $2 \times La_4Ti_3O_{12} + 3 \times LaTiO_3$ or ...5656...; $La_{13}Ti_{10}O_{39}$: $3 \times La_4Ti_3O_{12} + LaTiO_3$ or ...445...; etc. However, in practice, it is difficult to synthesise these compounds in a pure form because of the decrease in the energy differences between the homologues with increase in their ordinal number.

The population by B cations of the entire group of three face-linked octahedra is possible in the presence of an additional stabilising factor such as the formation of metal–metal bonds. Thus, in the $BaRuO_3$ structure, where the valence state

of ruthenium permits the formation of Ru–Ru bonds, all three adjacent octahedra are populated with formation of the $[Ru_3O_{12}]$ clusters.[63] The Ru–Ru distance in this structure is 2.55 Å.

When the chhc structural fragment cannot be stabilised, the incorporation of the cation in the middle of the three face-linked octahedra is unfavourable as a result of the short metal–metal distances arising under these conditions and the strong electrostatic repulsion and leads to a change in the type of close packing and the formation of hexagonal analogues of perovskite with the joint population of the B sites by cations and vacancies. Thus a trigonal primitive hccch close packing arises in the compound $Ba_5Ta_4O_{15}$. The heterovalent substitution of Ta^{5+} by Ti^{4+} leads to the appearance of an additional amount of B cations,[64] which exerts a decisive influence on the type of close packing produced. On passing from $Ba_5Ta_4O_{15}$ to $Ba_{10}Ta_{8-0.8x}Ti_xO_{30}$ solid solutions [$(hcccc)_2$ close packing, $0.6 \leqslant x \leqslant 1.2$], the type of close packing changes, the unit cell parameter c is doubled, and the symmetry is altered from $P\bar{3}m1$ to $P6_3/mmc$. This is accompanied by the delocalisation of the cationic vacancies and the joint population of the cationic sites by tantalum atoms and vacancies takes place in the chc structural fragment present in the $Ba_{10}Ta_{7.04}Ti_{1.2}O_{30}$ structure.

If the sum of the formal charges on the A and B cations is less than six, the formation of anion-deficient hexagonal analogues of perovskite having the composition $ABO_{3-\delta}$ is possible. In this case, the formation of stable structural fragments may be associated with the location of anionic vacancies outside the B cations for which CN < 6.

A group of hexagonal perovskite-like oxides is known where the appearance of anionic vacancies is induced by the introduction of aluminium atoms into the B sublattice. The structure of β-Ba_2RAlO_5 (R = Sc, In) (Fig. 11) is based on the eight-layer $(hccc)_2$ close packing.[65,66] The arrangement of the scandium and aluminium atoms is entirely ordered, the B-sites in the vertex-linked octahedra being populated by scandium alone. The ordered population of the B sites leads to the location of the oxygen atom on the 6_3 axis and the formation of a tetrahedral environment around the aluminium atoms. The group of two face-linked octahedra is then transformed into a group made up of two Al_2O_7 tetrahedra linked via the vertices. The ordering of the scandium, aluminium, and oxygen atoms leads also to a change in the coordination polyhedra around the barium atoms. One-fourth of the barium atoms are located in an almost ideal cubooctahedron. For another fourth of barium atoms, the appearance and ordering of the anionic vacancies lead to the removal of three out of the six oxygen atoms of the equatorial environment of the barium atoms, the three remaining oxygen atoms being displaced from the ideal positions (the Ba – O distance is 3.345 Å) and building up the coordination polyhedron of the barium atom to a truncated trigonal bipyramid (CN = 9). For the remaining half of the barium atoms, the displacement of the oxygen atoms in the $BaO\square_2$ layer leads to the appearance of a kind of open polyhedron in the form of a nonagon produced after the removal of the oxygen atoms making up the common face of the cubooctahedra in the h layer.

The fragments of the β-Ba_2RAlO_5 and $Ba(Sr)ZrO_3$ close packing (type c layers) in the structures of compounds with the general composition $Ba_{5-y}Sr_yR_{2-x}Al_2Zr_{1+x}O_{13+x/2}$ (R = Sc, In, Y, Gd–Lu) having a 10-layer close packing of BaO_{3-x} $(hcccc)_2$ layers alternating along the sixfold axis may be regarded as intergrowth structures (Fig. 12).[67] We may note that the compounds Ba_2RAlO_5 (R = Nd – Lu, Y) crystallise in the monoclinic system. When the ratio of the structural fragments corresponds to $2 \times (Ba_2RAlO_5) + (BaZrO_3)$, the ideal composition of the compounds is described by the formula $Ba_5R_2Al_2ZrO_{13}$. The establishment of common dimensions of the fragments in the given instance should be facilitated by the joint population of the B sites by zirconium and R^{3+} cations.

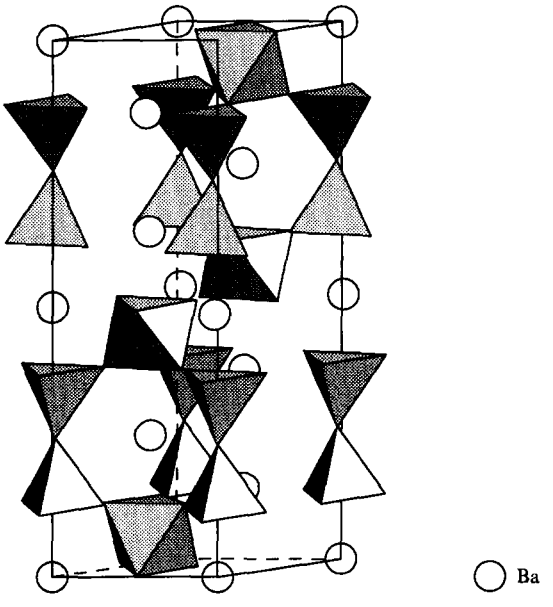


Figure 11. The crystal structure of β-Ba_2ScAlO_5.

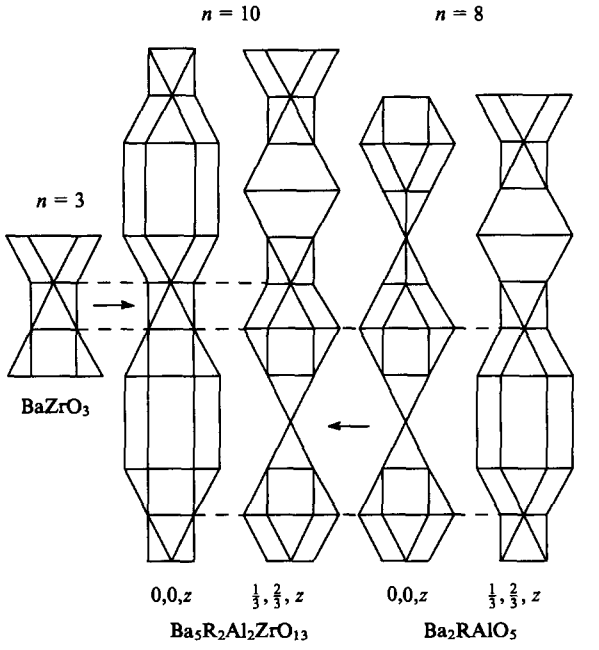


Figure 12. The structure of the compounds $Ba_5R_2Al_2ZrO_{13}$ resulting from the intergrowth of the Ba_2RAlO_5 and $BaZrO_3$ fragments.

The ionic radius of the R^{3+} cations exerts a significant influence on the stability of the compounds formed. Thus the formation of the compounds $Ba_5R_2Al_2ZrO_{13}$ was not observed for R = La – Eu. In this case, the radius of R^{3+} is too large for the accommodation of the ion in the octahedral vacancies within the close-packed BaO_{3-x} layers.

The significant difference between the ionic radii of R^{3+} (R = Gd – Lu; radii in the range 0.94–0.95 Å) and Zr^{4+} (0.72 Å) gives rise to the possibility of the existence of an ordered structure. The lanthanide cations are located in the octahedral vacancies of the type-β-Ba_2RAlO_5 block, whereas the Zr^{4+} cations are in the

$BaZrO_3$ block. In contrast to the $Ba_5R_2Al_2ZrO_{13}$ structures (R = Gd – Lu, Y), the structure of the Sc-containing compound is more disordered. In this structure, Sc^{3+} and Zr^{4+} occupy jointly the octahedral vacancies, which can be accounted for by the similarity of their ionic radii: 0.73 and 0.72 Å respectively. As a result of the statistical distribution, the cationic composition of the compound differs from the ideal composition and is expressed by the formula $Ba_5Sc_{1.33}Al_2Zr_{1.67}O_{13.33}$.

As in the β-Ba_2ScAlO_5 structure, in the $Ba_5R_2Al_2ZrO_{13}$ structures the oxygen vacancies are located in the h-type layers, which have the composition $BaO\square_2$. The remaining oxygen atom in this layer occupies a double position on the 6_3 axis, forming a common vertex of two Al_2O_7 tetrahedra. Under these conditions, some of the barium atoms achieve the same coordination environment as in the β-Ba_2ScAlO_5 structure. The change in the cationic composition following the substitution of some of the scandium atoms by zirconium atoms leads to the appearance of excess oxygen (compared with the ideal composition) and the composition of the h-type layer becomes $BaO_{1.33}\square_{1.67}$. The stable tetrahedral environment of the aluminium atoms prevents the delocalisation of the oxygen atom in the $\frac{1}{3}$, $\frac{2}{3}$, $\frac{1}{4}$ position and in the case of $Ba_5Sc_{1.33}Al_2Zr_{1.67}O_{13.33}$ the additional oxygen atom occupies the 0, 0, $\frac{1}{4}$ position, building up the nona-coordination polyhedron of the barium atoms to a decagon.

A characteristic feature of the crystal structure of $Ba_5In_2Al_2ZrO_{13}$ is the joint population of the B sites in the chc close packing fragment by indium and aluminium atoms, which is the cause of the delocalisation of the oxygen atom in the $\frac{1}{3}$, $\frac{2}{3}$, $\frac{1}{4}$ position. However, the compound with this structure is apparently metastable and has been obtained only on fusion of the specimen.

It is possible to distinguish three cases of the distribution of the cations among the B sites, which leads to three different types of location of the oxygen atoms in the BaO_{3-x} layers in the structures of the complex oxides $Ba_{5-y}Sr_yR_{2-x}Al_2Zr_{1+x}O_{13+x/2}$:

(1) the B sites in the chc fragment are occupied only by aluminium: the x, y, $\frac{1}{4}$ and x, y, $\frac{3}{4}$ layers have the composition $BaO\square_2$ and the arrangement of the oxygen atoms and of the anionic vacancies is fully ordered (the crystal structures of $Ba_5R_2Al_2ZrO_{13}$; R = Gd – Lu, Y);

(2) the B sites in the chc fragment are occupied statistically by atoms with stable octahedral and tetrahedral coordinations: the anion-deficient layers have the composition $BaO\square_2$ and the disposition of the oxygen atoms and the anionic vacancies is disordered (the crystal structure of $Ba_5In_2Al_2ZrO_{13}$);

(3) following the partial substitution of the R^{3+} cations by Zr^{4+}, the B positions in the chc fragments are occupied only by aluminium; the anion-deficient layers have the composition $BaO_{1.33}\square_{1.67}$ and the arrangement of the oxygen atoms is partly ordered (the crystal structure of $Ba_5Sc_{1.33}Al_2Zr_{1.67}O_{13.33}$).

In the cases examined above, the intergrowth structures are formed when the 'cubic' ABO_3 layers are incorporated in a multilayer close-packed structure. However, there exist hexagonal perovskites, where structurally isolated blocks, consisting of several 'cubic' and 'hexagonal' layers, alternate along the c axis.

The identical parameters a for the compounds $Ba_3Sc_4O_9$ [69–72] and β-Ba_2ScAlO_5 (5.794 Å) create ideal conditions for the formation of intergrowth structures. High-resolution electron microscope studies indicate the formation of two homologous series based on these compounds.[73,74] The compounds of the first series have the composition $Ba_{3n+8}Sc_{4n+4}Al_4O_{9n+20}$ (n = 2, 3, ...) (or, in a clearer form, $n \times Ba_3Sc_4O_9 + 2 \times Ba_4Sc_2Al_2O_{10}$). It is easily seen that for $n = 2$ the formula of the compound is $Ba_7Sc_6Al_2O_{19}$ (Fig. 13) and each succeeding member of the series is formed after the incorporation of an additional $Ba_3Sc_4O_9$ fragment. Compounds of the second series have the formula $Ba_{2n+3}Sc_{n+4}Al_nO_{5n+9}$ (n = 2, 3, ...) (or $Ba_3Sc_4O_9 + n \times Ba_4Sc_2Al_2O_{19}$), which is obtained following an increase in the number of $Ba_4Sc_2Al_2O_{10}$ blocks in the $Ba_7Sc_6Al_2O_{19}$ structure.

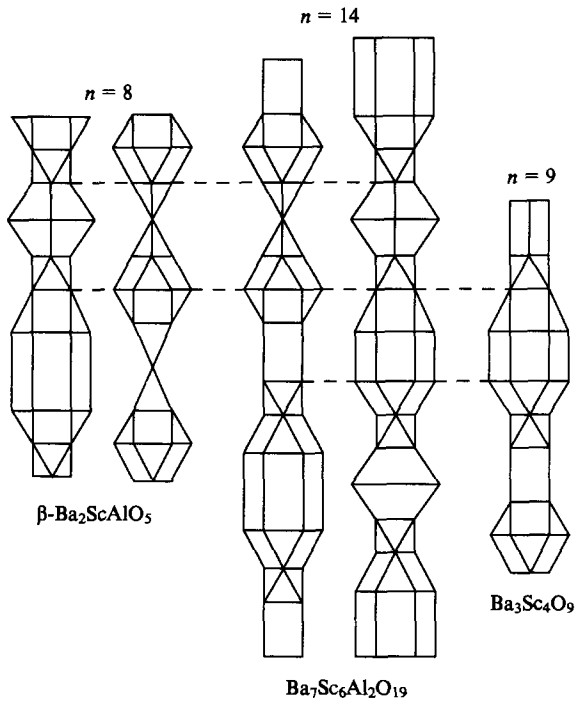


Figure 13. The structure of the compound $Ba_7Sc_6Al_2O_{19}$ resulting from the intergrowth of the β-Ba_2ScAlO_5 and $Ba_3Sc_4O_9$ fragments.

It is noteworthy that the members of homologous series with $n > 3$ were hardly observed or were present in the form of irregularly alternating sequences.

Barium ferrites form yet another group of hexagonal perovskites with intergrowth structures.[75,76] This family of compounds is obtained on 'by intergrowth' of $BaFe_{12}O_{19}$ structural blocks [M-type; $P6_3mmc$ (cchcc)$_2$] with $Ba_2M^{II}Fe_{12}O_{22}$ [Y-type: $R\bar{3}m$ (cchhcc)$_3$] or $M^{II}_2Fe_4O_8$ (M^{II} = Mg, Zn, Co) (*S*-type: $Fd3m$ spinel structure) in different proportions and sequences. The so called series of compounds M_2Y_n is formed along the $BaFe_{12}O_{19} - Ba_2M^{II}Fe_{12}O_{22}$ section. If the repeating parts of the sequences are denoted by M and Y, the compounds obtained have the composition M_2Y_n. Ordered phases with the ratios M : Y ranging from 2 : 1 to 2 : 11 have been obtained for them. Phases with even more complex ratios of the fragments have been discovered with the aid of high-resolution electron microscopy.

Compounds in the structures of which blocks having similar constructions and compositions alternate were described above. Thus a single principle governing the disposition of the cations among the crystallographic sites is maintained in all the structures based on the close packing of AO_3 layers. However, there are examples of crystal structures resulting from the intergrowth of blocks, which have at first sight both different compositions and constructions. Such compounds are chloro-oxoruthenates. Their structures are made up of fragments alternating in an ordered manner, one of which has the composition $[Ba_2Cl_2]^{2+}$, while the other is a fragment of the close-packed BaO_3 layers.[77–79] The structure of $Ba_5RuTaO_9Cl_2$ (Fig. 14) is made up of the close-packed fragments separated by two $[BaCl]^+$ layers, each of which is constructed in the same way as the $BaO\square_2$ layer in the compounds $Ba_5R_2Al_2ZrO_{13}$. Some of the barium atoms have under these conditions a coordination environment with CN < 12, where some of the oxygen atoms have been replaced by chlorine.

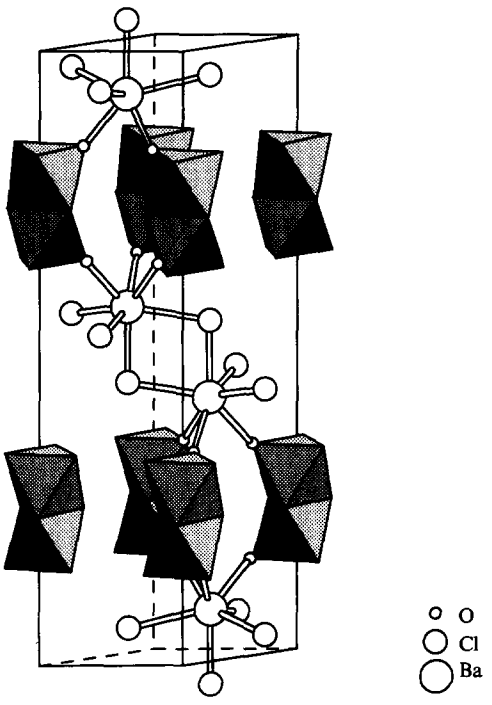


Figure 14. The crystal structure of $Ba_5RuTaO_9Cl_2$.

IV. Conclusion

The value of the prediction of the composition of new phases with high-temperature superconducting properties has been demonstrated in relation to complex copper oxides. New ternary copper, mercury, and barium oxides having high transition temperatures for superconduction have been obtained with the aid of this principle. This is a consequence of the fact that in this instance the CuO_2 layers are least distorted. The replacement of mercury by thallium, bismuth, or lead decreases T_c owing to the distortions of the CuO_2 layer under the influence of the lone pairs of the cations of the given elements.

The formation of oxygen vacancies in coherent intergrowth structures containing blocks of the NaCl and CaF_2 types together with CuO_2 layers alters the type of coordination from the octahedron to the tetragonal pyramid or a dumbbell, depending on the electronic structures of the corresponding ions.

A series of phases, differing in the layered structure and symmetry in the close packing, arise in compounds with alternation of structural blocks along the threefold axis of the perovskite structure (which is a prototype structure). In this case, the common dimensions of the fragments are achieved by altering the cationic composition in the A and B sublattices of the initial structural blocks.

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Sulfenyl† chlorides in organic synthesis

I V Koval'

Contents

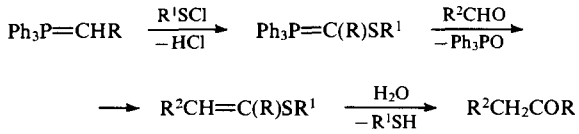
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Abstract. The results of studies concerned with the use of sulfenyl chlorides in organic synthesis are described systematically and surveyed. The methods of synthesis of sulfenyl chlorides are also considered. The bibliography includes 271 references.

I. Introduction

Sulfenyl chlorides, which are compounds of divalent sulfur, are highly reactive, and this has led to their extensive employment in organic synthesis. As a consequence of the high polarity and low strength of the S–Cl bond, sulfenyl chlorides readily react with both nucleophiles and electrophiles, which permits their employment for the synthesis of compounds with S–C, S–N, S–O, S–S, S–P, S=O, S=N, etc. bonds. These compounds include sulfides, disulfides, sulfenamines, sulfenates, sulfonates, sulfonyl chlorides, and other valuable products of fine organic synthesis.

Sulfenyl chlorides play an important role in multistep reactions, where they are employed to generate the sulfide functional group, the subsequent specific transformation of which may lead to a wide variety of products of organic synthesis.[1,2] For example, the synthesis of ketones from phosphorus ylides includes a stage in which the sulfide group is generated with the aid of sulfenyl chlorides, this being followed by its removal in the last stage of the synthesis.[3,4]



R = H, Me, COOEt, CN, COPh, 2-$NO_2C_6H_4$;

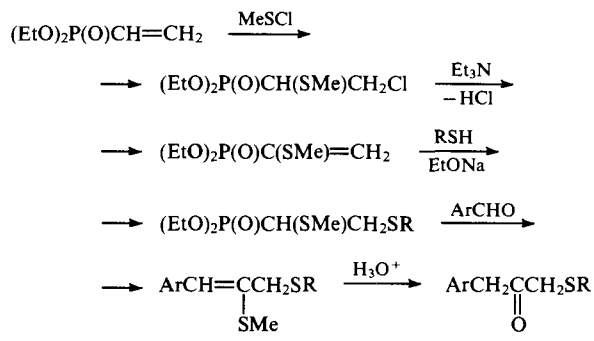
R^1, R^2 = Alk, Ar.

† It is appreciated that the name 'sulfenyl' is no longer accepted terminology under IUPAC recommendations [*A Guide to IUPAC Nomenclature of Organic Compounds, Recommendations 1993* (Oxford: Blackwell Scientific)]. The extensive use of the term, however, in the Russian literature makes it impracticable to effect a change in this review, but modern nomenclature is more likely in any subsequent review.

I V Koval' Department of Chemical Technology of Macromolecular Compounds, Ukrainian Chemico-technological University, prosp. Gagarina 8, 320005 Dnepropetrovsk, Ukraine. Fax (7-056) 247 33 16

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A similar synthetic procedure is employed in the preparative synthesis of α-alkylthioketones from diethyl vinylphosphonates.[1]



The primary products of the reactions of sulfenyl chlorides, for example β-chloroalkyl aryl sulfides, which play an extremely important role in β-arylthioalkylation reactions, have also found extensive applications in organic synthesis.

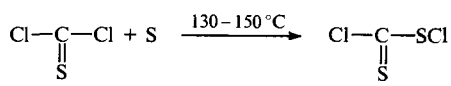
Bifunctional sulfenyl chlorides, i.e. compounds containing together with the sulfenyl chloride group also other functional groups (Cl, Br, C=O, S–Cl, ClC=O, ClC=N, etc.) are synthetically very important. A whole series of preparative methods of synthesis of diverse sulfur-containing heterocyclic compounds from these products have been developed.

Apart from fine organic synthesis, certain sulfenyl chlorides are employed in macromolecular chemistry as monomers,[5] in the production of widely known biologically active preparations such as phthalan, captan, euparen, and euparen M,[6–8] and also in the manufacture of pharmaceutical preparations[7] and vulcanising agents,[9] which makes them promising for practical purposes.

II. Methods of synthesis

1. Syntheses based on elemental sulfur and its inorganic derivatives

Elemental sulfur is relatively rarely employed in the synthesis of sulfenyl chlorides, which is due to the need for its activation.[10] A single instance of the direct application of elemental sulfur in the synthesis of chlorothiocarbonylsulfenyl chloride by its reaction with thiophosgene has been described in the literature.[11]



Inorganic derivatives of sulfur, for example sulfur chlorides, are much more frequently used in the synthesis of sulfenyl chlorides. Sulfur monochloride is employed in the form of the $SF_4-HF-S_2Cl_2$ system. Several ways of using this system in the synthesis of sulfenyl chlorides have been developed. One of them involves the interaction of the system with alkenes. For example, the reaction of the system with 1,2-dichlorodifluoroethene leads to the formation of 1,2-dichloroperfluoroethanesulfenyl chloride.[12] It is believed[13] that SF_4 and HF promote in this instance the ionisation of S_2Cl_2 and hence its addition to the double bond. The formation of a sulfenyl chloride is also favoured by the presence of fluoride and chloride anions in the reaction mixture.

$$S_2Cl_2 \xrightarrow{HF,\ SF_4} Cl^- + \overset{+}{S}SCl$$

$$SF_4 + 4\,Cl^- \xrightarrow[-4\,F^-]{} SCl_4 \longrightarrow SCl_2 + Cl_2$$

$$CFCl{=}CFCl + \overset{+}{S}SCl \longrightarrow \left[\overset{+}{C}FClCFClSSCl \xrightarrow{F^-} CF_2ClCFClSSCl\right] \xrightarrow{Cl_2} CF_2ClCFClSCl + SCl_2$$

Perfluoroethane-, perfluoro(1-methylethane)-, and perfluoro(1-methylpentane)sulfenyl chlorides have been synthesised similarly.[14,15]

It has been established[12] that the interaction of the $SF_4-HF-S_2Cl_2$ system with asymmetric alkenes, for example with chlorotrifluoroethene, leads to the formation of a mixture of two regioisomers, which is a disadvantage of the method.

$$CF_2{=}CFCl \longrightarrow CF_3CFClSCl + CF_2ClCF_2SCl$$

A second aspect of the use of this system to synthesise sulfenyl chlorides involves its reaction with certain inorganic and organic reagents and subsequent chlorolysis of the products.[16,17]

$$(EtOOC)_2CH_2 \xrightarrow[60\,^\circ C,\ 12\ h]{SF_4-HF-S_2Cl_2} [(EtOOC)_2CFS-]_2 \xrightarrow[28\,^\circ C,\ 4\ h]{Cl_2} (EtOOC)_2CFSCl$$

$$RCF{=}CF_2 \xrightarrow{SF_4-HF-S_2Cl_2} \left[\begin{matrix}RCFSCl\\|\\CF_3\end{matrix} + \begin{matrix}RCFSSCl\\|\\CF_3\end{matrix} + \begin{matrix}RCFSSSCFR\\|\quad|\\CF_3\quad CF_3\end{matrix}\right] \xrightarrow[100\,^\circ C]{Cl_2} \begin{matrix}RCFSCl\\|\\CF_3\end{matrix}$$

R = F, CF_3, Bu, C_6H_{13}.

$$CS_2 \xrightarrow{SF_4-HF-S_2Cl_2} [CF_3SSCF_3 + CF_3SSSCF_3] \xrightarrow{Cl_2} CF_3SCl$$

Several versions of the synthesis of sulfenyl chlorides from sulfur dichloride have been developed. The first of these consists in its addition to the multiple bonds of unsaturated compounds. For example, the synthesis of phosphorus-containing sulfenyl chlorides by the addition of SCl_2 to the C=C bonds of vinyl- and allyl-phosphonates has been described.[18]

$$(AlkO)_2P(O)CH{=}CH_2 \xrightarrow{SCl_2} (AlkO)_2P(O)CH(CH_2Cl)SCl$$

$$R_2P(O)CH_2CH{=}CH_2 \xrightarrow{SCl_2} R_2P(O)CH_2CH(Cl)CH_2SCl$$

R = Cl, C_2H_5O.

The formation in certain cases of a mixture of two isomeric sulfenyl chlorides which are difficult to separate, as happens, for example, in the reaction of SCl_2 and methyl methacrylate,[19] should also be included among the disadvantages of this method.

$$MeOCOC(Me){=}CH_2 + SCl_2 \longrightarrow \begin{cases} MeOCOC(Me)(SCl)-CH_2Cl & 71\% \\ MeOCOC(Me)(Cl)-CH_2SCl & 29\% \end{cases}$$

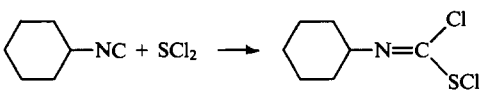
In the presence of fluorosulfonic acid, sulfur dichloride reacts with hexafluoropropene by a coupled addition mechanism, the subsequent elimination of hydrogen chloride, and the formation of the corresponding sulfenyl chloride.[20,21]

$$CF_3CF{=}CF_2 \xrightarrow[-HCl]{SCl_2,\ HSO_3F,\ 40-60\,^\circ C} \begin{matrix}CF_3-CF-CF_2OSO_2F\\|\\SCl\end{matrix} \quad 75\%$$

Under the conditions of specific solvation of the S–Cl bond (in acetonitrile, benzonitrile, SO_2, etc.), SCl_2 reacts with hexafluorodimethylketene, affording the corresponding sulfenyl chloride.[22]

$$(CF_3)_2C{=}C{=}O + SCl_2 \longrightarrow (CF_3)_2C\begin{matrix}C(O)Cl\\SCl\end{matrix}$$

The addition of sulfur dichloride to isonitriles is used in the synthesis of chloroiminomethanesulfenyl chlorides.[11]



The second version of the use of sulfur dichloride in the synthesis of sulfenyl chlorides involves the sulfenylation of CH acids, for example isobutyronitrile in the synthesis of α-cyanoisopropanesulfenyl chloride.[23]

$$Me_2CHCN + SCl_2 \longrightarrow \begin{matrix}Me_2C-SCl\\|\\CN\end{matrix}$$

2. Syntheses based on thiols

The chlorolysis of the S–H bond in thiols on treatment with chlorinating agents is used very frequently in the synthesis of sulfenyl chlorides. A series of preparative methods of synthesis of arene-,[24] polyfluoroalkane,[25,26] and trichlorothiophene-sulfenyl chlorides[27] have been developed on the basis of this reaction. In order to avoid the hydrolysis of the sulfenyl chlorides formed and also to diminish the possibility of *C*-chlorination, the reaction is carried out in anhydrous inert solvents in the absence of ultraviolet light. This is a three-stage process with participation of disulfides as intermediates.[24,28]

$$RSH + Cl_2 \longrightarrow RSCl + HCl$$

$$RSH + RSCl \longrightarrow RSSR + HCl$$

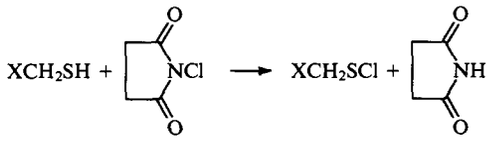
$$RSSR + Cl_2 \longrightarrow 2\,RSCl$$

Sulfuryl chloride is a milder chlorinating agent than chlorine.[24,28] It too can induce *C*-chlorination, which has been observed in the case of methane-thiols with functional group substituents.[29,30]

$$XCH_2SH + 3\,SO_2Cl_2 \longrightarrow XCCl_2SCl + 3\,HCl + 3\,SO_2$$

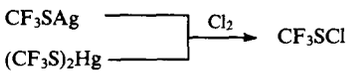
X = CN, $PhSO_2$, ArNHCO, RCO etc.

N-Chlorosuccinimide is frequently employed as a chlorinating agent in order to avoid the chlorination of α-C–H bonds.[31,32]



X = Ph, EtOOC, HOOC.

In the case of unstable or gaseous thiols, the use of their silver or mercury salts is more convenient.[33]



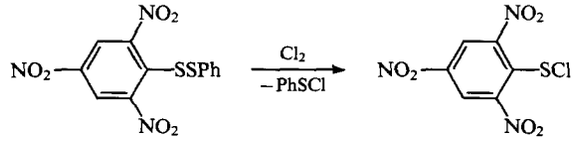
3. Syntheses based on disulfides

The chlorolysis of the S–S bond in disulfides on treatment with chlorine or other chlorinating agents in anhydrous organic solvents is one of the commonest methods of synthesis of sulfenyl chlorides.[24,28,32–44]

$$RSSR + Cl_2 \longrightarrow 2\,RSCl$$

R = Alk, Ar, Het, $CH_2ClCH(CF_3)$, $CF_3CHClCH_2$, $CF_3OCFClCF_2$, CF_2ClCF_2, CCl_2FCF_2, $CF_3CF_2CF_2$, $CF_3(CF_2)_6$, $(CF_3)_2CFOCF_2$, $(CF_3)_2CF$ etc.

Since the rate of chlorolysis of the S–S bond in disulfides depends on the nucleophilicity of the sulfur atoms, electron-accepting groups attached to a sulfur atom hinder the process. In such cases, it is recommended[45,46] that catalysts such as iodine, aluminium and iron chlorides, oleum, sulfuric acid, etc. be employed. In order to reduce the influence of strong electron-accepting groups on the chlorination process, asymmetric compounds, containing an electron-donating group as well as an electron-accepting group, are sometimes employed instead of symmetrical disulfides.[47]



In the case of disulfides containing α-C–H bonds, there is a possibility, of the chlorolysis also of C–H bonds together with that of the S–S bond.[24,28,48] In order to avoid this process, it is recommended that sulfuryl chloride,[49–53] *N*-chlorosuccinimide,[54] and other *N*-halo-derivatives[55,56] be used as chlorinating agents.

4. Syntheses based on sulfides

One of the important methods of synthesis of sulfenyl chlorides is the specific chlorolysis of one of the C–S bonds in sulfides. This method makes it possible to obtain sulfenyl chlorides with a wide variety of structures, including those containing powerful electron-accepting groups attached to the sulfur atom. The ease of chlorolysis of the C–S bond in sulfides is determined primarily by the nature of the leaving group, the structure of the initial sulfide, and the chlorolysis conditions. Sulfides containing a readily removable group such as the benzyl,[57–65] acyl,[61,66–68] and *tert*-butyl[69] groups are most often employed in the synthesis of sulfenyl chlorides.

$$RSCH_2Ph + Cl_2 \longrightarrow RSCl + PhCH_2Cl$$

R = 2,4,6-$(NO_2)_3C_6H_2$, CHF_2, CCl_2F, CF_3, C_2HF_4, $(CF_3)_2CHCF_2$, CF_3CFCl, $(CF_3)_2CF$, $CHFClCF_2$, $(CF_3)_2C{=}CF$, $(CF_3)_2C{=}C(I){-}C_2F_5$ etc.

$$RSAc + SO_2Cl_2 \longrightarrow RSCl + AcCl + SO_2$$

R = Me, Bu, Bu^i, Bu^t, 2-MeC_6H_4, Ph, $PhCH_2$, 4-$NO_2C_6H_4$, $MeOCOCH_2CH_2$, $PhC{\equiv}C$.

$$RSCMe_3 \xrightarrow[10\,^\circ C]{SO_2Cl_2} RSCl + Me_3CCl + SO_2$$

R = $MeOCOCH(CF_3)CF_2$, $MeOOC{=}CF(CF_3)$.

A series of methods of synthesis of sulfenyl chlorides involving the chlorination of sulfides containing leaving groups such as the chloromethyl,[33] methyl,[70] and ethyl[71] groups have been described.

$$CF_3SCH_2Cl + Cl_2 \longrightarrow CF_3SCl + CH_2Cl_2$$

$$XC(=O)CH_2SMe + 3\,SO_2Cl_2 \longrightarrow XC(=O)CCl_2SCl + MeCl + 3\,SO_2 + 2\,HCl$$

X = Ph–N(CHMe$_2$)–

$$MeOCOCF_2CF_2SEt + Cl_2 \xrightarrow[-EtCl]{CF_3COOH,\ 25\,^\circ C} MeOCOCF_2CF_2SCl$$

It has been noted[72] that the interaction of 1-thiocyanatobutan-3-ol with phosphorochloridous tetraethyldiamide in the presence of triethylamine at 30 °C proceeds with the cleavage of the C–S bond and the formation of 3-hydroxybutanesulfenyl chloride.

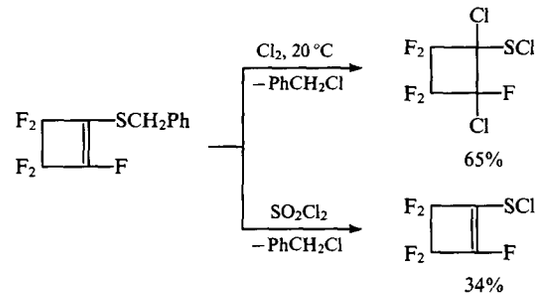
$$HOCH(Me)CH_2CH_2SCN + (Et_2N)_2PCl \longrightarrow HOCH(Me)CH_2CH_2SCl + (Et_2N)_2PCN$$

The chlorolysis of the C–S bond in sulfides containing active α-C–H bonds is accompanied by the *C*-chlorination of the alkyl group, which is used in the synthesis of dichloromethanesulfenyl chlorides with functional group substituents.[70,73]

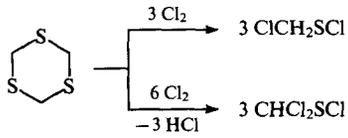
$$XCH_2SCH_2Ph + 2\,SO_2Cl_2 \xrightarrow[-2\,SO_2,\ -2\,HCl]{} [XCCl_2SCH_2Ph] \xrightarrow[-SO_2]{SO_2Cl_2} XCCl_2SCl + PhCH_2Cl$$

X = CN, $C_6H_4SO_2$, EtOCO, 4-ClC_6H_4OCO, HOCO, Alk_2NCO, ArNHCO, CF_3 etc.

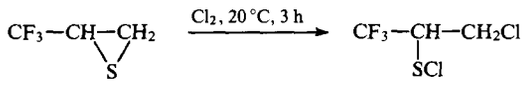
The chlorolysis of the C–S bond in alkenyl benzyl sulfides is accompanied as a rule by the addition of chlorine to the C=C bond.[58,63] The use of sulfuryl chloride instead of chlorine rules out the side reaction, as happens, for example, in the chlorination of benzyl pentafluorocyclobutenyl sulfide.[58]



Cyclic sulfides undergo chlorolysis to form sulfenyl chlorides. For example, the chlorination of trithiane with chlorine leads to chloromethane- and dichloromethane-sulfenyl chlorides depending on the conditions.[74]

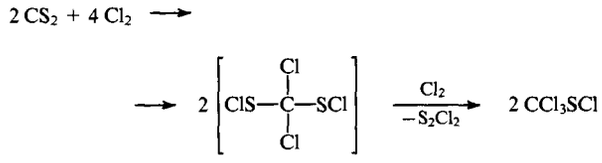


The analogous chlorination of trifluoromethylthiirane yields 1-chloro-2-chlorosulfenyl-3,3,3-trifluoropropane.[75]

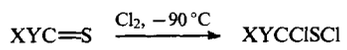


5. Syntheses based on thiocarbonyl compounds

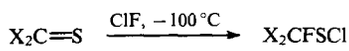
The use of thiocarbonyl compounds in the synthesis of sulfenyl chlorides is based on the addition of chlorine to the C=S bond. For example, reaction of Cl_2 with carbon disulfide is the basis of the industrial synthesis of trichloromethanesulfenyl chloride (TCMSC).[33]



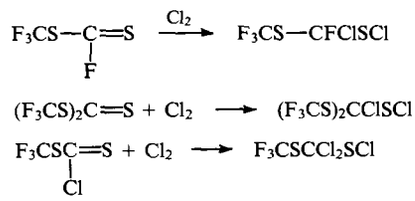
This reaction has been used to synthesise perhaloalkanesulfenyl chlorides.[63,76-83]



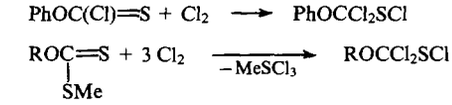
X = Cl, Br, F, CF_3, Et; Y = Br, F, $(CF_3)_2CH$, $(CF_3)_2CCl$.



X = Cl, Br, F.

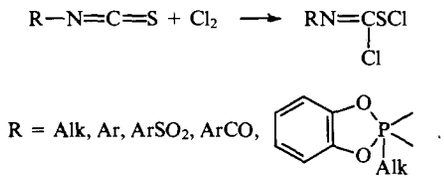


The addition of chlorine to the C=S bond in chlorides and esters of thiocarbonic and dithiocarbonic acids is the basis of the synthesis of α,α-dichloromethanesulfenyl chlorides with functional group substituents.[74]



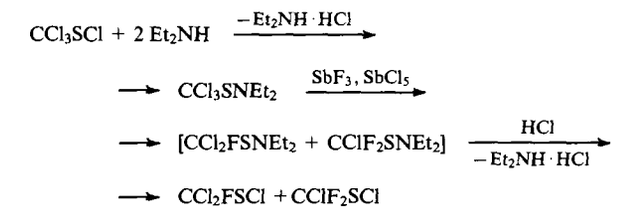
R = Me, Et.

One of the methods of synthesis of chloroiminomethanesulfenyl chlorides is based on the addition of chlorine to the C=S bond in isothiocyanates.[28,83,84]

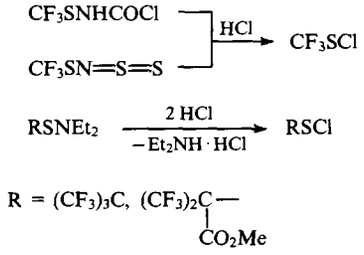


6. Syntheses based on sulfenamides

A familiar procedure for the formation of the sulfenyl chloride group involves heterolytic cleavage of the S–N bond in sulfenamides on treatment with gaseous HCl.[85-87] However, this reaction is used fairly rarely, since in most cases sulfenamides are obtained from the sulfenyl chlorides into which they are converted on hydrochlorolysis of the S–N bond. As a synthetic procedure, the conversion of the sulfenyl chloride group into the sulfenamide group with subsequent hydrochlorolysis of the S–N bond is used to protect the sulfenyl chloride group in the modification of groups attached to the sulfur atom, as happens, for example, in the conversion of TCMSC into dichlorofluoro- and chlorodifluoro-methanesulfenyl chlorides.[33]

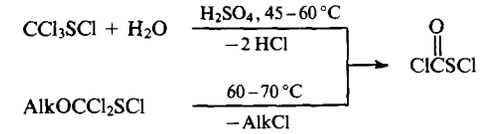


Instances of the synthesis also of other fluoroalkanesulfenyl chlorides using the hydrochlorolysis of the S–N bond in the corresponding sulfenamides are known.[88-90]



7. Modification of the functional groups in sulfenyl chlorides

The specific modification of the various functional groups attached to the sulfur atom in sulfenyl chlorides has been used very frequently in the synthesis of new types of these compounds. TCMSC is particularly valuable in this respect. Its partial hydrolysis in concentrated sulfuric acid leads to chlorocarbonylsulfenyl chloride,[11,33,74] which is also formed on thermolysis of alkoxydichloromethanesulfenyl chlorides.[11]



Alk = Me, Et.

The interaction of TCMSC with potassium fluoride can lead to the stepwise substitution of the chlorine atoms by fluorine.[33]

$$CCl_3SCl \xrightarrow[-KCl]{KF} CFCl_2SCl \xrightarrow[-KCl]{KF}$$

$$\longrightarrow CF_2ClSCl \xrightarrow[-KCl]{KF} CF_3SCl$$

A relatively large number of sulfenyl chlorides have been obtained by modification of the COCl group of chlorocarbonylsulfenyl chloride. For example, the replacement of the chlorine atom in this group by fluorine can be achieved with the aid of antimony trifluoride.[82]

$$ClC(=O)SCl \xrightarrow{SbF_3} FC(=O)SCl$$

The chlorine atom is replaced by the alkoxy-group in the interaction of chlorocarbonylsulfenyl chloride with alcohols in molar proportions of 1:1.[11]

$$ROH + ClC(=O)SCl \xrightarrow[-HCl]{} ROC(=O)SCl$$

R = Me, Et, Pr, C_8H_{17}, $ClCH_2CH_2$, $PhCH_2CH_2$, $MeOCH_2CH_2$.

8. Other methods of synthesis

Among other methods of synthesis, mention may be made of (a) the addition of sulfenyl chloride to the C=S bond in thiocarbonyl compounds:[82]

$$F_2C{=}S + F_3CSCl \longrightarrow CF_3CSCF_2SCl;$$

(b) the chlorolysis of the S–P bond in the alkyl esters of phosphorothioic acids:[68]

$$RSP(=O)(OEt)_2 \xrightarrow{SO_2Cl_2} RSCl + (EtO)_2P(O)Cl + SO_2,$$

R = $(CF_3)_2CHCF_2$, $(CF_3)_2CHCO$;

(c) the chlorolysis of the S–Si bond in thiosilanes.[91]

$$RSSiMe_3 \xrightarrow[-Me_3SiCl]{Cl_2} RSCl$$

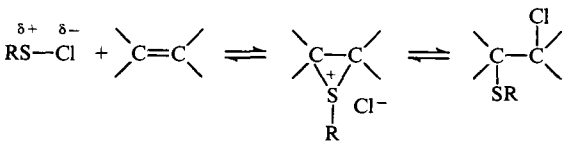
III. Syntheses based on sulfenyl chlorides

1. Syntheses of sulfides

The synthesis of sulfides from sulfenyl chlorides has been described in detail in the present author's earlier review[2] and in the literature quoted therein and only the synthesis of sulfides with functional group substituents, which play an important role in organic synthesis, will therefore be considered in the present review.

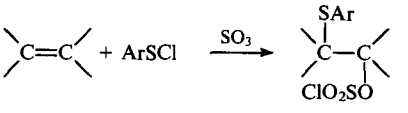
a. Synthesis of aryl β-chloroalkyl sulfides

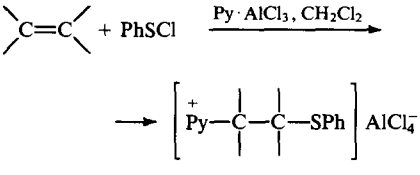
A classical method of synthesis of β-chloroalkyl sulfides involves the addition of sulfenyl chloride to the C=C bond in unsaturated compounds, which proceeds under mild conditions and with high yields.[2,4,24,28,46,92–97] The mechanism of this reaction has been discussed in detail in a series of review publications.[2,4,24,28,46] It has been suggested that the reaction proceeds via an Ad_E2 mechanism, in which an episulfonium ion is a cationic intermediate and which leads as a rule to stereospecific *trans*-addition.[28]



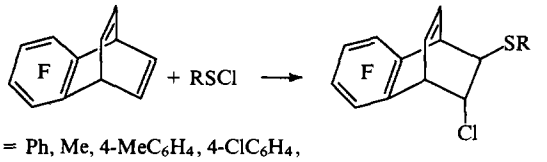
Quantum-mechanical calculations for the $C_2H_4SH^+$ ion have shown[98] that the bridged episulfonium ion is more stable as an intermediate than a linear carbenium ion. When the process is subject to kinetic control, the composition of the products of the addition reaction reflects the relative rate of substitution at the ring carbon atom of the episulfonium ion. The presence of α-substituents, which increase the reactivity in reactions of the S_N2 type (Ph, C=O, C≡N, CH=CH_2, etc.), increases the relative rate of addition, whereas alkyl groups or other bulky substituents diminish the relative rate of this reaction. Terminal alkenes therefore react with sulfenyl chlorides by anti-Markovnikov addition, whereas styrenes, acrylic acid derivatives, and dienes combine with sulfenyl chlorides in accordance with the Markovnikov rule.[28,99]

In order to increase the effective electrophilicity of the episulfonium ion and to substitute the chloride anion by other nucleophiles, it has been suggested that the coupled addition of sulfenyl chlorides be carried out in the presence of strong electrophiles such as $LiClO_4$,[100–103] SO_3,[104] and $PyAlCl_3$.[105] The episulfonium cations formed under these conditions react even with weak nucleophiles such as acetonitrile.[100–103]

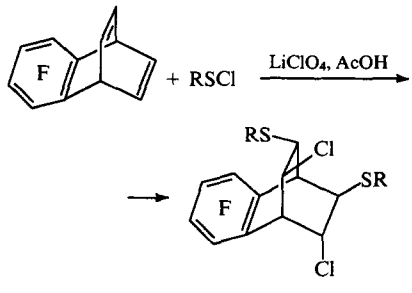




The use of lithium perchlorate in the reaction of sulfenyl chlorides with polycyclic dienes induces various side processes (skeletal rearrangements, etc.). For example, the addition of sulfenyl chlorides to tetrafluorobenzobarrelene in CH_3COOH, CH_3NO_2, and CH_2Cl_2 takes place in the *exo*-position with formation of *trans*- β-halo-substituted sulfides, whereas in the presence of lithium perchlorates the reaction proceeds with participation of two C=C bonds.[106]

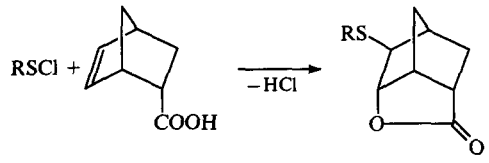


R = Ph, Me, 4-MeC_6H_4, 4-ClC_6H_4,
2-$NO_2C_6H_4$, 4-$NO_2C_6H_4$, 2,4-$(NO_2)_2C_6H_3$.



R = 4-MeC_6H_4.

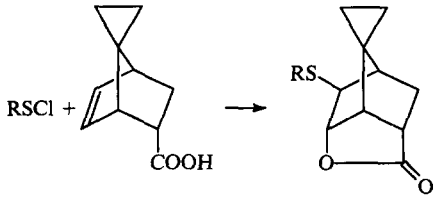
It has been noted[107] that the addition of polyfluoroalkanesulfenyl chlorides to norborn-5-ene-2-carboxylic acid under mild conditions (−20–0 °C) is accompanied by the lactonisation of the adducts.



R = $ClCH_2CH_2\underset{\displaystyle CF_3}{\underset{|}{C}}H$, CF_2ClCF_2, $CFCl_2CF_2$,

$ClCH_2\underset{\displaystyle CF_3}{\underset{|}{C}}Cl$, $MeOOC\overset{\displaystyle CF_3}{\overset{|}{C}}CF_3$

Spiro(2-carboxybicyclo[2.2.1]hept-5-ene-7,1'-cyclopropane) reacts similarly with sulfenyl chlorides.[108]



R = $ClCH_2\underset{\displaystyle CF_3}{\underset{|}{C}}H$, $MeOOC\overset{\displaystyle CF_3}{\overset{|}{C}}CF_3$

Under more severe conditions (20 °C and above), the formation of mixtures of the corresponding lactones and the products of the *endo*- and *exo*-addition to the C=C bond was observed.[108]

In certain cases, the stability of the episulfonium ion diminishes so much that the addition of sulfenyl chlorides to the C=C bond proceeds with participation of an open-chain carbenium ion with loss of stereospecificity.[15] Examples of such reactions are the addition of 2,4-dinitrobenzenesulfenyl chloride to *cis*-anethole[109] and also the addition of benzenesulfenyl chloride to strained cyclobutenes.[110] It has been noted[111] that the addition of sulfenyl chlorides to alkenes in weakly polar solvents proceeds via intermediates less polar than episulfonium salts. Kinetic studies of the addition of arenesulfenyl chlorides to *para*-substituted styrenes led to the conclusion[111] that a whole range of structures from nonpolar (σ-sulfurane) to ionic (episulfonium ion) as intermediates is possible. It has also been suggested that an ion-pair mechanism may be possible in the case of the addition of sulfenyl chlorides to alkenes in acetic acid.[112]

In the presence of Lewis acids ($TiCl_4$, $LiClO_4$) and also on dissolution in liquid SO_2, β-chloroalkyl sulfides are readily converted into episulfonium salts, which are widely used in β-arylthioalkylation reactions in order to expand the range of sulfides with functional group substituents.[10,112,113] However, it has proved more convenient to carry out this reaction using the aryl β-chloroalkyl sulfide–$TiCl_4$ (or $ZnCl_2$, $SnCl_4$) system, by-passing the stage involving the formation of a stable episulfonium salt, as happens, for example, in the interaction with trimethylsilyl ethers of enols (Scheme 1).[10,114–119]

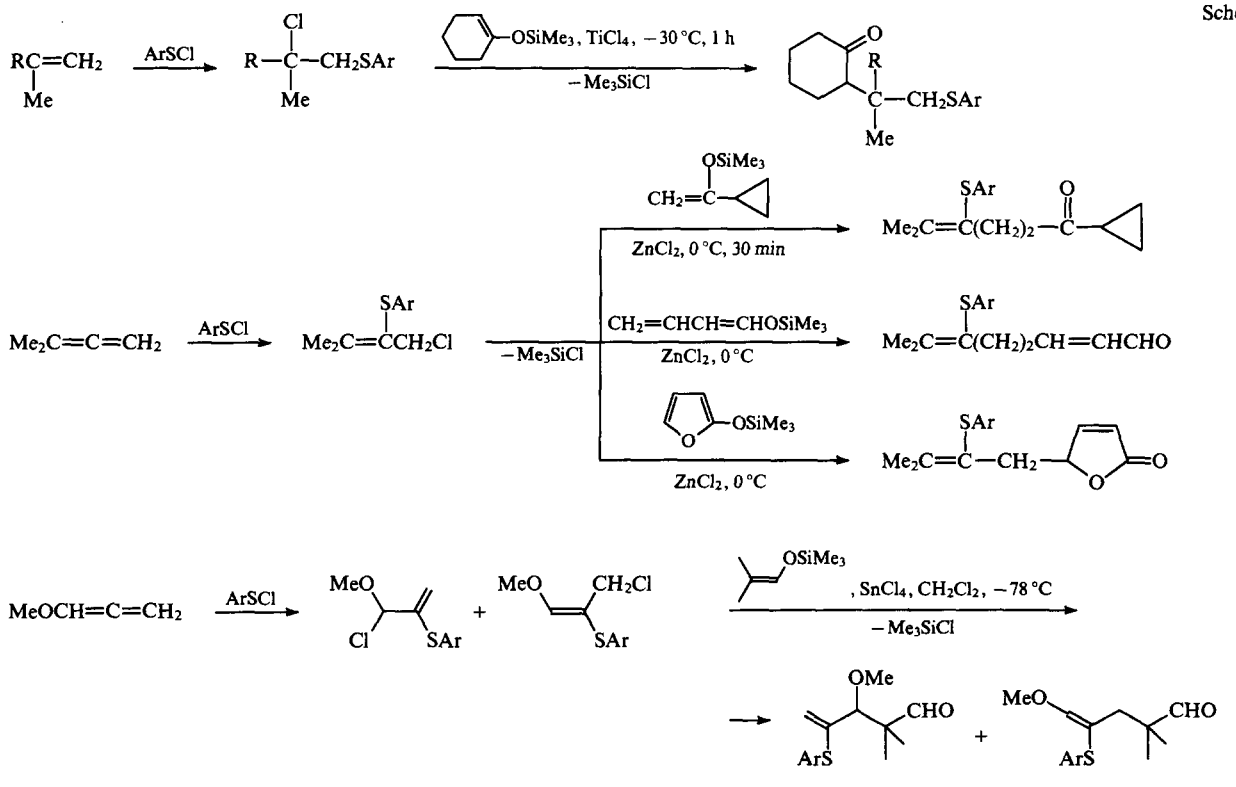
According to Ibragimov and Smit,[117] the β-arylthio-α-alkoxyalkylation of various types of trimethylsilylenol ethers is accompanied by their reaction with the products of the addition of arene-sulfenyl chlorides to vinyl ethers (Scheme 2).

According to Belen'kii[10] and Ibragimov et al.,[120] the overall outcome of these reactions reduces to the chemoselective aldol condensation of two carbonyl compounds with the simultaneous introduction of a γ-arylthio-substituent, which leads to the additional possibility of subsequent reactions at this centre.

Similar results have been obtained when methyl trimethylsilyl acetals of ketene were used as π-donors (Scheme 3).[10,121]

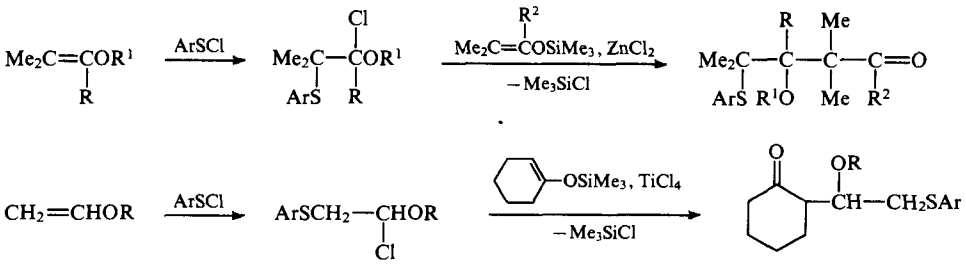
In the presence of $TiCl_4$ or $ZnBr_2$, allylsilanes also react with aryl β-haloalkyl sulfides (Scheme 4).[121–123]

Scheme 1

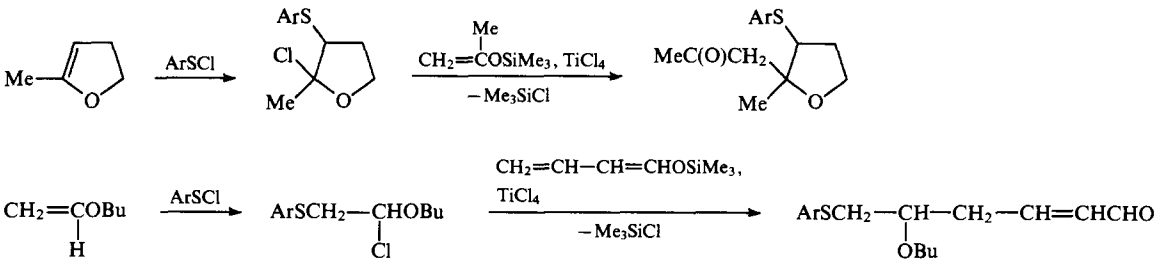


Ar = 4-MeC_6H_4, 4-ClC_6H_4, 2,4,6-$Me_3C_6H_2$.

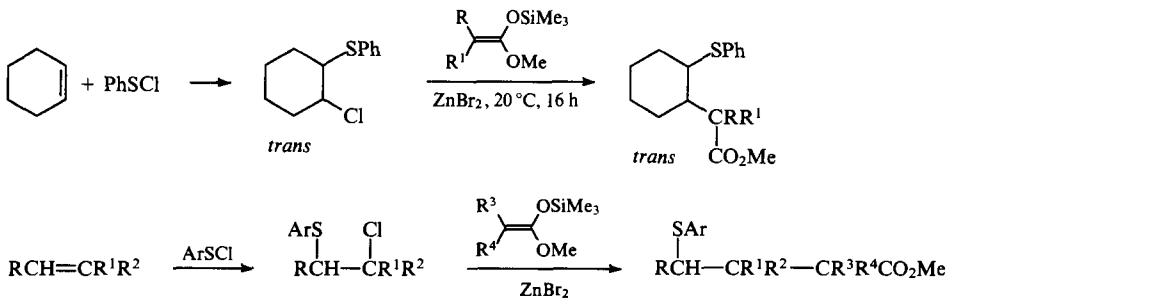
Scheme 2



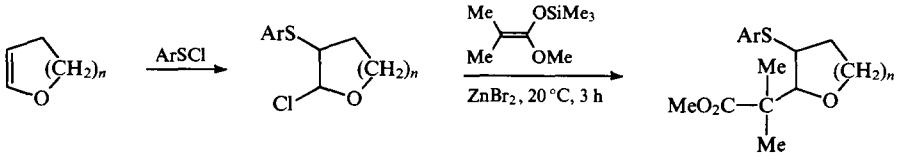
R = Me, Bu^t.



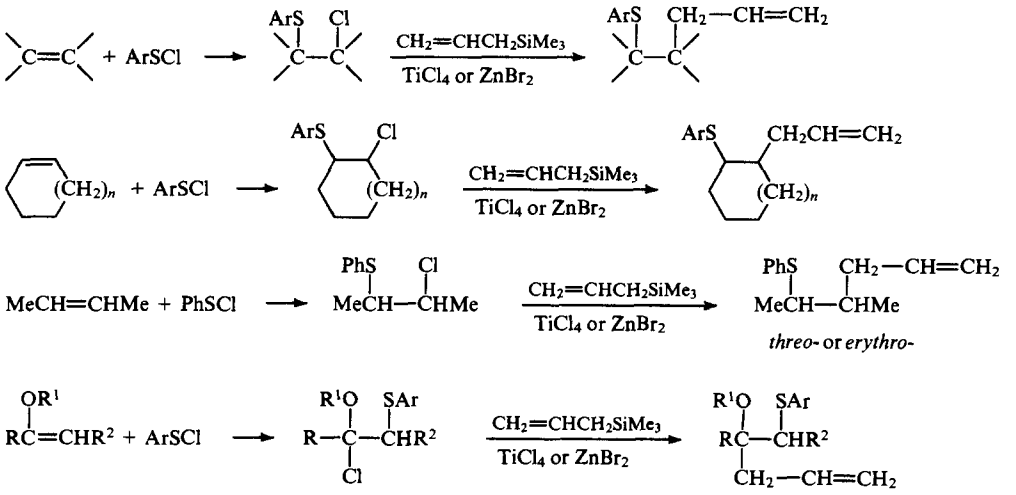
Scheme 3



R = R^1 = R^2 = R^3 = R^4 = H, Alk.

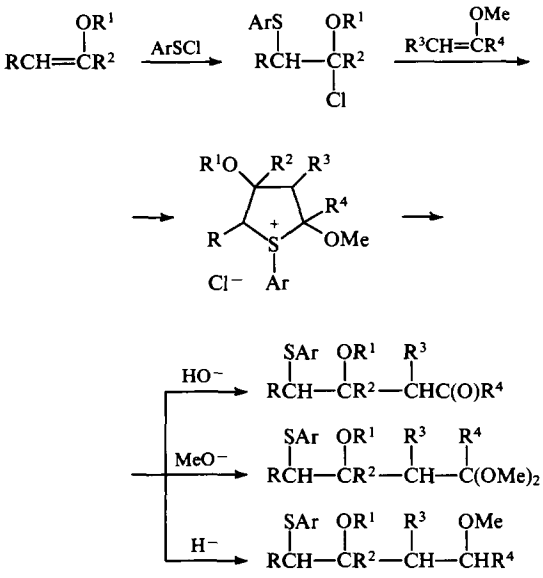


Scheme 4

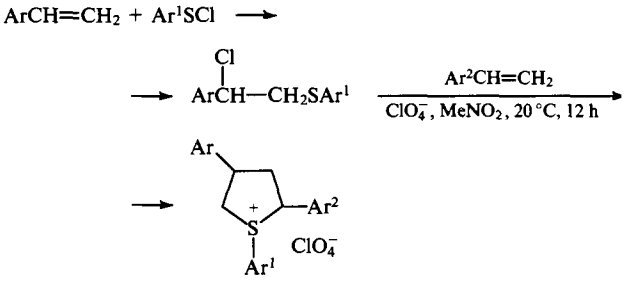


R = R^2 = H; R^1 = Et; R = H, R^1 + R^2 = $-(CH_2)_2-$; R = Me, R^1 + R^2 = $-(CH_2)_2-$.

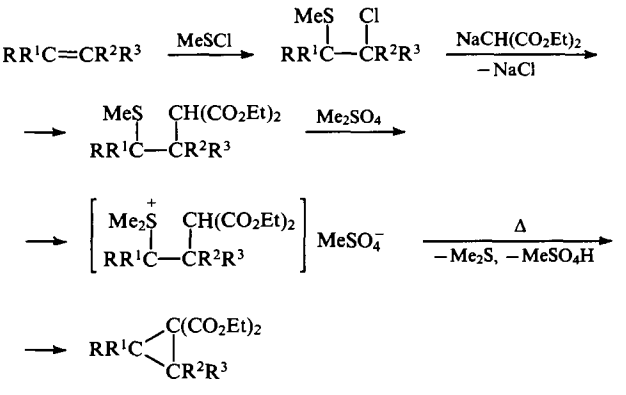
In the interaction of aryl β-chloroalkyl sulfides with vinyl ethers in proportions of 1:1, cyclic S-cationoid intermediates are formed. These react further with nucleophiles to form various sulfides having functional group substituents.[10,122,123]



β-Chloroalkyl sulfides react similarly with styrene and its homologues,[124] which involves the stabilisation of the intermediates in the form of tetrahydrothiophenium perchlorate.

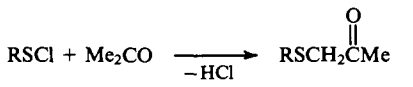


The reaction of β-chloroalkyl sulfides with *C*-nucleophiles, which may be used to create new carbon–carbon bonds, is synthetically very important. However, it is not always possible to achieve this reaction, since it has been noted,[10] for example, that, in the presence of *C*-nucleophiles such as organolithium or organomagnesium compounds, β-chloroalkyl sulfides undergo elimination. Only when sodiomalonic ester was used as the *C*-nucleophile was it possible to obtain the corresponding β-aryl(alkyl)thioalkylation products, which were subsequently converted into cyclopropane derivatives.[125]



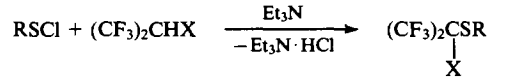
b. Syntheses of oxo-substituted sulfides

One of the commonest methods of synthesis of oxo-substituted sulfides is the sulfenylation of carbonyl compounds containing reactive C–H bonds. For example, sulfenyl chlorides react relatively easily in the cold with ketones having α-hydrogen atoms, forming β-oxo-substituted sulfides.[33]



R = Ar, Alk.

Fluorine-containing CH acids interact with sulfenyl chlorides only in the presence of triethylamine.[126]



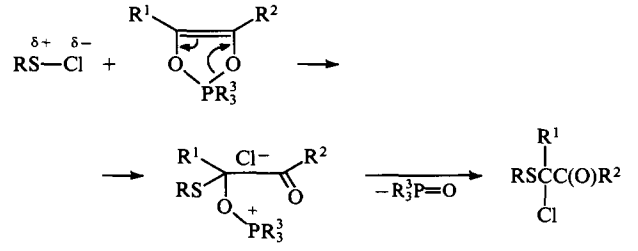
X = PhCO, CF_3CF_2CO, FCO.

In their reactions with sulfenyl chlorides, phosphorus ylides containing a carbonyl group readily exchange a hydrogen atom of the methylene group for an alkylthio- or arylthio-group even in the absence of bases.[3]

Dibenzoylmethane,[127,128] acetoacetic ester,[129,130] acetylacetone,[131] and even malonic ester[132,133] react similarly with alkanesulfenyl chlorides.

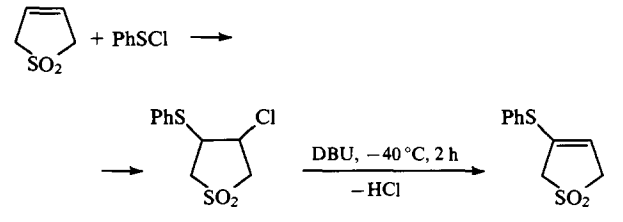
Another aspect of the use of sulfenyl chlorides in the synthesis of oxo-substituted sulfides involves the reaction of sulfenyl chlorides with vinyloxy[131–137] and divinyloxy-silanes[138] and also with the enols of dibutylborinates.[139] This reaction proceeds via stages involving 1,2-addition of the sulfenyl chloride and the elimination of chlorotrimethylsilane or dibutylchloroborane.

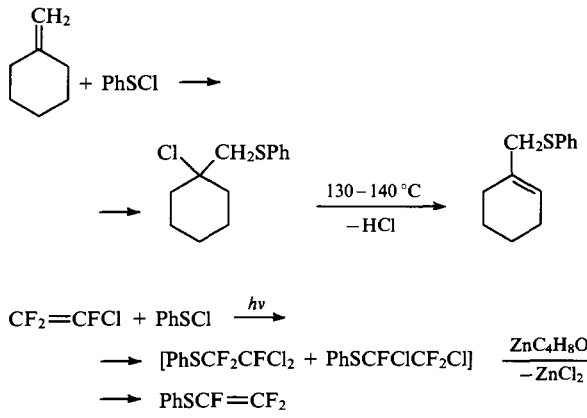
The synthesis of β-oxoalkyl sulfides from sulfenyl chlorides and 1,3,2-dioxaphospholenes has been described.[140] It has been suggested[28] that this reaction proceeds via a polar mechanism.



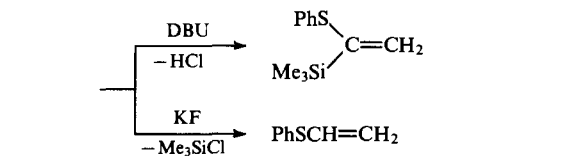
c. Synthesis of unsaturated sulfides

Several variants of the synthesis of unsaturated sulfides from sulfenyl chlorides have been developed. One of them involves the addition of sulfenyl chlorides to the C=C bond of unsaturated compounds with subsequent dehydrochlorination or dechlorination of the adducts. This variant has been used widely in the syntheses of vinyl[8,141] and allyl sulfides.[142,143] Potassium *tert*-butoxide, 1,5-diazabicyclo[5.4.0]undec-5-ene (DBU), triethylamine, and other organic bases are used as the dehydrochlorinating agents.

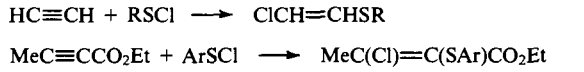




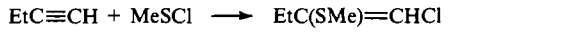
β-Chloro-α-(trimethylsilyl)ethyl phenyl sulfide, which is a product of the reaction of benzenesulfenyl chloride with trimethylvinylsilane, can undergo dehydrochlorination or dechlorotrimethyldesilylation, depending on the conditions, with formation of two different vinyl sulfides.[144]



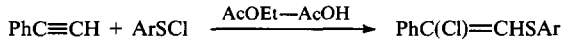
2-Chlorovinyl sulfides are formed as a result of the reaction of sulfenyl chlorides with ethyne and its homologues.[10,145,146]



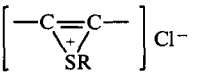
This reaction is slower than that of sulfenyl chlorides with alkenes, catalysts, for example aluminium chloride, being used sometimes to accelerate it.[10] The addition of sulfenyl chlorides to alkylethynes is mainly anti-Markovnikov and the products formed are not isomerised further.



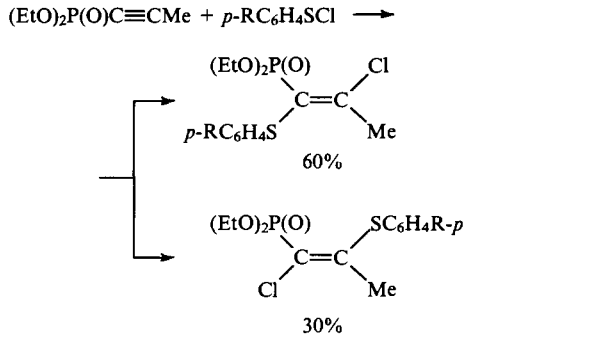
The mode of addition is influenced appreciably by the nature of the solvent and of the substituents. For example, the content of the Markovnikov addition product increases in acid media, a small amount of the *cis*-adduct being also formed together with the *trans*-adducts under these conditions.



It has been suggested[10] that Markovnikov addition occurs predominantly in those cases where the reaction conditions and the nature of the substituents favour the formation of a highly polar intermediate of the thiirenium salt type.

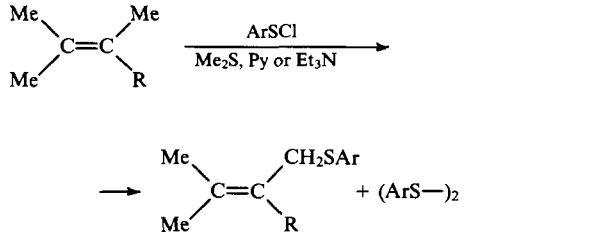


In anti-Markovnikov addition, the intermediate formed initially apparently decomposes. The addition of arenesulfenyl chlorides to diethyl propynylphosphonate takes place stereoselectively with formation of two regioisomers having the (*E*)-configuration in proportions of 2:1.[147]



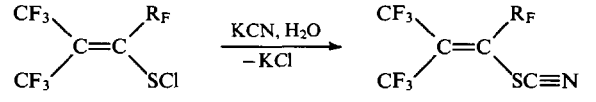
R = H, Me.

It has been noted[148] that, when internal alkenes reacted with arenesulfenyl chlorides in the presence of dimethyl sulfide, pyridine, or triethylamine, the hydrogen of the alkene methyl group is substituted by the arenesulfenyl fragment with formation of unsaturated sulfides. A proportion of the sulfenyl chloride is then converted into the disulfide.

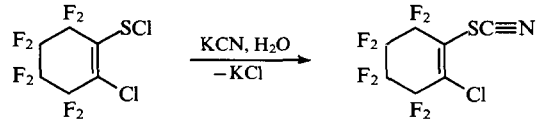


R = CH_3, 4-$MeOC_6H_4$; Ar = 4-MeC_6H_4, 4-ClC_6H_4.

The synthesis of perfluorinated α,β-unsaturated thiocyanates, by reaction of perfluorinated α,β-unsaturated sulfenyl chlorides with potassium cyanide in an aqueous medium, has been described.[149] This reaction proceeds under mild conditions (5–10 °C, 20 min) and gives high yields of the target products (50%–70%).

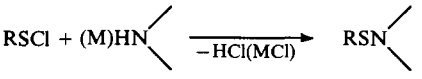


R_F = F, C_2F_5.



2. Syntheses of sulfenamides

One of the most important reactions of sulfenyl chlorides is that with compounds containing N–H or N–M (M = Na, K, Ag) bonds.



A whole series of preparative methods of synthesis of sulfenamides, including biologically active preparations, have been developed on the basis of this reaction.[13,85–87,150] Depending on the nature of the sulfenyl chloride and the compound containing the NH group, the sulfenylation is carried out in anhydrous inert organic solvents in the presence of hydrogen chloride acceptors (pyridine, triethylamine) or aqueous alkaline media. The sulfenylation of ammonia,[151–154] primary[155–159] and

secondary[160–165] amines, hydrazines and hydrazides,[28] the amides of carboxylic,[165–171] sulfonic,[172–177] and phosphoric[178,179] acids, cyanamide,[180,181] imides,[27,160] phosphine imines[182–184] and sulfine imines,[185,186] imidoesters,[187] sulfinamidines,[188] silazanes,[89,189–191] glycine derivatives,[192–197] and nitrogen-containing heterocyclic compounds[33,198] has been described. Instead of amines and amides, their silylated derivatives are introduced in certain cases into the reaction with sulfenyl chlorides. The interaction of these derivatives with sulfenyl chlorides entails the cleavage of the N–Si bond and the formation of the N–S bond.[199,200]

$$2\,ArSCl + (Me_3Si)_2NR \xrightarrow[-2\,Me_3SiCl]{} (ArS)_2NR$$

Ar = 4-$NO_2C_6H_4$, $PhCH_2$, Ac, $PhSO_2$

$$RSCl + Me_3SiN(Me)_2 \xrightarrow[-Me_3SiCl]{} RSN(Me)_2$$

R = Me, CCl_3, Ph, 2-$NO_2C_6H_4$.

The second aspect of the use of sulfenyl chlorides in the synthesis of sulfenamides involves their addition to the C≡N bond.[33] The reactions of TCMSC with 2,4-dimethylphenyl cyanate[33,201] and *N*-benzoylcyanamide,[202] of dichlorofluoromethanesulfenyl chloride with chlorocyanogen,[203] and of trifluoromethanesulfenyl chloride with tetracyanoethene[203] and chloro-cyanogen[204] take place in this way.

$$X{-}C{\equiv}N + ClSR \longrightarrow X{-}\underset{\displaystyle Cl}{\underset{|}{C}}{=}NSR$$

X = 2,4-$Me_2C_6H_3O$, PhCONH, $(NC)_2C{=}CCN$, Cl;

R = CCl_3, CF_3.

In the presence of mercury difluoride, trifluoromethanesulfenyl chloride adds readily to the C=N bond of chlorocyanogen and trifluoroacetonitrile and trichloroacetonitrile.[205] The interaction is accompanied by the substitution of chlorine by fluorine.

$$CF_3SCl \xrightarrow{HgF_2,\ 20\,^\circ C} \begin{cases} \xrightarrow{ClCN} CF_3N(SCF_3)_2 \\ \xrightarrow{CF_3CN} CF_3C(F){=}NSCF_3 \\ \xrightarrow{CCl_3CN} CCl_3C(F){=}NSCF_3 \end{cases}$$

The reactions of sulfenyl chlorides with cyanamide and its *N*-alkyl derivatives are accompanied by the sulfenylation of the amido-group.[206,207]

$$3\,XNHC{\equiv}N + 4\,RSCl \xrightarrow{0\,^\circ C,\ Et_2O} 2\,RSN(X)C(Cl){=}NSR + XNHCN\cdot 2\,HCl$$

R = CCl_3, $CFCl_2$, CF_3.

The third aspect of the use of sulfenyl chlorides in the synthesis of sulfenamides involves their conversion into sulfenyl isocyanates and subsequent treatment of the latter with ammonia, amines, or alcohols.[208–211] As a rule sulfenyl isocyanates are synthesised in situ by the interaction of sulfenyl chloride with AgOCN or NaOCN in anhydrous inert organic solvents.

$$RSCl + MOCN \xrightarrow[-MCl]{} RSNCO \longrightarrow$$

$\xrightarrow{NH_3}$ RSNHCONH$_2$

$\xrightarrow{R^1NH_2}$ RSNHCONHR^1

$\xrightarrow{R^2_2NH}$ RSNHCONR$^2_2$

$\xrightarrow{R^3OH}$ RSNHCOOR^3

$R^1 = R^2$ = Alk, Ar; R^3 = Alk, Bz; M = Ag, Na.

3. Syntheses of thiocarbonyl compounds

On treatment with bases (triethylamine, NaOH, etc.), sulfenyl chlorides containing reactive α-C–H bonds generate thioaldehydes, which are used in organic synthesis as highly reactive intermediates.[1,43]

$$EtOCCH_2SCl \xrightarrow[-HCl]{Et_3N} EtOC(=S)-CH$$

Certain sulfenyl chlorides give rise to thioaldehydes as a result of photolysis. For example, the photolysis of ethanesulfenyl chloride by irradiation with UV light at a wavelength of 365 nm has been recommended[212] as a preparative method of synthesis of thioacetaldehyde. Sulfenyl chlorides containing a *sp*-hybridised C atom at the S atom readily isomerise to thioketenes.[67]

$$PhC{\equiv}CSCMe \xrightarrow{SO_2Cl_2} [PhC{\equiv}CSCl] \longrightarrow \begin{matrix} Ph \\ \diagdown \\ Cl \end{matrix}\!\!>C{=}C{=}S$$

Treatment of perhaloalkanesulfenyl chloride with a solution of Na_2CS_3 in chloroform or of $BaCS_3$ in the CH_3CN-H_2O mixture leads to the formation of the polysulfide derivatives of polythiocarboxylic acids $(RSS)_2C=S$ (R = CCl_3, CCl_3CCl_2, CF_3CCl_2, $CClF_2CCl_2$).[213] A series of preparative methods of synthesis of thiocarbonyl dihalides, based on the reduction of perhalomethanesulfenyl chlorides, have been developed. For example, heating of TCMSC with tetralin leads to the formation of thiophosgene.[24,33]

$$CCl_3SCl \xrightarrow[-Cl_2]{C_{10}H_{12},\ 200\,^\circ C} \begin{matrix} Cl \\ \diagdown \\ Cl \end{matrix}\!\!>C{=}S$$

In the presence of tin, dichlorofluoromethanesulfenyl chloride and chlorodifluoromethanesulfenyl chloride are reduced to thiocarbonyl chloride fluoride and thiocarbonyl difluoride respectively.[33]

$$CFCl_2SCl \xrightarrow{40\,^\circ C} \begin{matrix} F \\ \diagdown \\ Cl \end{matrix}\!\!>C{=}S$$

$$CF_2ClSCl \xrightarrow{20\,^\circ C} \begin{matrix} F \\ \diagdown \\ F \end{matrix}\!\!>C{=}S$$

4. Syntheses of sulfenic acid esters

Sulfenic acid esters are formed in the reactions of sulfenyl chlorides with alkoxides (phenoxides) or with alcohols (phenols) in the presence of pyridine or triethylamine.[13,24,33,159] The reaction does not always proceed smoothly, especially in the case of aliphatic sulfenyl chlorides and alcohols. This is due to the fact that, by virtue of the high nucleophilicity of the sulfur atom, the sulfenate formed may react with the sulfenyl chloride to form a disulfide and other side products, which reduce the yield and hinder the isolation of the sulfenates.[28] The reaction proceeds more smoothly in the case of sulfenyl chlorides containing powerful electron-accepting groups at the sulfur atom, which reduce the nucleophilicity of the sulfur atom in the resulting sulfenate and therefore hinder its interaction with the sulfenyl chloride. For example, relatively stable sulfenates have been obtained in the reaction of polyfluoroalkanesulfenyl chlorides with alcohols on heating[69] and also in the presence of hydrogen chloride acceptors (triethylamine, pyridine)[214–216] or with alkali metal[217] and mercury[218] alkoxides and phenoxides.

$$R_FSCl + ROH \xrightarrow[-HCl]{\Delta} R_FSOR$$

$R_F = CF_3, (CF_3)_2CHCF_2$;

R = Et, 4-$MeOC_6H_4CH_2$, $CF_3SNHCH_2CH(Ph)$.

$$R_FSCl + ROH \xrightarrow[-HCl]{Et_3N \text{ or } C_5H_5N} R_FSOR$$

$R_F = CF_3, (CF_3)_2CHCF_2$; $CF_3CH(CH_2Cl)$;

R = Alk, Ar, 4-$MeOC_6H_4CH_2$.

$$R_FSCl + RONa \xrightarrow[-NaCl]{THF,\ 20\,^\circ C,\ 3\ h} R_FSOR$$

$R_F = CF_3CPh_2$;

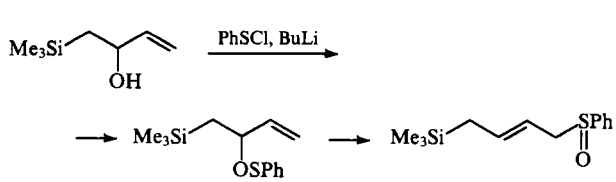
R = Bu^tCH_2, $PhCH_2O(CH_2)_2$, 4-$NO_2C_6H_4$, $Me(CH_2OCH_2)_3CH_2$.

$$R_FSCl + ROHgCl \xrightarrow[-HgCl_2]{0\,^\circ C,\ 24\ h} R_FSOR$$

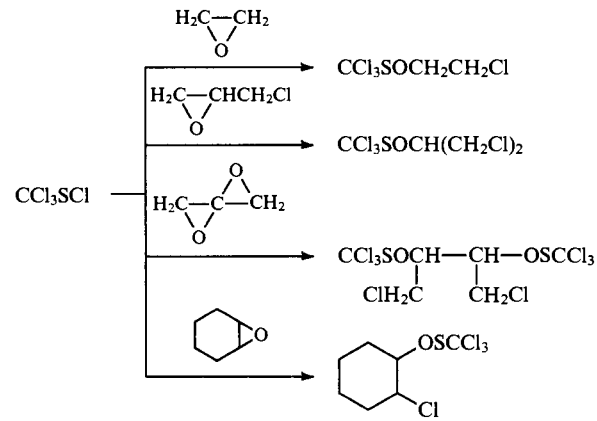
R_F = CF_3, CF_3CO; R = $(CF_3)_3C$.

The stable esters of 2,4,6-trinitrobenzenesulfenic,[47] 2,4-dinitrobenzenesulfenic,[4,28] trichloromethanesulfenic,[33] and dichlorofluoromethanesulfenic[33] acids have been described. In the sulfenylation of phenols and naphthols, it is better to employ their sodium salts, which rules out the competing electrophilic substitution of the hydrogen atoms of the benzene ring.[8] The introduction of the corresponding alkoxides instead of alcohols into the reaction with TCMSC, especially in the presence of an excess of the alkoxides, leads to the formation of alkyl orthocarbonates.[219] The above methods are unsuitable for the synthesis of allyl sulfenates, with the exception of the allyl esters of 2,4-dinitrobenzenesulfenic acid, because the esters formed are readily converted into allyl sulfoxides as a result of a 2,3-sigmatropic rearrangement.[33]

$$RSCl + HOCH_2CH{=}CH_2 \xrightarrow[-HCl]{C_5H_5N} [RSOCH_2CH{=}CH_2] \longrightarrow R\overset{\overset{O}{\|}}{S}CH_2CH{=}CH_2$$



The chloroalkyl esters of trichloromethanesulfenic acid are formed in the reaction of TCMSC with 1,2-epoxides.[33]



5. Syntheses of the thiolo-esters of sulfinic, sulfonic, carboxylic, and phosphoric acids

The hydrolysis of sulfenyl chlorides leads to the formation of a mixture of products in which the thiolo-esters of sulfinic or sulfonic acids predominate. This is determined both by the structure of the initial sulfenyl chloride and the hydrolysis conditions.[13,33] For example, in a study of the hydrolysis of dichlorofluoromethane- and chlorodifluoromethane-sulfenyl chlorides in a neutral medium, it has been possible[220] to isolate the thiolo-esters of sulfinic acids. The thiolo-esters of sulfonic acids are one of the products of the hydrolysis of sulfenyl chlorides in acid media.[221]

$$4\,RSCl + 2\,H_2O \xrightarrow{H^+} RSO_2SR + RSSR + 4\,HCl$$

The formation of the corresponding thiolosulfonate in the reaction of *p*-chlorobenzenesulfenyl chloride with anhydrous formic acid has been noted.[222] The interaction of sulfenyl chlorides with sulfinic acids[28,223] or their silver[28] and sodium[174] salts leads to asymmetric thiolosulfonates.

$$RSO_2H(M) + R^1SCl \xrightarrow[-HCl(MCl)]{} RSO_2SR^1$$

R, R^1 = Alk, Ar.

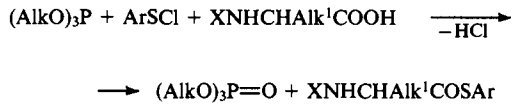
M = Na, Ag.

The thiolo-esters of carboxylic acids are formed on interaction of arenesulfenyl chlorides with triphenylphosphine or with trialkyl phosphites in the presence of carboxylic acid salts. It has been suggested[224] that the quasi-sulfonium salt **A** is an intermediate in this reaction. Its interaction with the carboxylate anion leads to the final products.

$$R_3P + ArSCl \longrightarrow \underset{\mathbf{A}}{(R_3PSAr)^+Cl^-} \xrightarrow[-NaCl]{R^1COONa} (R_3PSAr)^+R^1COO^- \longrightarrow (R_3POCOR^1)^+(SAr)^- \longrightarrow R_3P{=}O + RCOSAr$$

R = Ph, AlkO; R^1 = Ar, Alk.

The analogous reaction of arenesulfenyl chlorides with trialkyl phosphites and *N*-acylaminoacids in the presence of bases has been proposed as a preparative method of synthesis of the aryl thiolo-esters of carboxylic *N*-acylaminoacids.[225,226]



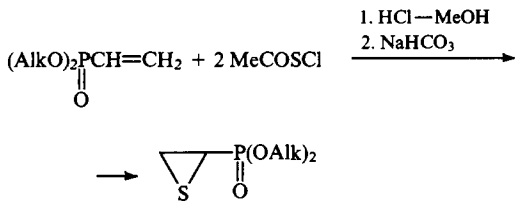
X = CF_3CO, Ph, $PhCH_2OCO$.

The syntheses of the thiolo-esters of phosphonic acids and other phosphorus-containing compounds from sulfenyl chlorides have been described in detail in a monograph[4] and also in a review[33] and in the literature quoted therein. For this reason they will not be considered here.

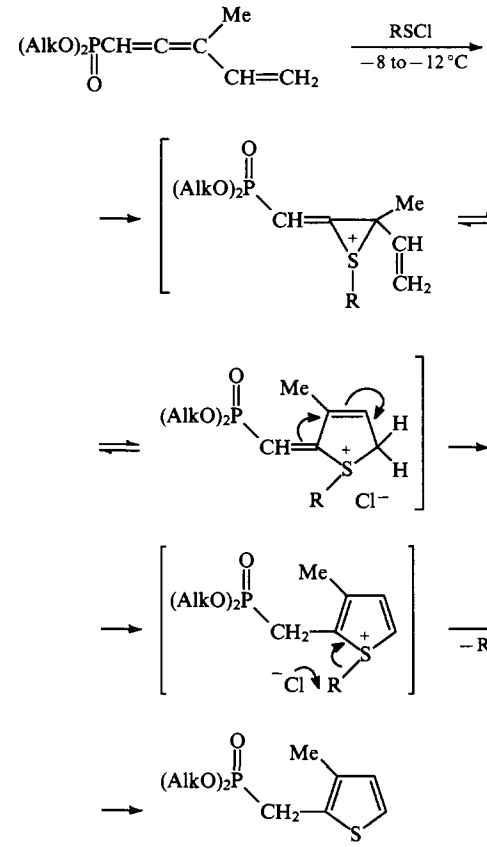
6. Syntheses of heterocyclic compounds

a. Syntheses based on monofunctional sulfenyl chlorides

The use of monofunctional sulfenyl chlorides in the synthesis of heterocyclic compounds is based on their addition to the C=C bond of unsaturated compounds with subsequent cyclisation of the resulting intermediates.[4,13,33] For example, the synthesis of the dialkyl esters of 1,2-epithioethylphosphonic acid has been described.[227] It is based on the addition of acetylsulfenyl chloride [1-oxoethanesulfenyl chloride (Ed. of translation)] to the alkyl esters of vinylphosphonic acid and subsequent treatment of the resulting adduct with a solution of hydrogen chloride in methanol and then with sodium bicarbonate.



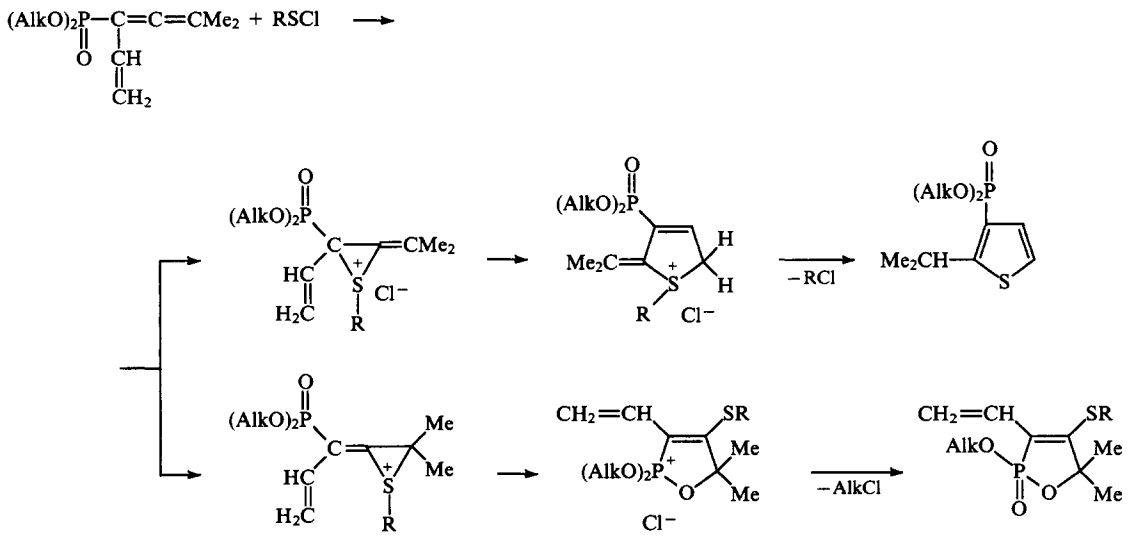
It has been noted[4,228,229] that the introduction of the vinyl group in the 3-position in allenylphosphonate leads to a system of double bonds, to which alkanesulfenyl chlorides add relatively easily with formation of an episulfonium ion capable of ring expansion to a five-membered cyclic compound followed by conversion into a thiophene derivative.

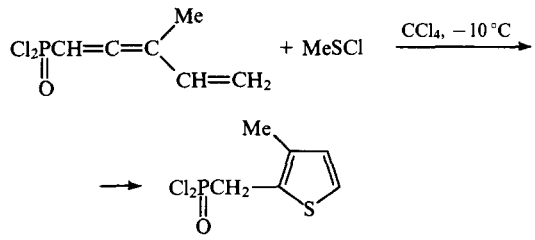


The analogous reaction of alkanesulfenyl chlorides with allenylphosphonates containing a vinyl substituent in the 1-position leads to a mixture of 3-vinyl-1,2-oxaphosphol-3-enes and phosphorylated thiophenes, the ratio of which is influenced by the reaction temperature (Scheme 5).[4,228,230]

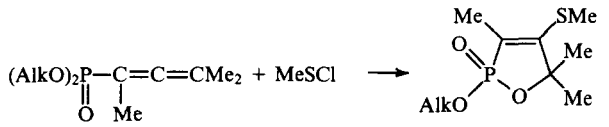
Derivatives of 2,2-dichlorophosphorylmethylthiophene are formed in 53% yield as a result of the addition of methanesulfenyl chloride to alkyl-1,2,4-trienylphosphonic dichlorides.[231]

Scheme 5

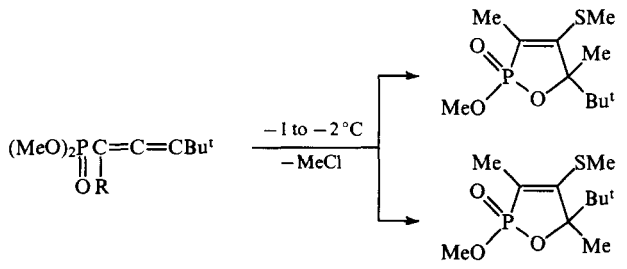




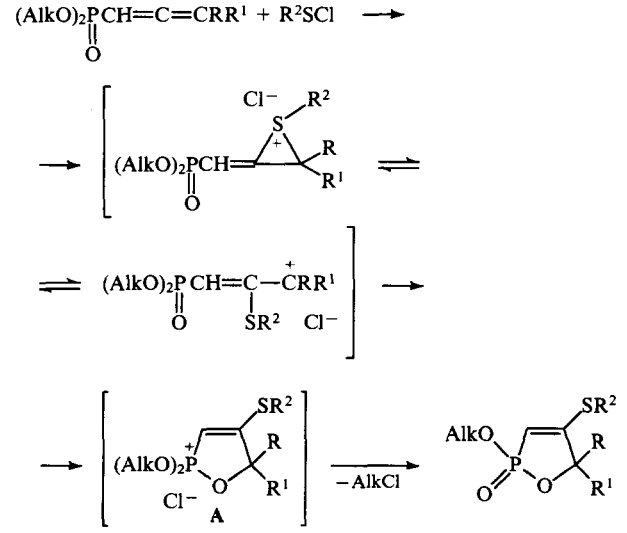
The addition of methanesulfenyl chloride to 1,3,3-trimethylallenylphosphonates leads to the derivatives of 1,2-oxaphosphol-3-ene.[228]



In the case of 1,3,3-trisubstituted allenylphosphonates containing the *tert*-butyl group in the γ-position, a mixture of two stereoisomers is formed. This has been demonstrated by NMR spectroscopy.[232]



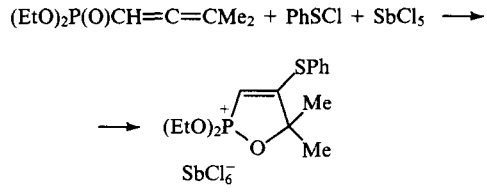
The addition of sulfenyl chlorides to the dialkyl esters of 3,3-disubstituted allenylphosphonic acids, the rearrangement of the episulfonium ion, cyclisation, and dealkylation result in the formation of 4-organylthio-1,2-oxaphosphol-3-enes.[233–237]



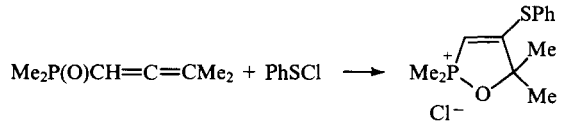
R, R^1 = Alk or R + R^1 = $-(CH_2)_5-$.

R^2 = Me, Et, Pr^i, Ph, 2,4-$(NO_2)_2C_6H_3$.

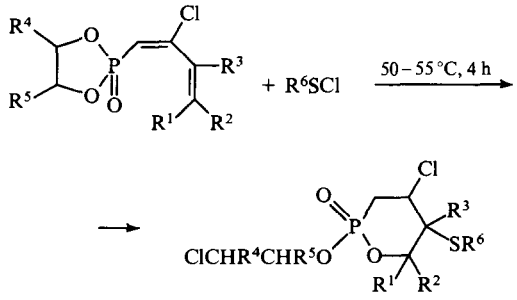
The formation of the intermediate phosphonium salt **A** has been demonstrated by its isolation in the form of 1,2-oxaphosphol-3-enium hexachloroantimonate.[238]



A quasi-phosphonium salt has also been isolated in the reaction of benzenesulfenyl chloride with dimethyl(3-methylbuta-1,2-dienyl)phosphine oxide in the cold.[234]



In chloroform or dichloroethane, alkanesulfenyl chlorides react with 1,3,3-dioxaphospholane 2-oxides to form 1,2-oxaphosphorines.[239]

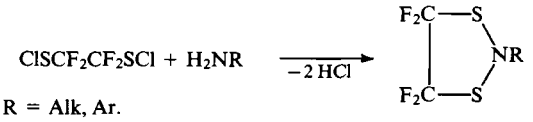


R^1 = R^2 = R^3 = R^4 = R^5 = H, Me; R^6 = Me, Pr^i.

The addition of arenesulfenyl chlorides to 2-allylphenols and subsequent cyclisation of the resulting adducts lead to the formation of 2-phenylthiomethylbenzofurans.[240]

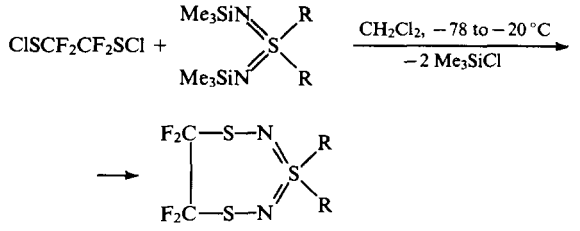
b. Syntheses based on bifunctional sulfenyl chlorides

Bifunctional sulfenyl chlorides are more widely used in the synthesis of heterocyclic compounds.[13] For example, a series of *N*-substituted 1,3,2-dithiazolidines have been obtained by the reaction of tetrafluoroethane-1,2-disulfenyl chloride with primary amines.[156]



R = Alk, Ar.

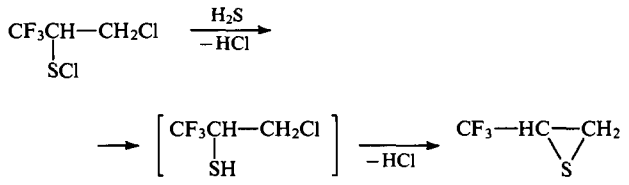
The interaction of the same disulfenyl chloride with *N*,*N*′-bis(trimethylsilyl)sulfodiimides affords high yields of 1,3,5-trithia-2,4-diazepines.[13]



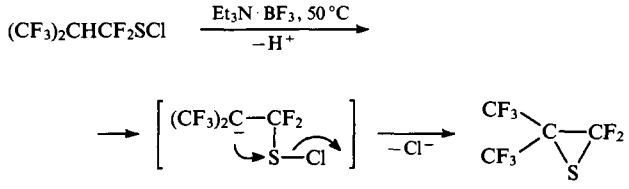
R = Alk, Ar.

Numerous heterocyclic compounds have been obtained from other polyfluoroalkanesulfenyl chlorides. The capacity of these sulfenyl chlorides for ring formation is determined primarily by

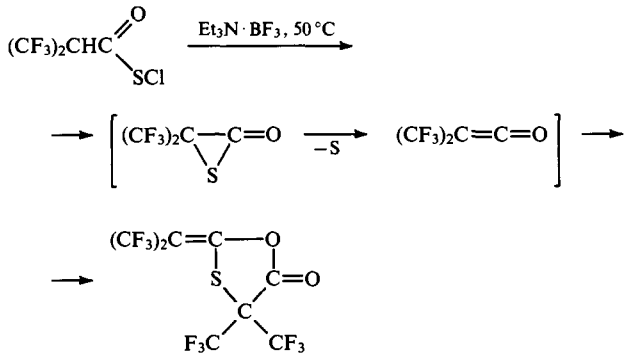
anionotropic transformations in the C–C–S three-centre systems.[13,241] It has been noted[242] that, on treatment with H_2S in *N*-methylpyrrolidinone, 3-chloro-1,1,1-trifluoropropane-2-sulfenyl chloride is readily converted into trifluoromethylthiirane. 3-Chloro-1,1,1-trifluoropropane-2-thiol is an intermediate in this reaction.



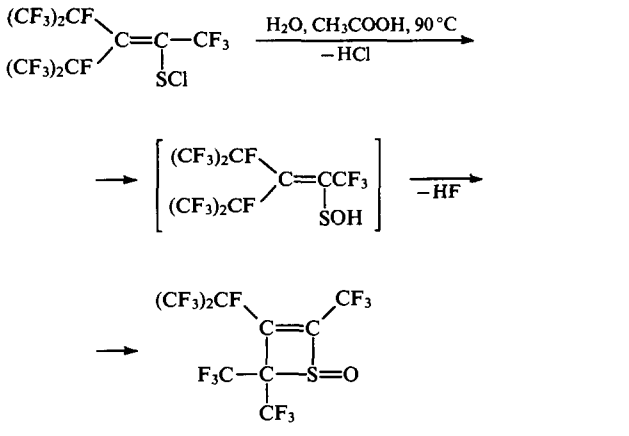
The dehydrochlorination of 2-hydroperfluoroisobutanesulfenyl chloride in the presence of the complex $Et_3N \cdot BF_3$ leads to the formation of perfluoro-2,2-dimethylthiirane.[69]



In the case of 3,3,3-trifluoro-2-(trifluoromethyl)-1-oxopropanesulfenyl chloride, the reaction proceeds in a more complex manner. The thiirane formed as a result of the 3-chlorination of this sulfenyl chloride is desulfurised under the reaction conditions, being converted into bis(trifluoromethyl)ketene, which subsequently react with the thiirane via a [3 + 2]-cycloaddition mechanism.[69]



The formation of the thietene ring has been observed[13,243] in the acid hydrolysis of perfluoro-3-isopropyl-4-methylpent-2-ene-2-sulfenyl chloride. An unstable sulfenic acid is an intermediate product of this reaction.



TCMSC has found extensive applications in the synthesis of heterocyclic compounds.[33] Thus the interaction of this compound with a 25% aqueous solution of ammonia in the benzene–water two-phase system leads to the formation of 2,3,7,8-tetrachloro-5,10,11,12-tetrathia-1,4,6,9-tetrazatricyclo-[5.3.11^{2,6}]-dodeca-3,8-diene.[244]

The interaction of TCMSC with aromatic amines results in the formation of unstable *N*-aryltrichloromethanesulfenamides, which are converted into 2,5-diaryl-3,3,6,6-tetrachloro-1,4-dithia-2,5-diazines in the presence of bases or on heating.[201]

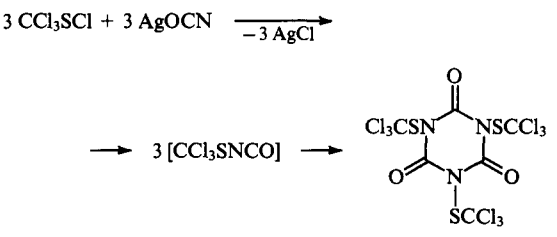
The reaction of TCMSC with 2-aminopyridine leads to the formation of 2-(*N*-trichloromethanesulfenyl)aminopyridine, which is converted into 3-(2-pyridylimino)-3*H*-1,2,4-thiadiazolo-[4,3-α]pyridine in the presence of an excess of the aminopyridine.[201,245]

When TCMSC is heated with carboxylic acid amides in dioxane, 5-aryl-1,3,4-oxathiazol-2-ones are formed.[246] *N*-Aroyltrichloromethanesulfenamides are intermediates in this reaction. In the presence of bases, they undergo the heterocyclisation reaction.[86,175,247,248]

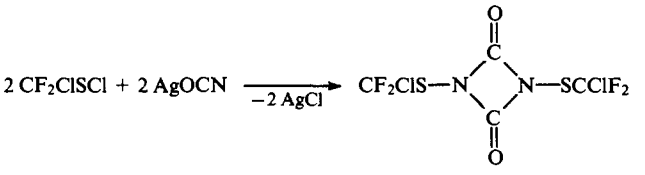
A series of 1,2,4-thiadiazole derivatives have been obtained by the reaction of TCMSC with carboxylic acid amidines and *S*-alkylisothiuronium salts.[33]

Dichloromethane- and dichlorofluoromethane-sulfenyl chlorides react similarly with carboxylic acid amidines.[28,33]

Treatment of TCMSC with silver isocyanate leads to the unstable trichloromethanesulfenyl isocyanate, which trimerises to 1,3,5-tris(trichloromethanesulfenyl)-2,4,6-trioxo-1,3,5-triazine.[249]



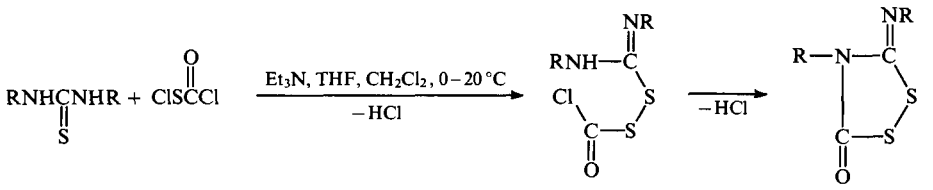
The analogous reaction of silver isocyanate with chlorodifluoromethanesulfenyl chloride leads to the formation of 1,3-bis(chlorodifluoromethanesulfenyl)-2,4-dioxo-1,3-diazetidine.[208,209]



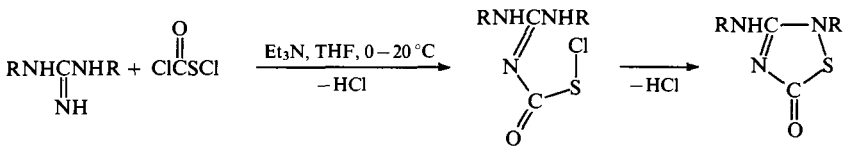
Chlorocarbonylsulfenyl chloride is of considerable preparative importance for the synthesis of various five-membered nitrogen and sulfur-containing heterocyclic compounds.[11] The two reaction centres (sulfur and carbon) as well as the high lability of the S–Cl and C–Cl bonds impart to this reagent a set of properties which are extremely valuable for heterocyclisation reactions. Depending on the nature of the bifunctional compound, chlorocarbonylsulfenyl chloride may react with the latter, a C or the S atom participating in the first stage of the reaction, while in the second stage the second reaction centre is involved, as happens, for example, in the interaction of chlorocarbonylsulfenyl chloride with thiourea, urea, and guanidine derivatives (Scheme 6).[250]

A whole series of preparative methods of synthesis of various five-membered heterocyclic compounds from chlorocarbonylsulfenyl chloride and 1,3-bifunctional compounds, presented in Scheme 7, have been developed.[11]

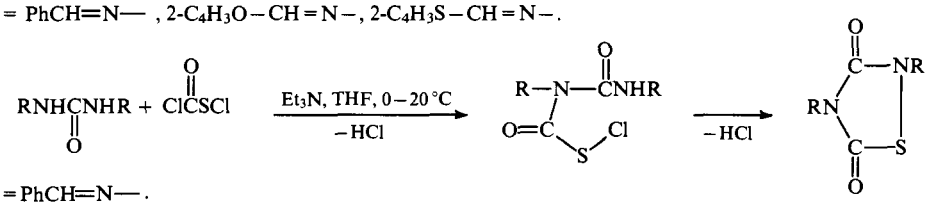
Scheme 6



R = Ph, XCH=N— (X = Ph, 2-C_4H_3O, 2-C_4H_3S, 2-C_5H_4N, 3-C_5H_4N).



R = PhCH=N— , 2-C_4H_3O–CH=N–, 2-C_4H_3S–CH=N–.

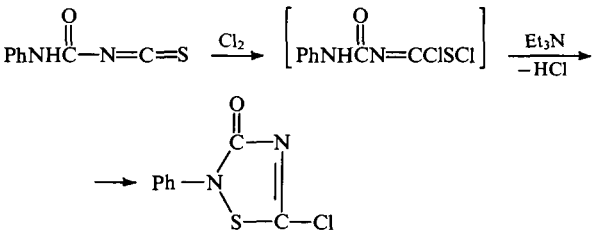


R = PhCH=N—.

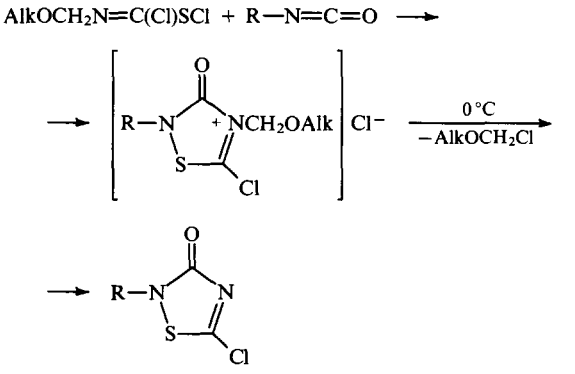
The interaction of chlorocarbonylsulfenyl chloride with derivatives of benzamide oxime in acetonitrile in the presence of triethylamine leads to the formation of two products — 3-aryl-1,2,4-thiadiazol-5-ones and 3-aryl-1,2,4-oxadiazol-5-ones.[251]

The condensation of chlorocarbonylsulfenyl chloride with 2-aminothiazole in tetrahydrofuran in the presence of bases takes place with formation of 2,3 fused thiadiazolone, whereas the condensation in chloroform leads to 3,4 fused thiadiazolone.[252]

Numerous methods of synthesis of five-membered nitrogen-containing heterocycles have been developed on the basis of chloroiminomethanesulfenyl chlorides. However, many of these methods have so far been inadequately tested and it is not clear whether they are of a general character. On the other hand, the majority of these compounds are unstable, their synthesis and their reactions being carried out in situ, which also limits their application in the syntheses of heterocycles. For example, the synthesis of 5-chloro-3-oxo-2-phenyl-1,2,4-thiadiazoline, described in the literature,[11] involves the chlorination of phenylcarbamoyl isothiocyanate followed by the treatment of the intermediate chloro(phenylcarbamoylimino)methanesulfenyl chloride with a tertiary amine.

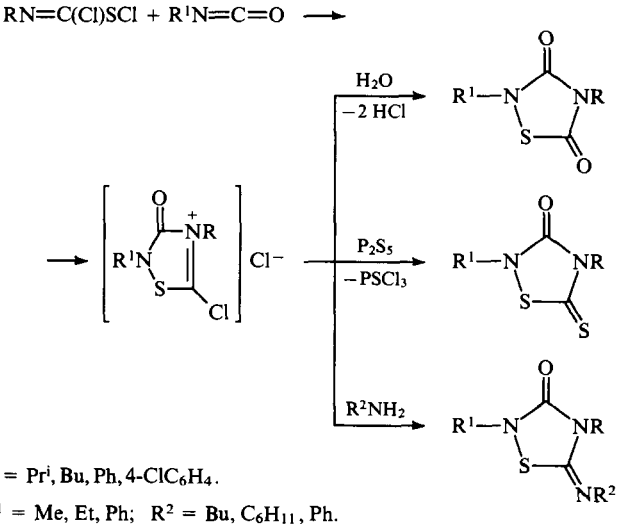


Similar compounds are formed in the interaction of alkoxymethylimino(chloro)methanesulfenyl chlorides with isocyanates. The intermediate formed in the first stage of this reaction is converted into the final product by elimination of an alkyl chloromethyl ether.



R = Me, Pr^i, Ph, 2-BrC_6H_4, 3,4-$Cl_2C_6H_3$, 4-$EtOC_6H_4$.

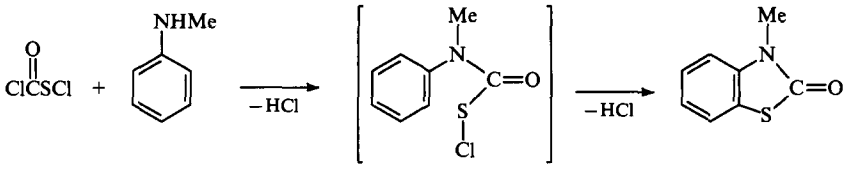
The intermediates formed in the reactions of chloro(imino)-methanesulfenyl chlorides with isocyanates interact relatively easily with various nucleophiles, affording five-membered heterocyclic compounds containing both sulfur and nitrogen.[253,254]

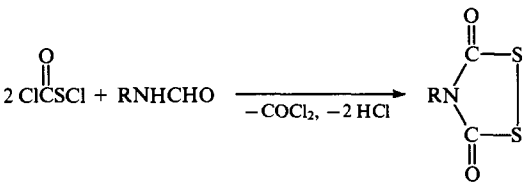


R = Pr^i, Bu, Ph, 4-ClC_6H_4.

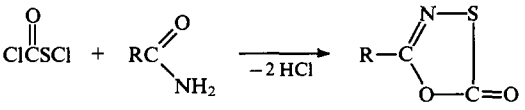
R^1 = Me, Et, Ph; R^2 = Bu, C_6H_{11}, Ph.

Scheme 7

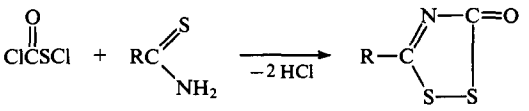


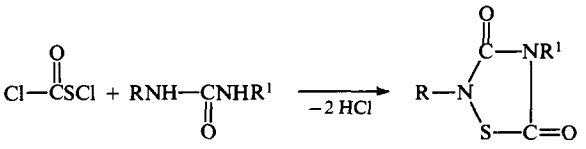


R = Me, C_5H_{11}, Ph, 3,4-$Cl_2C_6H_3$, 3-Cl-4-$MeOC_6H_3$.



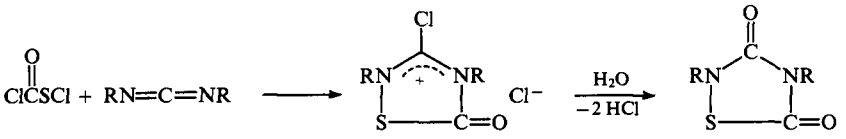
R = 2-$MeOC_6H_4$, 3-$MeOC_6H_4$, 4-$MeOC_6H_4$, 2-BrC_6H_4, 2-IC_6H_4, 2-MeC_6H_4.

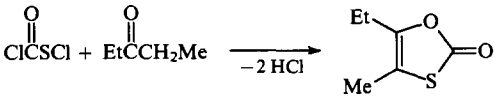


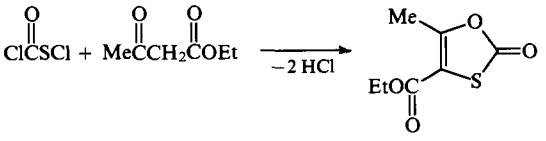


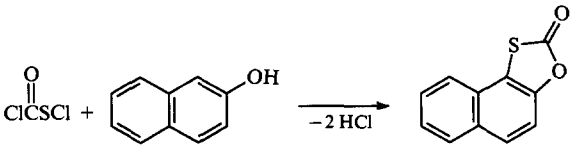
R = Me, $MeOCH_2$, C_6H_{11}, Ph, 2-$CF_3C_6H_4$, 3,4-$Cl_2C_6H_3$, 3-Cl-4-MeC_6H_3;

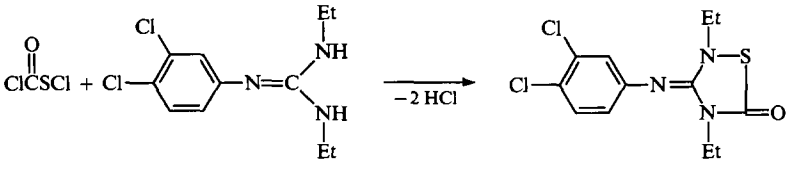
R^1 = Me, $MeOCCH_2$, C_6H_{11}, Ph.



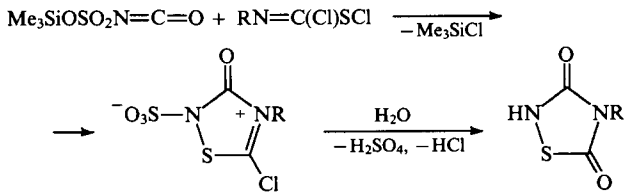






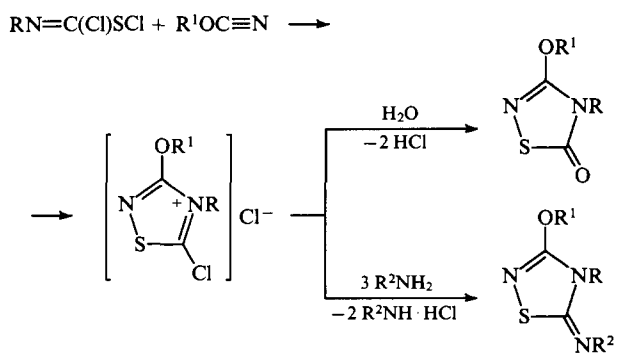


The interaction of chloro(imino)methanesulfenyl chlorides with trimethylsiloxysulfenyl isocyanate takes place with cleavage of the Si–O bond and the formation of a product having a dipolar structure, the hydrolysis of which affords 1,2,4-thiadiazolidine-3,5-diones.[254]



R = Me, Bu, $PhCH_2$, Ph, 3,4-$Cl_2C_6H_3$.

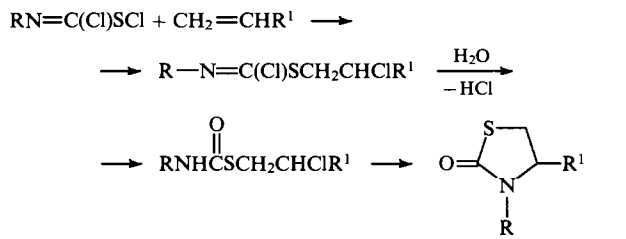
The addition of chloro(imino)methanesulfenyl chlorides to the C≡N bond of cyanates also proceeds with formation of intermediates, the hydrolysis and aminolysis of which lead to derivatives of 1,2,4-thiadiazoline.[11]



R = Me, Ph; R^1 = CCl_3CH_2, Ph, 3-$NO_2C_6H_4$.

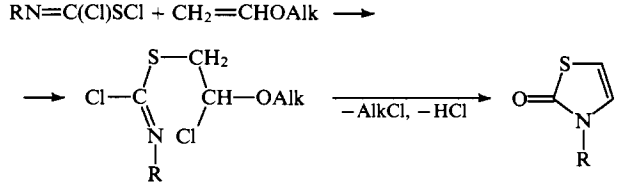
R_2 = Me, 4-ClC_6H_4.

The addition of chloro(imino)methanesulfenyl chlorides to the C=C bond of alkenes is accompanied by the formation of adducts, the hydrolysis of which leads to the S-esters of thiocarbamic acid, which cyclise to 2-oxo-1,3-thiazolidines.[255]



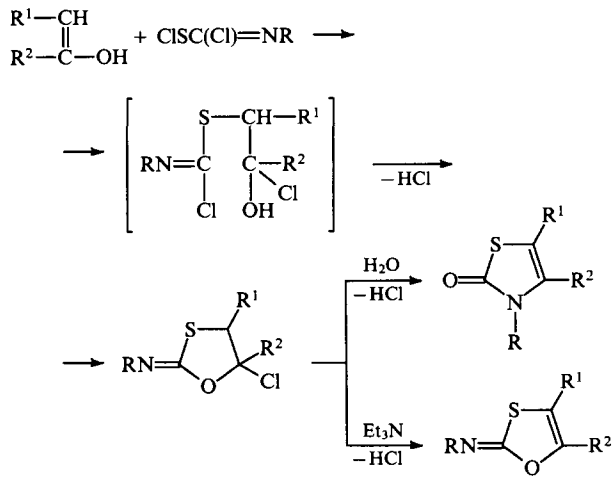
R = Me, Ph, R^1 = Alk.

In additions to vinyl ethers, the cyclisation of the adducts proceeds with elimination of an alkyl halide and hydrogen chloride and the formation of 2-oxo-1,3-thiazolines.[256]

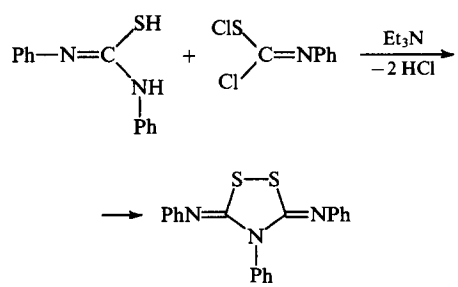


R = Me, Bu, Ph.

The enolic form of ketones react with chloro(imino)-methanesulfenyl chlorides to give adducts which are stabilised on intramolecular cyclisation.[256]



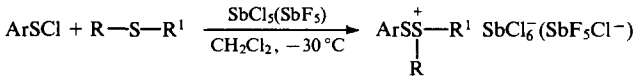
Diphenylthiourea reacts with chloro(*N*-phenylimino)-methanesulfenyl chloride in the thiolo-form with formation of 3,5-bis(phenylimino)-4-phenyl-1,2,4-dithiazolidine.[11]



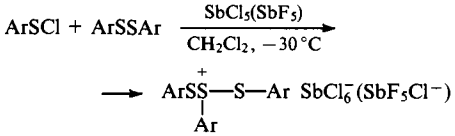
7. Syntheses of compounds of tetravalent and hexavalent sulfur

a. Syntheses of arylthiosulfonium and aryl(bisarylthio)sulfonium salts

Arylthiosulfonium and aryl(bisarylthio)sulfonium salts belong to a special type of derivatives of tetravalent sulfur, namely to the class of S-cationoid compounds with a positive charge on one of the sulfur atoms. These salts are formed relatively easily on interaction of sulfenyl chlorides with sulfides[257] and disulfides[258] in the presence of Lewis acids such as $SbCl_5$ or SbF_5.



Ar = Ph, 4-MeC_6H_4, 4-ClC_6H_4; R = R^1 = Me, Ph;

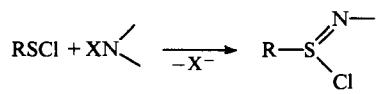


Ar = Ph, 4-MeC_6H_4, 4-ClC_6H_4.

Arylthiosulfonium and aryl(bisarylthio)sulfonium salts have found applications in organic synthesis as agents transferring the RS^+ groups in Ad_E reactions with alkenes.[259]

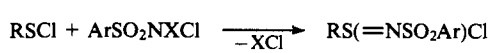
b. Syntheses of iminosulfinic acid chlorides.

The use of sulfenyl chlorides in the synthesis of iminosulfinic acid chlorides is based on their oxidative imination by *N*-halo-compounds, as a result of which the valence of the sulfur atom of the sulfenyl chloride increases by two units and combines with the imino-group.[186,260,261]



X = Cl, Br.

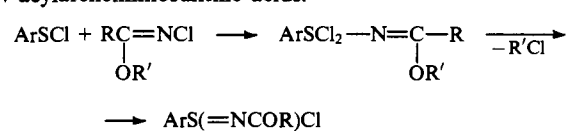
For example, it has been noted that arenesulfenyl chlorides react in anhydrous organic solvents with *N*-chloro- and *N,N*-dichloroamides of arenesulfonic acids with formation of the chlorides of *N*-arenesulfonylareneiminosulfinic acids.[260,261]



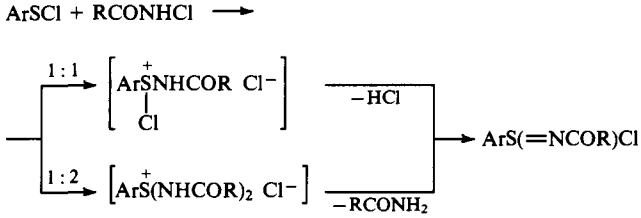
R = Ph, 4-MeC_6H_4, 4-$NO_2C_6H_4$, 4-ClC_6H_4, 2-$NO_2C_6H_4$.

Ar = Ph, 4-MeC_6H_4, 4-ClC_6H_4; X = Na, Cl, Me_3Si.

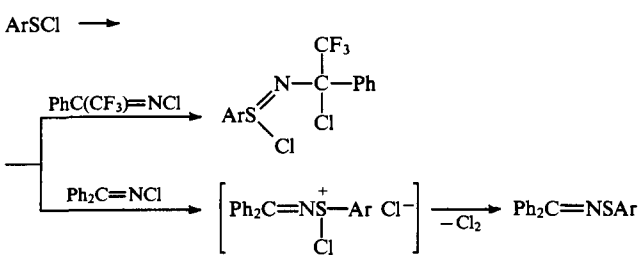
N,N-Dichlorourethanes and esters of *N*-chloroiminocarbonic acid,[260] *N*-chloro-*N*-trimethylsilyl-*tert*-butylamine,[262] the *N*-chloroamides of carboxylic acids,[263] and *N*-chloroketimines[264] are used as iminating agents in order to obtain the chlorides of *N*-substituted iminosulfinic acids containing other substituents at the nitrogen atom. The reactions of arenesulfenyl chlorides with *N*-chloroiminocarbonic acid esters proceed with formation of sulfuranes in the first stage. As a result of the elimination of an alkyl halide, the sulfuranes are converted into the chlorides of *N*-acylareneiminosulfinic acids.[265]



Depending on the reactant ratio, *N*-acylamino(aryl)chlorosulfonium chlorides or bis(*N*-acylamino)(aryl)sulfonium chlorides are intermediates in the reactions of arenesulfenyl chlorides with the *N*-chloroamides of carboxylic acid.[263]



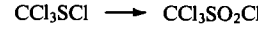
Arenesulfenyl chlorides do not react unambiguously with *N*-chloroketimines.[264] The formation of the corresponding acid chlorides has been observed in the reaction of arenesulfenyl chlorides with *N*-trifluoromethylphenylketimine, whereas the reaction with *N*-chlorodiphenylketimine leads to the corresponding sulfenamide.



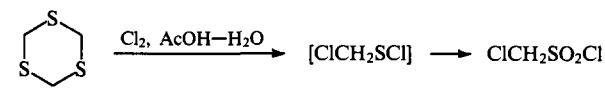
Arenesulfenyl chlorides do not react with *N*-chlorobis(trifluoromethyl) ketimine.[264]

c. Syntheses of sulfonic acid chlorides

Sulfenyl chlorides which are resistant to hydrolysis are relatively easily converted into sulfonic acid chlorides on treatment with oxidants, which is sometimes used in preparative organic chemistry.[13,33] For example, the oxidation of trichloromethanesulfenyl chlorides by various oxidants constitutes the basis of a preparative method of synthesis of trichloromethanesulfonic acid chloride.



Chlorine in an aqueous medium,[266] chlorine in acetic acid,[267] nitric acid,[268] and hydrogen peroxide[269] are used as oxidants. The same oxidants are employed in the synthesis of trifluoromethanesulfonic acid chloride[270] from trifluoromethanesulfenyl chloride. It has been noted[271] that the hydrolysis of trithiane in dilute acetic acid, which results in the formation of chloromethanesulfonic acid chloride, proceeds via an intermediate stage involving the formation of chloromethanesulfenyl chloride.



* * *

It is seen from the present review that the use of sulfenyl chlorides in fine organic synthesis, which has reached a large scale in recent years, is based on the characteristic features of their reactivity and in the first place on the high lability of the S–Cl bond, as a result of which sulfenyl chlorides are widely employed in reactions with diverse reagents in order to generate the S–C, S–N, S–O, S–S, S–P, S=O, S=N, etc. bonds. The ease of addition of sulfenyl chlorides to the C=C bond of unsaturated compounds with formation of β-chloroalkyl sulfides is likewise widely used in fine organic synthesis for the introduction of the β-arylthioalkyl groups into the molecules of various organic compounds. A feature of the reactivity of bifunctional sulfenyl chlorides which is of very great synthetic importance is their tendency to form heterocycles on interaction with various polyfunctional compounds, which has also been reflected in the present review.

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Inhomogeneity in the molecular structure of cellulose nitrates

V I Kovalenko

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Abstract. The results of studies on the molecular structures of cellulose nitrates and related saccharide nitrates are surveyed. The inhomogeneity of the structures of cellulose nitrates can be analysed on three hierarchical levels: in terms of the composition of the elementary units, in terms of the distribution of the elementary units along the chain, and in terms of their distribution in the bulk phase. The possibilities of the NMR and FT-IR spectroscopy for studies of these structural levels are discussed. A simple method has been developed for the estimation of the molecular-structural inhomogeneity of cellulose nitrates. It is shown that this inhomogeneity is determined by the inhomogeneity of the nitration process. A procedure is proposed for taking into account the diffusion of the nitrating agent in studies of the kinetics of the inhomogeneous reactions. The bibliography includes 121 references.

I. Introduction

Cellulose nitrates (CN) are polymers the production of which always took place long before studies of their structural characteristics. For this reason, the technology of the preparation of cellu-lose nitrates has been largely based on empirical rules and has been developed by the method of trial and error. Despite the large scale production of cellulose nitrates for gunpowders, rocket fuels, varnishes, dyes, biological membranes, ionising radiation detectors, etc., the characteristics of their molecular structure, as manifested in the properties of these polymers, have not so far been investigated: the structure–property correlations have not been found. There are comparatively few surveys of studies on the structure of cellulose nitrates.[1–14] However, recently studies on the detailed molecular structure of cellulose nitrates have received a fresh stimulus from the development of molecular spectroscopic methods yielding data with a high information content — high-resolution ^{13}C and ^{15}N NMR and FT-IR spectroscopy.

The present review is devoted mainly to studies on the molecular structure of cellulose nitrates and on their structural inhomogeneity.

V I Kovalenko Molecular Spectroscopy Laboratory, Kazan State Technological University, ul. Karla Marksa 68, 420015 Kazan, Russian Federation. Fax (7-843) 276 54 03.

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II. Molecular structure of cellulose nitrates

Cellulose nitrates constitute a family of incompletely substituted cellulose esters having the general formula $-[-C_6H_7O_2.(ONO_2)_x(OH)_{3-x}-]_n-$, where $0 < x \leqslant 3$. Cellulose nitrates with different values of x have different properties, the most important of which are solubility and plasticisability. The principal feature of cellulose nitrates is their heterounit structure. In the general case, cellulose nitrate chains include eight types of elementary unit: one unsubstituted glucopyranose ring; three monosubstituted (2-, 3-, and 6-monosubstituted) pyranose rings; three disubstituted (2,3-, 2,6-, and 3,6-disubstituted) pyranose rings; and one 2,3,6-trisubstituted pyranose ring (Fig. 1).

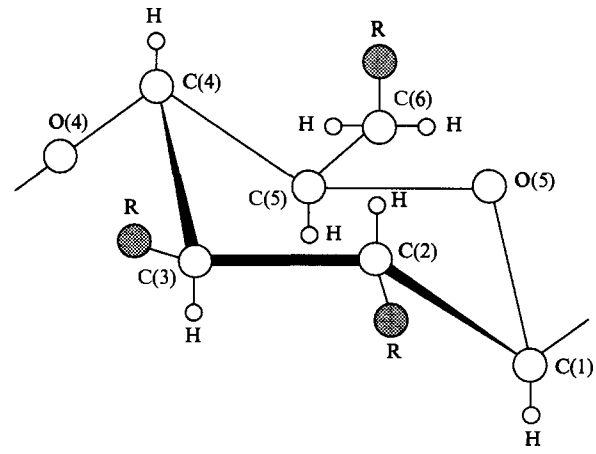


Figure 1. The numbering of the atoms in the elementary unit of cellulose nitrate. R = —OH or $-ONO_2$.

1. Conformation of the cellulose nitrate macromolecule

Like the majority of crystalline polymers, cellulose nitrates give rise to a diffraction pattern with a small number of reflections, from which it is difficult to obtain complete information about the conformation of the cellulose nitrate chains. The unit cell parameters of cellulose nitrates (with a nearly limiting degree of substitution) have been found.[1,15–17] The parameters of the orthorhombic unit cell found by different workers agreee fairly closely, which makes it possible to regard them as reliable (Table 1).

Table 1. The unit cell parameters of cellulose nitrate.

Degree of substitution	a/nm	b/nm	c(IP)/nm[a]	Ref.
2.8	0.90	1.39	2.56	1
2.8			2.57	15
2.8	0.855	1.230	2.54	16
2.9	0.90	1.224	2.54	17
2.9	0.90	1.46	2.54	17

[a] The parameter c corresponds to the identity period.

The identity period (IP) of 2.54 nm and the corresponding meridianal reflections on the diffraction patterns of cellulose trinitrates (CTN) indicate directly that the cellulose nitrate chains are packed in the form of a 5_2 helix (five elementary units for two turns of the helix). Cellulose has IP = 10.3 Å, which corresponds to a 2_1 helix (a planar zig-zag conformation with two units per identity period).[18]

Consequently the appearance of bulky nitrate substituents on passing from cellulose to CTN is accompanied by the uncoiling of the macromolecular helix (the twist angle of the helix varies from 180° for cellulose to 144° for cellulose nitrate). The question of the parallel or antiparallel arrangement of the chains in crystalline cellulose nitrates has so far remained open.[17] We are aware of only one study[19] in which the most favourable conformations of isolated chains of CTN and cellulose di- and mono-nitrates were calculated by the method of molecular mechanics. Structural models, consistent with experimental data and corresponding to the deepest minima on the potential energy surface for the macromolecules, were constructed. A chain conformation close to 2_1 obtains for cellulose mononitrates, which probably reflects the smaller 'saturation' of the polymer skeleton by nitrate groups compared with CTN. Conformational states of the chains ranging from the 2_1 helix to the 5_2 helix, depending on the degree of substitution of the cellulose nitrates, are probably possible for cellulose nitrates with degrees of substitution less than three.

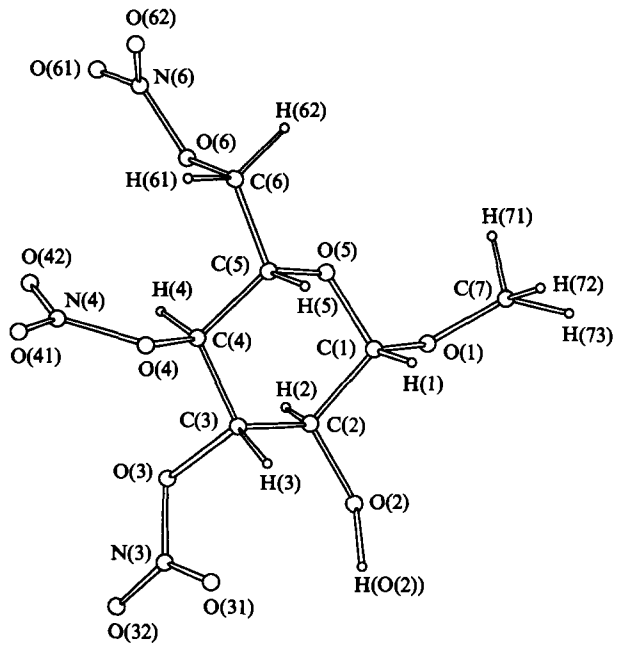


Figure 2. The geometry of the molecule of the 3,4,6-trinitrate of methyl β-D-glucopyranoside.[26]

2. Conformation of the glucopyranose ring

Unfortunately there are no direct experimental data concerning the conformation of the pyranose ring in cellulose nitrates. It has been demonstrated in a review[18] that the glucopyranose ring in cellulose and model saccharides[20] has the $^4C_1$ (chair) conformation with an equatorial disposition of the substituents. The ring conformations in the cellulose nitrate chain have been calculated by the method of molecular mechanics and it has been shown that the $^4C_1$ chair conformation is the most favourable.[11,21,22] A series of studies on the X-ray diffraction of model glucoside and cellobioside nitrates have been published recently.[23–29] They were concerned with the 2,3-dinitrates of methyl 4,6-*O*-ethylidene-β-D-glucopyranoside (2,3-DNMEG) (the α- and β-anomers), the 3,6-dinitrate of methyl 4-*O*-methyl-β-D-glucopyranoside (3,6-DNMMG), the 2,4,6- and 3,4,6-trinitrates of methyl β-D-glucopyranoside (2,4,6- and 3,4,6-TNMG) (Fig. 2), the 2,3,4,6-tetranitrate of methyl β-D-glucopyranoside (2,3,4,6-TNMG) (Fig. 3), and the 6,6′-dinitrate and the 2,3,6,2′,3′,4′,6′-heptanitrate of methyl β-D-cellobioside (6,6′-DNMC and 2,3,6,2′,3′,4′,6′-HNMC) (Figs 4 and 5).

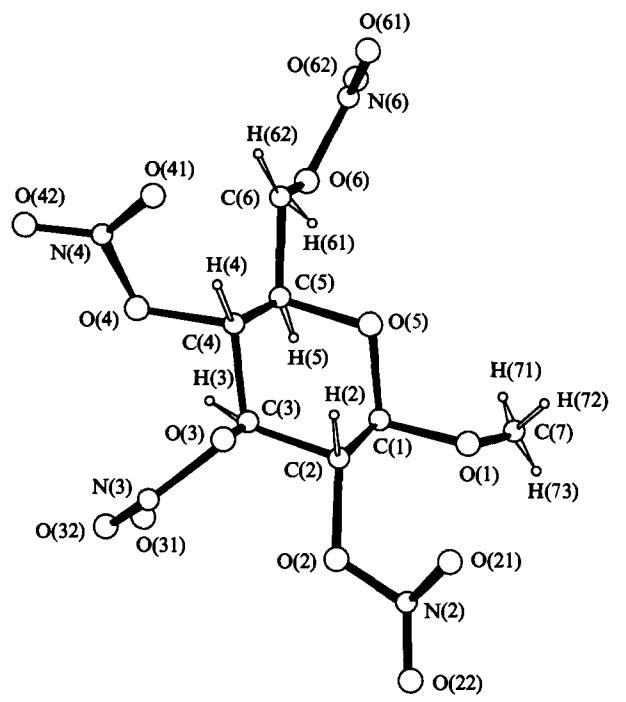


Figure 3. The geometry of the molecule of the 2,3,4,6-tetranitrate of methyl β-D-glucopyranoside.[27]

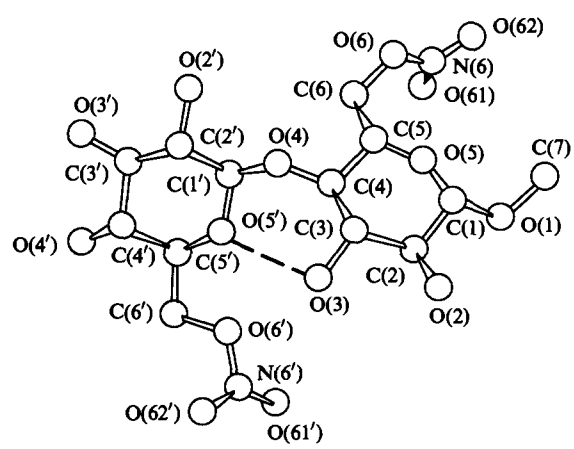


Figure 4. The geometry of the molecule of the 6,6′-dinitrate of methyl β-D-cellobioside.[28]

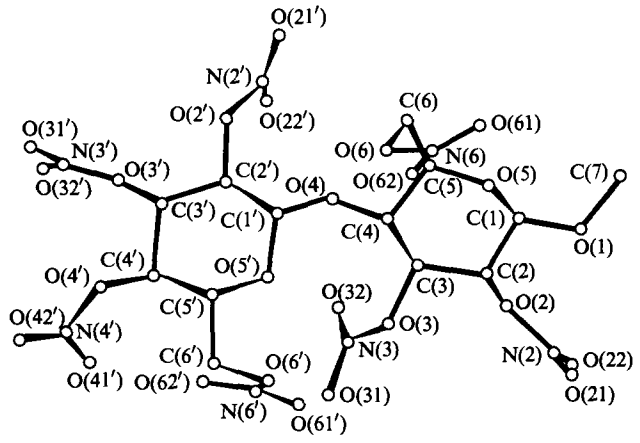


Figure 5. The geometry of the molecule of the 2,3,6,2',3',4',6'-heptanitrate of methyl β-D-cellobioside.[29]

Without exception, they all have the $^4C_1$ conformation of the glucopyranose ring regardless of the number of substituting nitrate groups or the presence of the second ring in 2,3-DNMEG.

Thus it is evident that the conformation of the glucopyranose ring is fairly stable. One must recall that, in an attempt to describe the conformation of the CTN chain, Watanabe and coworkers[15,30] used the 'half-boat' conformation, assuming erroneously that the conformation of the nitrate groups along the cellulose nitrate chain is more 'rigid' than the conformation of the pyranose rings. The 'half-boat' conformation has also been used for the description of the model of the folded chain of cellulose II.[31] However, later studies demonstrated that this model conflicts with the concept underlying the biosynthesis of cellulose.[9]

3. Conformations of the nitrate groups

Calculations for cellulose and cellobiose nitrates[32] as well as for fragments of the CTN chains,[11,21,22] carried out by methods of molecular mechanics, have shown that a large number of stable conformers are possible for the nitrate group in the C(6) position†. This is evidently determined by the presence of two conformational degrees of freedom — the internal rotations relative to the C(5)–C(6) and C(6)–O(6) single bonds. X-Ray diffraction studies on model saccharide nitrates confirm the results of the calculations: different C(4)C(5)C(6)O(6) and C(5)C(6)O(6)N(6) torsional angles for the given fragment are observed in the crystal (Table 2).

The nitrate groups in all the compounds investigated are planar. The internal rotation of the nitrate groups in cellulose nitrates in the 2- and 3-positions takes place relative to the C(2)–O(2) and C(3)–O(3) bonds [C(1)C(2)O(2)N(2) and C(2)C(3)O(3)N(3) torsional angles]. However, their close proximity limits their mutual orientation. These groups have different locations relative to the pyranose ring. The results of calculations have shown that both groups 'tend' to achieve a mutually perpendicular disposition.[32] According to X-ray diffraction data, the angles between the planes of the nitrate groups, for example in 2,3-DNMEG,[23] are 82° for the α-anomer and 76° for the β-anomer, whereas in 2,3,4,6-TNMG the angle is 75°.[27] The $-CONO_2$ groups are significantly nonplanar. The maximum displacement of the carbon atom from the plane of the nitrate group reaches 23° for 2,3-DNMEG and 21° for 2,3,6,2',3',4',6'-HNMC.

In conclusion of this section, we emphasise that its main aim was not so much the discussion of controversial problems concerning the conformational state of cellulose nitrates as the description of the most important and reliable parameters necessary for the consideration of the molecular-structural inhomogeneity of cellulose nitrates. Readers who are interested may obtain the necessary details from the literature sources quoted.

† The term 'conformer' is understood as the mutual disposition of atoms in the molecule or its fragment which corresponds to global or local energy minima, whilst the term 'conformation' implies any kind of their mutual disposition.[81]

Table 2. The torsional angles (deg) in the molecules of the monosaccharide and disaccharide nitrate single crystals.

Angle	2,3-DNMEG[a]	3,6-DNMMG	2,4,6-TNMG	3,4,6-TNMG	2,3,4,6-TNMG	6,6'-DNMC[b]	2,3,6,2',3',4',6'-HNMC[b]
C(1)C(2)O(2)N(2)	−80.5 / 88.4	–	122.3	–	97	–	95.3 / 95.4
C(2)O(2)N(2)O(21)	19.5 / −156.4	–	−177.3	–	−163.5	–	1.8 / −158.5
C(2)C(3)O(3)N(3)	104.7 / 99.0	−117.4	–	−97.5	−120	–	−130.9 / −146.8
C(3)O(3)N(3)O(31)	174.4 / 172.8	−0.5	–	−17.2	−6.1	–	177.5 / 178.5
C(3)C(4)O(4)N(4)	–	–	134.9	127.9	not quoted	–	– / 136.8
C(4)O(4)N(4)O(41)	–	–	−170.1	−175.8	−5.5	–	– / 5.8
C(4)C(5)C(6)O(6)	−57.6 / −56.8	53.3	59.2	60.4	not quoted	−176.7 / −178.4	42.5 / −179.1
C(5)C(6)O(6)N(6)	–	−178.0	−162.7	−169.1	not quoted	−95.7 / −23.0	101.4 / 93.7
C(6)O(6)N(6)O(61)	–	−2.0	179.8	177.1	−169.5	−171.5 / −174.5	−2.7 / −178.6

[a] Numerator — α-anomer, denominator — β-anomer.
[b] Numerator — first pyranose ring, denominator — second pyranose ring.

III. High-resolution NMR studies on the molecular structure of cellulose nitrates

The development of the experimental NMR technique has significantly expanded the scope of studies on the detailed molecular structure of cellulose nitrates. Interesting results have been obtained with the aid of high-resolution ^{13}C NMR spectroscopy in solution.[33-44] At the beginning of the 1980s, two publications appeared independently on the analysis of the NMR spectra of cellulose nitrates and their analogues,[33,34] in which the ^{13}C NMR spectra of cellulose nitrates were interpreted for the first time. Wu[33] showed that, with the aid of NMR, it is possible not only to distinguish the signals of the carbon atoms sensitive to the location of the nitrate groups but also to determine the ratio of the types to units with different numbers of nitrate groups. A rigorous interpretation of the NMR spectra of cellulose nitrates has now been achieved based on numerous studies of the NMR spectra of model nitrates[34,39,43] and specially synthesised cellulose nitrates,[33,35,36,41] as well as on calculations of the chemical shifts of the nuclei from their increments[41,44] (Table 3).

Cellobiose octanitrate (CON) is the closest structural analogue of CTN. In CON, it is possible to differentiate a molecular fragment (Fig. 6) which gives rise to NMR signals least perturbed by the terminal sections of the molecules which are not similar to those in the CTN. Analysis of the chemical shifts of the nuclei (Table 3) showed that the positions of these particular signals in the spectra are closest to the positions of the CTN signals. It has been suggested that the neighbouring elementary units exert a significant influence on the chemical shifts of the nuclei of the glucoside ring.[34,36] Together with this, it is also necessary to take into account the conformational state of the chains and substituents in cellulose nitrates. The 10% solutions of cellulose nitrates employed in the NMR experiments are very different from the equilibrium solutions, in which there is no interchain interaction and homogeneous conformations of the macromolecules are achieved.[9] In this case, the differences between the chemical shifts of CON and CTN under identical experimental conditions may be accounted for by the following factors: (1) the inadequacy of the model (Fig. 6), (2) the more extensive conformational set of the CTN chains, (3) the influence of neighbouring units on one another, and (4) the heterounit structure in the case of cellulose nitrates with a degree of substitution less than 3. The differences between the positions of the signals of the tetranitrate of methyl glucoside, cellobiose octanitrate, and CTN hardly exceed 1 ppm (Table 3). This is evidence indicating that the mutual influence of the units in cellulose nitrates is insignificant (for example, a change of solvent leads to similar differences between the chemical shifts and one may expect that different solvents may ultimately act specifically on the conformations of the cellulose nitrate chains). Consequently the parameters which influence significantly the magnitudes of the chemical shifts of cellulose nitrates are the heterounit structure of the polymer and the differences between

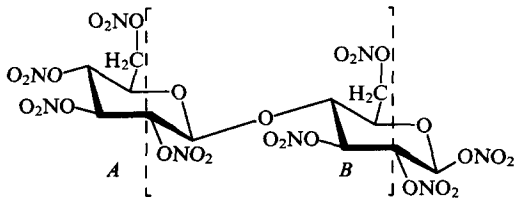


Figure 6. The structural formula of cellobiose octanitrate. The molecular fragment modelling CTN is shown in square brackets.

the conformational states of the cellulose nitrate chains. An important conclusion which follows from the analysis of the data in Table 3 is that the NMR spectrum actually corresponds to a single elementary unit of CTN; the influence of the neighbouring units (at least for the modern apparatus with a resolution corresponding to 100 MHz) is negligible.

The ^{13}C NMR spectrum of a cellulose nitrate specimen with a degree of substitution of 1.2 in solution in DMSO shows clearly (Fig. 7) that the main group of lines is concentrated in the region of 70-90 ppm where the signals of different nuclei overlap. The most remote and nonoverlapping region, 95-105 ppm, belongs to the signals from the C(1) atoms. By analysing carefully the chemical shifts for selectively substituted nitrates of methyl glucosides and cellulose nitrates with different degrees of substitution (Table 4), it is possible to separate reliably the signals obtained from different elementary units of cellulose nitrates.

Table 4. The chemical shifts (ppm) for the resonances of the C(1) carbon atom in the nitrates of methyl β-D-glucosides (NMG) and in cellulose nitrate.

Positions of nitrate groups	NMG[39]	CN[41]	CN[44]
2	101.6	99.7	(99.0)
2,3	101.6	(100.9)	(98.6)
2,4	101.4	–	–
2,6	101.4	98.8	(97.3)
2,3,6	101.6	100.0	(98.3)
2,4,6	101.35	–	–
2,3,4,6	101.4	–	–
Unsubstituted unit	104.8	104.4	(103.1)
6	104.85	103.5	(102.8)
3	104.3	(106.1)	(102.4)
3,6	104.95	105.2	(103.0)
3,4,6	104.45		

Note. The chemical shifts calculated from the increments are given in brackets.

Table 3. The chemical shifts (δ/ppm) of the 2,3,4,6-tetranitrate of methyl β-D-glucoside, β-cellobiose octanitrate, and cellulose trinitrates.

Atom	δ(2,3,4,6-TNMG) according to data in Refs		δ(CON-*A*) according to data in Refs		δ(CON-*B*) according to data in Refs		δ(CTN) according to data in Refs		
	39	43	34	43	34	43	34	43	41
C(1)	101.4	101.35	100.1	100.26	96.1	96.64	100.1	100.14	100.0
C(2)	79.1	79.06	78.5	78.58	74.8	74.73	78.3	79.28	80.6
C(3)	78.8	79.06	78.6	78.58	79.0	78.96	79.4	78.06	79.5
C(4)	76.9	76.88	76.0	75.94	76.75	77.02	76.8	77.02	77.2
C(5)	70.35	70.30	69.8	69.66	72.6	72.50	71.7	71.37	71.9
C(6)	71.1	71.12	70.5	70.65	70.1	70.23	70.6	70.72	71.9

Note. Here and henceforth the chemical shifts corresponding to those of CTN are underlined (Fig. 6). The last column presents data for a solution of CTN in dimethyl sulfoxide, while the remaining columns present data for solutions in acetone-d_6.

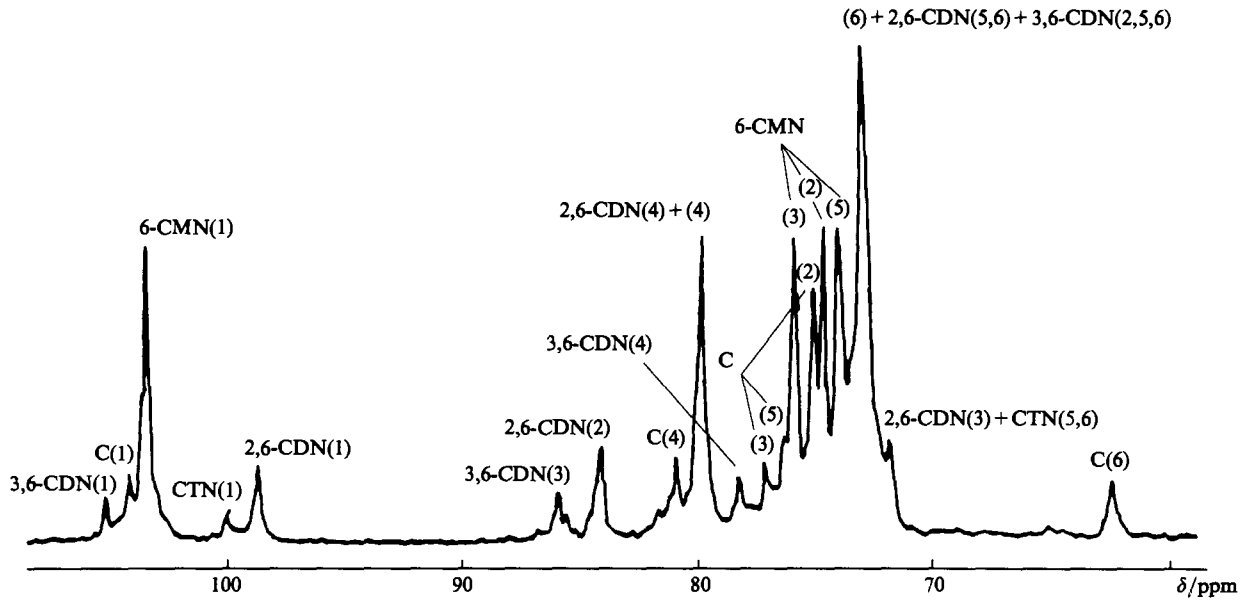


Figure 7. The ^{13}C NMR spectrum of a cellulose nitrate specimen with a degree of substitution of 1.2 in solution in DMSO showing the assignments of the signals to the corresponding units (the number of the ring carbon atom is indicated in brackets).[41]

The presence of the nitrate group in the 2-position is characterised by the presence of C(1) signals in the region of 100 ppm for any types of substitution in the remaining positions (see Table 4), whilst its absence leads to the displacement of the signals of the C(1) atom to the region of 104 ppm. Apparently this is a convenient analytical feature for the determination of the type of substitution. Analysis of the chemical shifts of the C(1) atom for model nitrates of methyl β-D-glucosides has confirmed the above conclusion that the conformational state of the cellulose nitrate chains influences significantly the positions of the signals in the NMR spectrum. Evidently the conformer most stable for the given solvent is formed in the model nitrates, this being indicated by the small differences between the maximum and minimum chemical shifts (Table 4). They also indicate that the C(1) nucleus is less 'sensitive' to the type of substitution in a small molecule than in a chain molecule and this is also evidence for the greater conformational freedom of the cellulose nitrate macromolecules. In order to detect more detailed effects (such as the influence of neighbours), it is necessary to increase significantly the resolution afforded by the spectrometer. For example, comparison of the spectra of the same cellulose nitrate specimen obtained on instruments with different working frequencies shows a marked increase in the complexity of the spectrum, which undoubtedly reflects the influence of secondary effects. However, the interpretation of such spectra still remains difficult.

Analysis of the NMR spectra demonstrated the similarity of the Overhauser effects and the spin–lattice relaxation times for all the carbon nuclei of the glucopyranose ring of cellulose nitrates, which had been indicated earlier by Wu[33] and Clark.[35] This agrees well with the fact that the charges on different oxygen atoms in glucose and its nitrates, obtained from quantum-chemical calculations, are similar.[46] Taking this into account, it is possible to carry out quantitative measurements of the partial degrees of substitution in the 2-, 3-, and 6-positions and also to find the fractions of units with different types of substitution in cellulose nitrates. A series of publications have appeared[33, 35–37, 40, 44, 47–54] whose authors measured the contents of the principal types of units in cellulose nitrates. It is noteworthy that the contents of 2-mono-, 3-mono-, and 2,3-di-nitrate units in cellulose nitrates are very low and for this reason they are usually not measured. (An exception is a study[44] where it was shown that the fractions of the above units are 0.039, 0.021, and 0.047 respectively.)

Progress in the study of the detailed structure of cellulose nitrates was achieved after high-resolution ^{13}C NMR spectra had been obtained in the solid state.[7, 8, 55–59] New results were obtained with the aid of this method, from which it was possible to trace the characteristic features of the formation of the cellulose nitrate matrix during the nitration of cellulose and, at the same time, to assess the conformational rearrangement of the macromolecules. A characteristic feature is that the transition of solutions to the solid phase of cellulose nitrates leads to appreciable downfield shifts and a significant broadening of the lines in the ^{13}C NMR spectra.[58] Thus the following values of δ were obtained for CTN:

C(1)	C(2)	C(3)	C(4)	C(5)	C(6)
101.8	72.1	72.1	72.1	72.0	72.0

The main cause of the change in δ (cf. Table 3) may be, first, the loss of mobility by the chains and, second, the differences between the conformational states of the cellulose nitrate macromolecules in solution and in the bulk phase. The latter are characterised by a much more diverse set of conformations of the chains and substituents. For the C(1) nucleus in solutions of cellulose nitrates (Table 4) it is possible to differentiate two groups of signals for the cellulose nitrate unsubstituted, or substituted, in the 2-position: (1) from the unsubstituted unit and the 6-mono-, 3-mono-, and 3,6-di-substituted units; (2) from the 2-mono-, 2,3-di-, 2,6-di-, and 2,3,6-tri-substituted units. This subdivision can be readily detected also in the NMR spectra of the solid[58, 59] in the form of broad maxima in the regions of 105 and 100 ppm respectively. Evidently, with increase in the degree of substitution of the cellulose nitrate, the increase in the maximum at 100 ppm and the decrease in that at 105 ppm are associated with the increased content of the trinitrate units and the decrease in the fraction of the mono- and di-substituted and unsubstituted units. It is therefore wrong to attribute the changes in the intensities of these signals solely to the conformational rearrangement of the cellulose nitrate with increase in the degree of substitution during the course of nitration.[59]

We are aware of only two papers devoted to the study of high-resolution ^{15}N NMR spectra in solution.[42, 43] The principal signals of the nitrogen nuclei of the nitrate groups, occupying the 2-, 3-, and 6-positions, were assigned in both studies (Table 5).

Table 5. Positions of the signals (ppm) in the high-resolution ^{15}N NMR spectra of solutions of cellulose nitrates and model nitrates.

Position of the nitrate group	2,3,4,6-TNMG[43]	CON[43]		CN[43]	CN[42]
		A	*B*		
2	335.2	332.8	333.7[a]	335.5[b]	−1.0[c]
3	335.3	335.2	334.5	336.9	−2.4
6	340.6	339.6	340.1	341.1	3.2

[a] See Fig. 9.
[b] Degree of substitution 2.72, solution in acetone-d_6, external standard — $^{15}NH_4Cl$ + HCl. [c] Degree of substitution 2.35, solution in dimethyl sulfoxide, external standard — $H^{15}NO_3$.

As can be seen from the data presented, there are significant discrepancies in the interpretation of the signals from the N(2) and N(3) atoms. The reasons for these are so far obscure, but the authors[42] confirm the validity of their interpretation by showing that the relative intensities of the signals agree well with the partial degrees of substitution determined from the ^{13}C spectra. Nevertheless, a detailed analysis of the ^{15}N NMR spectra is lacking to date.

Proton magnetic resonance of cellulose nitrates yields much less information than ^{13}C NMR.[33,43] Systematic analysis of the ^{1}H, ^{13}C, and ^{15}N NMR spectra combined with the analysis of the NMR spectra of selectively substituted model saccharide nitrates will probably assist progress in studies on the detailed molecular structure of cellulose nitrates.

IV. Infrared spectroscopic study of the structure of cellulose nitrates

The vibrational spectroscopy of cellulose nitrates is almost fully represented by IR spectroscopic studies. The measurement of the Raman spectra of cellulose nitrates still constitutes a difficult experimental task.

The first IR spectrum of cellulose nitrate was recorded about 25 years ago.[5,15] Since then, there have been numerous publications devoted to the experimental study of the molecular structure of cellulose nitrates and their analogues by IR spectroscopy[6,7,11,14,44,60–77] and also to theoretical calculations of the vibrational spectra of the latter.[66,78,79] The low-frequency IR spectra of cellulose nitrates[64,68,70] and the nitrates of low-molecular-mass hydrocarbons[73] have been investigated particularly vigorously at the present time (undoubtedly as a result of the appearance of commercial FT-IR spectrometers). A detailed analysis of these spectra and also of the low-frequency spectroscopic characteristics of structural modifications of cellulose has been presented in another review[14] and will not therefore be considered here‡.

The IR spectroscopic data obtained by Watanabe et al.[15] and Panov and Zhbankov[5] were subsequently refined and supplemented by Kovalenko et al.[76] on the basis of the analysis of the IR spectra of cellulose nitrate enriched in ^{15}N and also of the polarised IR measurements for oriented cellulose nitrate fibres.

In the study of the region 2800–2950 cm^{-1} corresponding to absorption due to the $\nu(CH)$ and $\nu(CH_2)$ stretching vibrations of cellulose nitrates enriched in ^{15}N, it was observed for the first time that there is a Fermi resonance of the $\nu_a(CH_2)$ stretching vibration and of the $\nu_a(NO_2)$ + $\nu_s(NO_2)$ sum frequency. The observed redistribution of the intensities and the frequency shifts due to the Fermi resonance explain satisfactorily the dependence of the intensities of the absorption bands due to the CH and CH_2 groups in this spectral range on the degree of substitution of cellulose nitrate which had been discovered earlier.[11,60,71]

Analysis of the IR spectra of highly dilute solutions of cellulose nitrates in tetrahydrofuran (THF) in the range 1600–1700 cm^{-1}, where the $\nu_a(NO_2)$ stretching vibration of the nitrate groups is observed, indicates a doublet structure of the band[44,63,76] with 1662 and 1646 cm^{-1} components (Fig. 8); the first was assigned to the absorption by the nitrate groups occupying the 2- and/or 3-positions and the second was assigned to the absorption by the nitrate groups in the 6-position in the pyranose rings of cellulose nitrate.[44,76] The second derivatives of the spectrum in this range have been obtained[44] and a third high-frequency component of the band was detected. According to the authors, it is associated with the steric hindrance generated by the pair of neighbouring nitrate groups in the 2- and 3-positions in the pyranose ring of the cellulose nitrate. However, it follows from X-ray diffraction and calculated data[21–23,27,29,32] that such hindrance does not occur even in crystals of the model nitrates and it is therefore difficult to expect their appearance in dilute cellulose nitrate solutions. In their next study, the same workers[80] present the spectrum of the same cellulose nitrate specimen but this time without the third component. We emphasise that the doublet structure is readily manifested on an FT-IR spectrometer, with a resolution of 1 cm^{-1}, whereas on the usual dispersion instruments it had been previously impossible to observe it.[11,61]

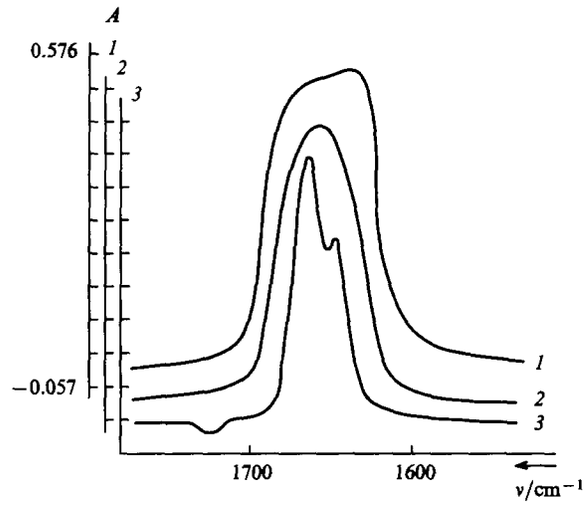


Figure 8. IR spectra of cellulose nitrate with a degree of substitution of 2.8. Specimen: (*1*) fibre; (*2*) film cast from an acetone solution; (*3*) dilute solution in THF.

A complex, diffuse contour of the $\nu_a(NO_2)$ band, the width of which reaches 90 cm^{-1}, can be observed in the IR spectra of fibrous and powdered cellulose nitrates (Fig. 8).[76,77] This width is due to the large set of conformational states of the chains and substituents. It has been suggested[11] that the extensive set of conformations can be accounted for by the inhomogeneity of the nitration of cellulose, where there is insufficient time for the chains to relax after the removal of the liquid phase and the conformations of the chains and the 'appendages' in cellulose nitrate are frozen. Comparison of the IR spectroscopic[77] and X-ray diffraction[82] data for the plasticisation of cellulose nitrates shows that the crystallinity of the cellulose nitrates does not contribute to the widening of the $\nu_a(NO_2)$ band; the narrowing of the band occurs before the plasticiser reaches the crystalline regions of the cellulose nitrate (Fig. 9). Consequently the conformational rearrangement of the chains accompanying their relaxation when the plasticiser is introduced leads to a decrease in

‡ We may note that the 516 and 490 cm^{-1} bands, which have a high dichroic ratio,[76] are due to the vibrations of the pyranose skeleton of the cellulose nitrate chain and are not associated with the vibrations of the trinitrate units as suggested in our earlier communication.[64]

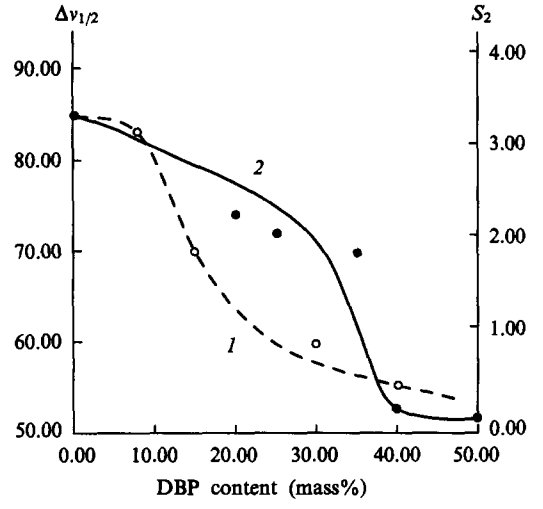


Figure 9. Dependence of the $\nu_a(NO_2)$ band width (curve *1*) in the IR spectra and of the crystallinity of cellulose nitrate S_2 (curve *2*) on the dibutyl phthalate content in the composition with cellulose nitrates.

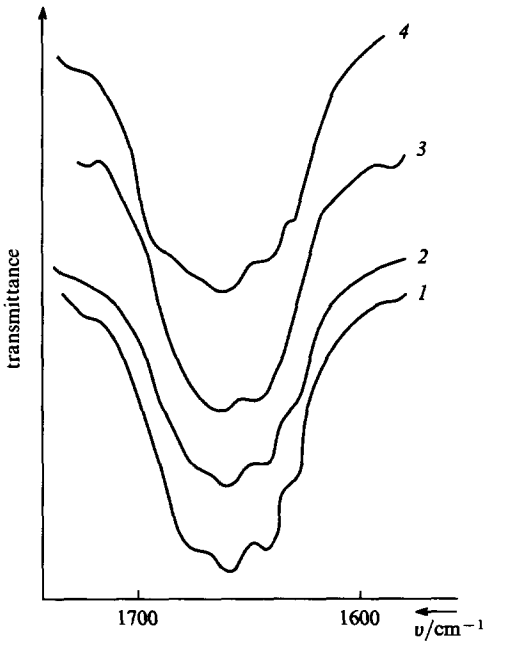


Figure 10. IR spectra of amorphous 2,3-DNMG (curve *1*), 2,3-DNMMG (curve *2*), 2,3,6-TNMMG (curve *3*), and 2,3,4,6-TNMG (curve *4*).

the diversity of the conformations of the nitrate groups and hence to a narrowing of the $\nu_a(NO_2)$ as well as the $\nu_s(NO_2)$ bands.[77]

Studies of the IR spectra of crystalline low-molecular-mass carbohydrate nitrates have been resorted to in the analysis of the complex contour of the $\nu_a(NO_2)$ band in the spectra of cellulose nitrates.[65-67,74] Unfortunately, in this case the transfer of the spectroscopic information obtained, which is itself extremely valuable, to cellulose nitrates is not always justified. Both the static field of the crystal and the Davydov (resonance) splitting are known to exert a significant influence on the position of the absorption band in the IR spectra of organic crystals. In all the crystalline nitrates of glucopyranosides investigated,[23-27] the primitive cell (which in this case is identical with the crystallographic cell) contains four molecules, and one must therefore expect four components due to the splitting of the band in the IR spectrum. Under these conditions, for example in the case of the 2,3,4,6-TNMG crystal, each molecule contains four nonequivalent nitrate groups: the primitive cell, which is in fact reflected in the IR spectrum, includes 16 spectroscopically nonequivalent nitrate groups. The contour of the $\nu_a(NO_2)$ band proves to be complex.[66,74] Effects characteristic of molecular crystals are virtually absent from cellulose nitrates as a consequence of the low crystallinity and defectiveness (owing to the heterounit structure) in the crystal packing of cellulose nitrates.[85] Incidentally, the picture is significantly different in the spectra of amorphous low-molecular-mass glucoside nitrates (Fig. 10): the triplet, doublet, and single $\nu_a(NO_2)$ bands observed in the spectra of 2,3,4,6-TNMG, 2,3-DNMMG, and 2,3-DNMG crystals are converted into bands which are now determined solely by the positions of the nitrate groups in the ring and by the conformational equilibrium in the molecules. For the same reason, it is necessary to treat with caution the application to cellulose nitrates data obtained for the $\nu_s(NO_2)$ band in the spectra of crystals of low-molecular-mass carbohydrate nitrates. In the cellulose nitrate spectrum, this band, like the $\nu_a(NO_2)$ band, is 'sensitive' to conformational rearrangements.[77]

The band due to the antisymmetric stretching vibrations of the nitrate groups in the cellulose nitrate spectra proved useful in determining the compositions of the elementary units[72] (in addition to ^{13}C NMR data): by measuring the ratio A_{1662}/A_{1648} of the optical densities of the components in the IR spectra of dilute cellulose nitrate solutions in THF, it is possible to estimate the ratio of different kinds of substituted cellulose nitrate units from the formula

$$\frac{A_{1662}}{A_{1648}} = \frac{[C_2] + [C_3] + 2\,[C_{23}] + [C_{26}] + [C_{36}] + 2\,[C_{236}]}{[C_6] + [C_{26}] + [C_{36}] + [C_{236}]}, \quad (1)$$

where $[C_{ijk}]$ is the fraction of units with a given type of substitution.

The ν(OH) stretching vibration bands are observed in the form of a broad band having a complex contour in the range 3300–3600 cm^{-1} in the IR spectra of cellulose nitrates with a degree of substitution less than three (Fig. 11). They are due to the hydroxy-groups of cellulose nitrate involved in the formation of hydrogen bonds. The most probable proton acceptors are the nitrate groups, the OH groups themselves, and the O(5) oxygen atoms of the pyranose rings. It has been shown[5-7,11,60-62] that the ~3570 cm^{-1} maximum is due to the hydroxy-groups involved in a weak hydrogen bond with the nitrate groups. At the same time, an absorption region with a maximum at 3430 cm^{-1} may be noted in the cellulose nitrate spectra (Fig. 11). It characterises the OH...OH type of intermolecular hydrogen bond and the O(3)H...O(5) intramolecular hydrogen bond in neighbouring glucopyranose rings.[86,87] Calculations by the method of molecular mechanics showed[19] that a hydrogen bond of the latter type occurs in cellulose mono- and di-nitrates and that the energies of the hydrogen bonds of both types

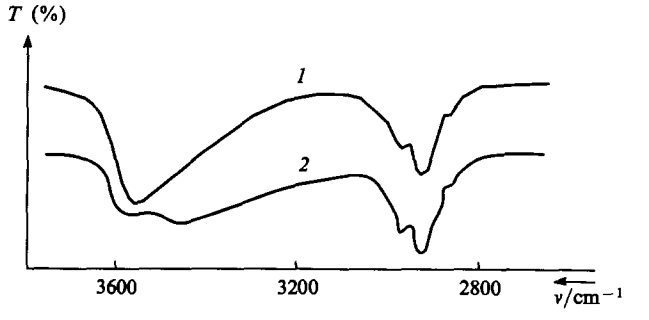


Figure 11. IR spectra of cellulose nitrates with a degree of substitution of 2.0 obtained by nitration in $HNO_3 + CH_2Cl_2$ (curve *1*) and $HNO_3 + H_2SO_4 + H_2O$ (curve *2*).

are similar§. As will be shown below, the ratio of the intensities of the ν(OH) bands at 3570 and 3430 cm^{-1} may be used to estimate the inhomogeneity in the mass distribution of the elementary units of cellulose nitrates.

V. Molecular spectroscopic study of the molecular-structural inhomogeneity of cellulose nitrates

The inhomogeneity in molecular-structure of cellulose nitrates with a degree of substitution less than three is associated with their heterounit structure and is determined by the inhomogeneity of the nitration process, where the final composition of the products depends significantly on the diffusional characteristics of the reaction system. In most cases, the initial cellulose and the final product (cellulose nitrate) are insoluble in the liquid reaction mass, and the morphological and fibrous structures of the initial cellulose are retained after nitration. By estimating the inhomogeneity of the cellulose nitrate with the given degree of substitution, it is possible to find a multiplicity of combinations of heterotypical units, which undoubtedly influence the properties of the cellulose nitrates. However, it has not previously been possible to estimate quantitatively the inhomogeneity of the cellulose nitrates. The methods based on the chemical or enzymic hydrolysis, which have been used successfully to determine the compositions of the elementary units of cellulose ethers, for example by Spurlin[88] and Reuben,[89] proved unsuitable for cellulose nitrates, since the elimination of the nitrate groups from the latter takes place significantly more readily than the dissociation of the glycosidic bonds.[90,91] For this reason, the determination of the composition of the elementary units and of the molecular-structural inhomogeneity of cellulose nitrates became possible only recently by virtue of the advances made in the study of the detailed molecular structures of cellulose nitrates by the high-resolution ^{13}C NMR and FT-IR spectroscopic methods.

1. Terminology

Since there is some terminological confusion in the literature on the molecular structure of cellulose esters, and the number of studies devoted to the inhomogeneity of such esters has been growing continuously, it has become necessary to define the terms used in the analysis of the molecular structure of cellulose esters — in this instance cellulose nitrates.

The degree of substitution γ is defined as the average number of substituting groups per glucopyranose ring in the cellulose nitrate macromolecule. The partial degree of substitution at the given carbon atom γ_i is the average number of substituting groups occupying the given position C_i. Clearly for cellulose nitrates we have

$$\gamma = \gamma_2 + \gamma_3 + \gamma_6.$$

For example, in the fully substituted CTN with a degree of substitution $\gamma = 3$, we have

$$\gamma_2 = \gamma_3 = \gamma_6 = 1.$$

The composition of the elementary units is expressed in fractions of unity and is defined by the relations[88]

$$s_0 + s_2 + s_3 + s_6 + s_{23} + s_{26} + s_{36} + s_{236} = 1,$$

where s_{ijk} is the fraction of units with the given type of substitution, and

$$c_0 + c_1 + c_2 + c_3 = 1,$$

where c_i are the fractions of unsubstituted and mono-, di-, and trisubstituted cellulose nitrate units. Evidently $c_0 = s_0$ and

$$c_1 = s_2 + s_3 + s_6,$$

$$c_2 = s_{23} + s_{26} + s_{36},$$

$$c_3 = s_{236}.$$

Here one may speak of six hypothetical cellulose nitrate homopolymers (cellulose 2-, 3-, and 6-mononitrates and 2,3-, 2,6-, and 3,6-dinitrates). The seventh homopolymer (CTN) does actually exist.

In the general case, the cellulose nitrate macromolecule represents an assembly of elementary units of eight types and an analogy with copolymers is appropriate here: statistical, block, etc.

2. Distribution of the units along the chain

The distribution of heterotypical units along the chain is also referred to as the microstructure or configuration of the chain.[92] By analogy with biopolymers, one may assume that each heterotypical cellulose nitrate unit represents a letter of the alphabet, so that the cellulose nitrate chain constitutes an eight letter 'word'. Unfortunately the current level of experimental technique does not permit the decoding of these cellulose nitrate 'words'. However, it is possible, in principle, to solve the problem of the frequency of the appearance of particular combinations of 'letters' for different methods of synthesis of cellulose nitrates. This problem has not yet been solved although the first attempts have already been made.[36,53]

3. Distribution of units in the bulk phase (in the matrix)

For the statistical distribution of the elementary units along the cellulose nitrate chain, one may expect that their distribution in the matrix is also statistical or homogeneous. The extreme case is the block character of the distribution of units along the chain. There is then a possibility of the aggregation of blocks of isotypical units into domains — three-dimensional regions of the cellulose nitrate matrix containing mainly chain fragments consisting of isotypical units. As a result of the inhomogeneous nature of the nitration of cellulose, a state intermediate between the cases quoted above occurs in the cellulose nitrate obtained.

The possibility of determining or estimating the composition of the elementary units, and of determining their distribution along the chain or in the bulk of the cellulose nitrate, gives rise to ways of analysing the inhomogeneity of cellulose nitrates, which is necessary both for the study of the mechanism and kinetics of the nitration of cellulose and for the preparation and processing of industrial cellulose nitrates.

4. Levels of inhomogeneity of cellulose nitrates

The molecular-structural inhomogeneity of cellulose nitrates is determined by a complex set of parameters: the composition of the nitrating mixture, the morphological structure of the initial cellulose determined by its origin (cotton, wood, linen, etc. celluloses), the conditions in the preparation of cellulose for nitration (activations of different kinds), and the nitration regimes. Naturally, without a logically well-founded subdivision in terms of the levels of inhomogeneity of cellulose nitrates, analysis of their properties becomes virtually impossible. For this reason, it has been suggested that their molecular-structural inhomogeneity be divided into several hierarchical levels:[72] in terms of the composition of the elementary units (compositional inhomogeneity); in terms of the distribution of heterotypical elementary units along the chain (configurational inhomogeneity); and in terms of the distribution of heterotypical elementary units in the cellulose nitrate matrix (matrix inhomogeneity).

5. Inhomogeneity of cellulose nitrates in terms of the composition of the elementary units

The compositions of the elementary units of cellulose nitrates[33,35,36,44,48–54] and of a number of other polysaccharide derivatives[93–96] have now been quite reliably determined by

§O K Nugmanov. Personal communication.

high-resolution ^{13}C NMR in solution. Systematic analysis of the inhomogeneity at this level is only possible when a single methodological approach, permitting a comparison of data obtained for different nitrating mixtures, initial celluloses, etc., is employed. Attempts to achieve such an approach have been undertaken,[36,97] but, in our view, they have not been successful, because the criteria employed were not clearly defined and there were no 'reference points' for the inhomogeneity of the cellulose nitrates. A simple scheme for the determination of the inhomogeneity of cellulose nitrates in terms of the composition of elementary units (suitable, incidentally, for any derivatives of cellulose and of polysaccharides in general) has been proposed.[86] The concepts of cellulose nitrates with limiting homogeneity and limiting inhomogeneity were introduced in the above study. Cellulose nitrates with integral degrees of substitution are assumed to have the limiting homogeneity: 1 — cellulose mononitrate, 2 — cellulose dinitrate, and 3 — cellulose trinitrate. Here no account is taken of the specific positions of the nitrate groups in the elementary unit. For degrees of substitution of 1.2 and 2.5, cellulose nitrates containing respectively 20% of disubstituted and 80% of monosubstituted units, and 50% of dinitrate and trinitrate units, are considered to be homogeneous to the limiting extent. Cellulose nitrates consisting only of trinitrates and unsubstituted units are considered to have the limiting inhomogeneity.

In order to measure the inhomogeneity of cellulose nitrates in terms of the composition of the units, one determines the sum of the deviations, $\Sigma\Delta_i$, of units of the given type (tri-, di-, and monosubstituted as well as unsubstituted) from cellulose nitrates homogeneous to the limiting extent and with the same degree of substitution:

$$\Delta_i = |a_i - a_i^0|,$$

where a_i and a_i^0 are the measured and calculated fractions of the ith type units respectively. Analogous calculations are performed for the hypothetical cellulose nitrates which are inhomogeneous to the limiting extent, whereupon the dependence of $\Sigma\Delta_i$ on the degree of substitution of the cellulose nitrate is represented graphically by the 'inhomogeneity trapezium' (Fig. 12), the base of which is the cellulose nitrate homogeneous to the limiting extent in terms of the composition of the elementary units ($\Sigma\Delta_i = 0$), while the other three sides bound the region of existence of cellulose nitrates with any homogeneity (with respect to the composition of the units).

Models of the esterification of cellulose have been analysed[88] in terms of the quasi-homogeneous approximation (with thermodynamic and kinetic monitoring of the reaction products) and calculations have been made of the fractions of the unsubstituted, monosubstituted, disubstituted, and trisubstituted units in accordance with the constants for the substitution of the hydroxy-groups in the 2-, 3-, and 6-positions in the glucopyranose rings. These were subsequently revised for cellulose nitrates.[33,40,97] The values of $\Sigma\Delta_i$ were calculated from these data and plotted (Fig. 12). The figure includes also all the available experimental data for cellulose nitrates. The inhomogeneity with respect to composition of elementary units is determined by the distance from the abscissa axis of the values of $\Sigma\Delta_i$ calculated from the experimental measurements. The cellulose nitrates obtained by nitration in mixtures of nitric and sulfuric acids and in solutions of nitrogen oxides in nitric acid, as well as denitrated cellulose nitrates, proved to be the most inhomogeneous. These results will be examined in detail in the next section. Here we may note the clarity of the proposed procedure and the possibility of comparing polysaccharide derivatives with any compositions of the elementary units. For example, in the selectively substituted cellulose 2,3-diacetate (degree of substitution 1.69), the compositional inhomogeneity is very low and $\Sigma\Delta_i = 0.18$.[93] Carboxymethylcellulose with a low degree of substitution (0.7) has $\Sigma\Delta = 0$,[94] whilst a cellulose ether (degree of substitution 1.27) also exhibits a high inhomogeneity

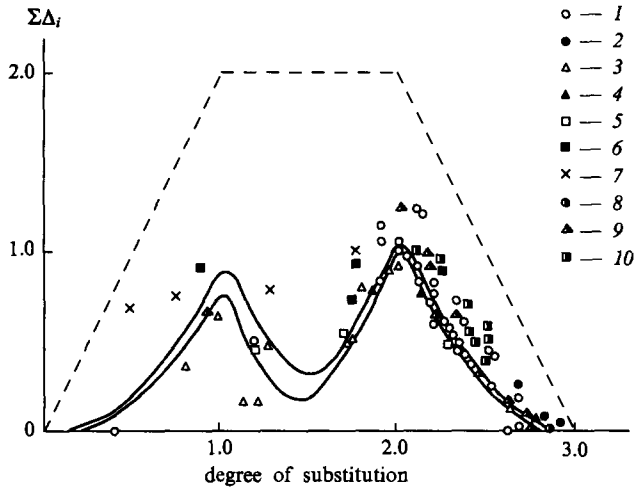


Figure 12. The sums of the deviations $\Sigma\Delta_i$, measured by ^{13}C NMR, of the compositions of the elementary units of cellulose nitrates obtained by nitration in the $HNO_3+H_2SO_4+H_2O$ [33,36,40,44,48–50,53] (curve *1*), $HNO_3+H_2SO_4$ [49] (curve *2*), HNO_3+H_2O [50,53,54] (curve *3*), and $HNO_3+CH_2Cl_2$ [40] (curve *4*) mixtures, in HNO_3 vapour [50,53,54] (curve *5*), in the $HNO_3+N_2O_5$ [50] (curve *6*), $HNO_3+N_2O_5+N_2O_4$ (Yu M Kargin, personal communication) (curve *7*), and $HNO_3+H_3PO_4+P_2O_5$ [35] (curve *8*) mixtures, and by denitration in the HNO_3+H_2O [35,50,53] (curve *9*) and $HNO_3+H_2SO_4+H_2O$ [48] (curve *10*) mixtures. Calculated sums of the deviations $\Sigma\Delta_i$: continuous curves — according to Spurlin:[88] upper curve — for the equilibrium constant ratios $K_6 : K_2 : K_3 = 10 : 1 : 1$, lower curve — for the rate constant ratios $k_6 : k_2 : k_3 = 10 : 1 : 1$; dashed line — calculated sums of the deviations $\Sigma\Delta_i$ for cellulose nitrates with the limiting inhomogeneity.

with respect to the composition of the elementary units with $\Sigma\Delta_i = 0.36$.[95] It is of interest that the amylose nitrates obtained by inhomogeneous nitration and having degrees of substitution of 1.69 and 2.17 are characterised by $\Sigma\Delta_i = 0.68$,[96] which is close to the value calculated by Spurlin's method (Fig. 12), whereas the homogeneously denitrated amylose nitrate with a degree of substitution of 1.89 has $\Sigma\Delta_i = 0.08$.

The limitation of the applicability of high-resolution NMR to polymer solutions should be noted. Only the dissolved part of the polymer contributes to the signal intensities, and for low degrees of substitution the solubility of cellulose nitrates in organic solvents is low. This is in fact the reason why the limiting homogeneity of the cellulose nitrate specimen with a degree of substitution of 0.4, found by Wu,[33] is a 'consequence' of neglecting this limitation.

Results obtained by IR spectroscopy may be used to estimate the inhomogeneity from the ratio of the optical densities of the 1662 and 1648 cm^{-1} bands by using Eqn (1). Unfortunately, this method too, which is simpler than the NMR procedure, suffers from a disadvantage — no account is taken of the unsubstituted units, i.e. the applicability of the method is limited to the region where the degree of substitution is greater than two, in which the fraction of these units becomes negligible.

6. Distribution of elementary units along the cellulose nitrate chain

Currently, the distribution of the elementary units along the cellulose nitrate chain is not susceptible to direct measurement, although it is possible in principle. Such distribution can, however, be inferred indirectly from combined data on the compositional and matrix inhomogeneities of cellulose nitrates. We may note that both the compositional and the configurational inhomogeneities of cellulose nitrates are characteristics of macromolecules; account must be taken of the fact that all the data presented here are estimates of both levels of

inhomogeneity, averaged over the entire assembly of macromolecules. If it is necessary to investigate the compositional inhomogeneity of the macromolecules themselves, one has to resort to methods developed for the investigation of the molecular-mass distribution of cellulose nitrates — for example fractionation, gel-permeation chromatography with different detection procedures, etc.

7. Distribution of heterotypical units in the cellulose nitrate matrix

The distribution of heterotypical units in the cellulose nitrate matrix has been investigated very fully. Most of the results have been obtained by X-ray photoelectron spectroscopy (XPS). This method yields information about the elementary composition of the material on the surface to a depth of the order of tens of nanometers.[8] By comparing the contents of nitrate groups on the surfaces of cellulose nitrate fibres, measured by the XPS method, and in the bulk of the material, it is possible to infer the matrix inhomogeneity of the cellulose nitrate. It has been shown[98] that nitration of cellulose by the $HNO_3 + H_3PO_4 + P_2O_5$ and $HNO_3 + P_2O_5 + H_2O$ mixtures proceeds uniformly on the surface and in the bulk of the fibres, attaining simultaneously identical degrees of substitution, whereas in nitration by the $HNO_3 + H_2SO_4 + H_2O$ mixtures the final degree of substitution is attained rapidly on the surfaces of the fibres but, even after nitration for 2 h, the degree of substitution within the fibres remains smaller than on the surface. Nitration of cellulose by a solution of the nitronium salt $NO_2^+BF_4^-$ in general takes place only on the surfaces of the cellulose fibres without involving the inner region.[99]

The results of X-ray phase analysis (XPA) have shown that the crystal structure of cellulose nitrate is already formed during the nitration process. In the nitration of cellulose by $HNO_3 + H_2SO_4 + H_2O$ mixtures, the reflections due to the nonnitrated regions of the cellulose are still observed, together with the reflections due to crystalline cellulose nitrates, even for a degree of substitution of 2.[100–103] Furthermore, on raising the water content in the above mixture from 0% to 15%, it was observed[52] that the inhomogeneity of the resulting cellulose nitrates diminished: the reflections due to crystalline cellulose vanish at lower degrees of substitution, while the formation of cellulose nitrate crystallites begins at higher degrees of substitution. Nitration of cellulose with the $HNO_3 + CH_2Cl_2$ mixture is characterised by the formation of a more homogeneous cellulose nitrate structure: the reflections due to cellulose have already disappeared for a degree of substitution of 0.1, whereas the crystallinity of the cellulose nitrates begins to be manifested only for a degree of substitution > 1.2.[102,104] It has also been shown by the XPA method that the products of the nitration of cellulose of different origins (cotton and wood celluloses) in the same nitrating mixture are different, the most homogeneous cellulose nitrates being obtained when cotton cellulose is employed.[103] The data obtained by high-resolution ^{13}C NMR in the solid state lead to similar conclusions.[10,105] Seemingly, by employing the XPA method for the analysis of the dynamics of the cellulose nitration process as a function of time, it is possible to discover the characteristics of the establishment of the inhomogeneity of the cellulose nitrates: the lower the degree of substitution at which the reflections due to crystalline cellulose vanish and the higher the degree of substitution at which the crystal packing of cellulose nitrate begins to be established, the more homogeneous is the cellulose nitrate obtained.

The establishment of the inhomogeneity of cellulose nitrates has been analysed by IR spectroscopy for two nitrating media — concentrated HNO_3 and the $HNO_3 + H_2SO_4 + H_2O$ mixture.[106] The ratios of the cellulose nitrate fractions soluble and insoluble in acetone were determined in samples taken during the nitration process, and the degrees of substitution of both fractions were found for each specimen from the formulae

$$\gamma_s = 3 - \frac{3-\gamma}{a_s(1 + a_u b_u/a_s b_s)}, \text{ and } \gamma_u = 3 - \frac{3-\gamma}{a_u(1 + a_s b_s/a_u b_u)},$$

where γ is the degree of substitution of the given cellulose nitrate specimen, γ_s and γ_u are the partial degrees of substitution, a_s and a_u are the mole fractions, and b_s and b_u are the relative optical densities of the ν(OH) bands due to the hydroxy-groups in the soluble (s) and insoluble (u) fractions of the cellulose nitrate respectively (Table 6). In order to estimate the inhomogeneity of the cellulose nitrate, the deviations of the partial degrees of substitution from the overall degree of substitution were calculated from the relations

$$\Delta_s = \frac{\gamma_s - \gamma}{\gamma}, \quad \text{and} \quad \Delta_u = \frac{\gamma - \gamma_u}{\gamma}.$$

Evidently the smaller the values of Δ_s and Δ_u, i.e. the closer the partial and overall degrees of substitution of cellulose nitrates, the greater the homogeneity of the latter. In the course of the nitration by the ternary mixture, the degrees of substitution of the

Table 6. Partial degrees of substitution of cellulose nitrate fractions soluble and insoluble in acetone.

γ	$10^{-2}\tau$/s		ρ (mass %)		γ_s		γ_u		Δ_s		Δ_u	
	I	II	I	II	I	II	I	II	I	II	I	II
1.2	–	0.15	–	55	–	1.9	–	0.6	–	0.58	–	0.50
1.4	–	0.25	–	61	–	2.0	–	0.7	–	0.42	–	0.50
1.4	–	0.30	–	61	–	1.9	–	0.8	–	0.57	–	0.43
1.5	–	0.60	–	68	–	2.0	–	0.7	–	0.47	–	0.53
1.7	0.15	–	68	–	1.9	–	1.3	–	0.12	–	0.24	–
1.8	0.20	–	67	–	2.0	–	1.4	–	0.11	–	0.24	–
1.9	–	1.8	–	83	–	2.2	–	0.8	–	0.16	–	0.58
2.0	0.25	–	69	–	2.2	–	1.6	–	0.10	–	0.20	–
2.2	0.30	–	76	–	2.4	–	1.7	–	0.09	–	0.23	–
2.3	–	7.8	–	99	–	2.3						
2.3	–	18	–	100	–	2.3						
2.5	1.8	36	100	100	2.5	2.5						
2.7	7.8	–	100	–	2.7	–						
2.7	18	–	100	–	2.7	–						
2.7	36	–	100	–	2.7	–						

Note. The following notation has been adopted: τ = nitration time; ρ = solubility; nitrating mixtures: I — 98% HNO_3; II — 39% HNO_3 + 56% H_2SO_4 + 5% H_2O.

fractions soluble and insoluble in acetone differ significantly from the degree of substitution of the specimen analysed, so that the inhomogeneity of the latter is appreciably greater than that of the cellulose nitrate obtained by nitrating cellulose with concentrated nitric acid.

The residual hydroxy-groups present in the elementary cellulose nitrate units (with the exception of the fully substituted ones) are a kind of label. They can form hydrogen bonds of different types in the cellulose nitrate matrix. Taking this into account, the distribution of the labels in the bulk of the cellulose nitrate has been estimated quantitatively.[86] Those cellulose nitrates in which there is a statistical distribution of the heterotypical units in the bulk phase are matrix-homogeneous. We therefore calculated[86,87] the ratio of the probabilities of the formation of weak hydrogen bonds between the hydroxy- and nitrate groups, of strong hydrogen bonds of the type OH...OH, and of intramolecular hydrogen bonds of the type OH(3)...O(5) from only the degree of substitution of the cellulose nitrates by means of the formula

$$P_r = k\frac{\gamma}{3-\gamma},$$

where k is a coefficient which takes into account the fraction of the intramolecular hydrogen bonds. The ratios A_{3570}/A_{3440}, reflecting the actual ratios of the different types of hydrogen bonds involving the residual OH groups in the cellulose nitrate and determined experimentally from the IR spectra, were used to plot the $P_r = f(\gamma)$ relation (Fig. 13). The relation between this level of inhomogeneity, determined by a somewhat different method, and the thermal stability of the cellulose nitrates has been demonstrated.[107]

We may note that there is complete agreement between the results of the measurements of both levels of inhomogeneity — compositional (Fig. 12) and matrix (Fig. 13) inhomogeneities. This evidently reflects their hierarchical relation because nitration in all the nitrating media examined above takes place inhomogeneously. It is quite likely that the use of nontraditional nitration methods, for example transesterification under homogeneous conditions or the application of new selectively substituting reagents, will lead to inconsistent data for different levels of inhomogeneity.

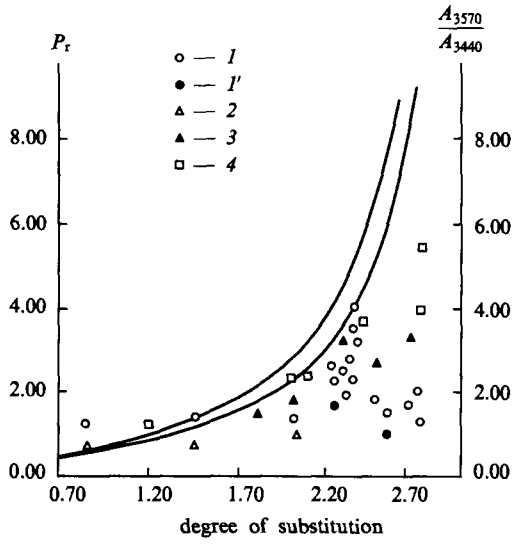


Figure 13. Deviations of the optical densities (A_{3570}/A_{3440}) of cellulose nitrates obtained by nitration in $HNO_3 + H_2SO_4 + H_2O$ (*1*, *1'*), $HNO_3 + H_2SO_4$ (*2*), $HNO_3 + H_2O$ (*3*), and $HNO_3 + CH_2Cl_2$ (*4*) mixtures. (*1'*) cellulose nitrate films cast from solutions in acetone; the P_r curves have been calculated for two values of k.[86]

VI. Inhomogeneity of the nitration and inhomogeneity of cellulose nitrates

Cellulose nitrates obtained by nitration with $HNO_3 + H_2SO_4$, $HNO_3 + H_2SO_4 + H_2O$, $HNO_3 + N_2O_5$, and $HNO_3 + N_2O_5 + N_2O_4$ mixtures, as well as the denitrated cellulose nitrates, are most inhomogeneous in terms of the composition of the elementary units and in the matrix. More homogeneous cellulose nitrates have been synthesised in liquid and gaseous nitric acid, in its aqueous solutions, and in nitric acid–dichloromethane mixtures. It was found that such subdivision in terms of inhomogeneity correlates satisfactorily with the presence or absence of nitronium ions NO_2^+ in the initial nitrating mixtures. Thus, in a mixture of sulfuric and nitric acids, the latter is dissociated to a considerable extent[108–111] with formation of the most inhomogeneous cellulose nitrates (Fig. 12). The addition of water to this mixture of acids lowers the NO_2^+ concentration[109,111] and the inhomogeneity of the cellulose nitrates in terms both of the composition of the elementary units and of the matrix (Fig. 13). Nitration with a solution of the nitronium tetrafluoroborate salt[99] leads to the formation of a surface layer of cellulose nitrates on nonnitrated cellulose fibres. The mixture of nitric acid with N_2O_5 is also characterised by a high concentration of nitronium ions.[112,113]

The content of nitronium ions in aqueous solutions of nitric acid with a HNO_3 concentration in excess of 80% is low;[114] the degree of ionisation of the acid varies within the limit of 0.03. The compositional inhomogeneity does not then exceed the values calculated by Spurlin's method and the matrix inhomogeneity of the cellulose nitrates obtained in 98% nitric acid is significantly lower than that of the cellulose nitrates synthesised in the $HNO_3 + H_2SO_4 + H_2O$ mixture (Table 6, Fig. 13). Nitronium ions have not been detected in the $HNO_3 + CH_2Cl_2$ mixtures,[115] which has been confirmed by studies on the Raman spectra of this mixture in the nitric acid concentration range from 30% to 80%. Cellulose nitrates obtained by nitration in this mixture are the most homogeneous (Figs 12 and 13).

Several points of view on the mechanism of the nitration of cellulose exist at the present time. The elementary step in the reaction reduces mainly to the $Cell-OH + NO_2^+$, $Cell-OH_2^+ + HONO_2$, and $Cell-OH_2^+ + N_2O_5$ interactions or their combinations.

In order to elucidate the relation between the inhomogeneity of the cellulose nitrate obtained and the presence of nitronium ions in the initial acid mixture, we shall consider the following scheme: the elementary step of the reaction requires an active pair consisting of the nitronium ion and a hydroxy-group of cellulose, the molecular form of nitric acid or N_2O_5, and the protonated form of the hydroxy-groups of cellulose. In this case, the nitration of cellulose must be regarded as the combination of three proceses occurring simultaneously:

(1) diffusion of the nitrating mixture to the polymer matrix;
(2) the formation of the active pairs;
(3) the interaction of the active pairs (nitration proper).

These processes are followed by the counterdiffusion of the species (molecules and ions) comprising the nitrating mixture and the low-molecular-mass reaction product in microregions of the matrix of the cellulose being nitrated. Since the rate of nitration (process 3) is significantly higher than the rates of the first two processes, the homogeneity of the cellulose nitrates obtained depends on the ratio of the rates of processes 1 and 2.

If the nitrating mixture contains initially the nitronium ions NO_2^+, i.e. both components of the active pair are already present in the reaction mass, process 2 is ruled out and the reaction proceeds topochemically (Fig. 14, curve *1*). The rate of this reaction is limited by the diffusion of nitronium ions into the cellulose matrix, and leads to the formation of an inhomogeneous cellulose nitrate. On the other hand, if process 2 plays a significant role, then the active pairs interact at the site of the increase in their concentration and, what is most important,

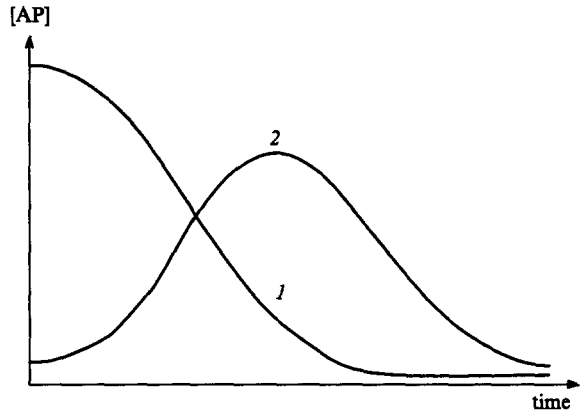


Figure 14. Variation of the concentration of the active pairs [AP] during the diffusion of the nitrating mixture into the cellulose matrix: (*1*) in the presence of both components of the pair at the beginning of nitration; (*2*) on formation of the active pairs during nitration.

under the conditions of a more or less uniform distribution resulting from the diffusion of the nitrating mixture (process 1) into the cellulose matrix (Fig. 14, curve *2*). The reaction then proceeds quasi-homogeneously and a more homogeneous cellulose nitrate is therefore formed. There is no doubt that the real nitration pattern is the average of those illustrated in Fig. 14. The rate of diffusion can evidently vary depending on the ability of the nitrating mixture to 'loosen' the cellulose matrix, but the formation of active pairs probably plays the main role in the establishment of the inhomogeneity.

The products of the denitration of cellulose nitrates obtained by treating the latter with solutions of nitric acid[35,50,53] or the sulfuric acid–nitric acid mixture[48] have the most inhomogeneous elementary units. Seemingly the denitration of cellulose nitrates has different features as regards both the mechanism[116] and the diffusional characteristics. Experimental data (XPA) have shown[36,48] that the denitration involves the cellulose nitrate crystallites to only a slight extent, the diffusion of the denitrating mixture in the latter being significantly limited. For this reason, the denitration proceeds mainly in the nonordered sections of the cellulose nitrate matrix, whereupon a considerable proportion of the dinitrate and trinitrate units, which constitute the bulk of the cellulose nitrate crystallites, are retained and the inhomogeneity of the denitrated cellulose nitrates increases. This has been confirmed by the finding that the last point for the denitration of cellulose nitrates by the acid mixture, corresponding to a degree of substitution of 2.1 (over a period of 7 days) (Fig. 12), fits on the calculated curve. The inhomogeneity of this cellulose nitrate is significantly lower, which can be accounted for by the disruption of the morphological structure,[48] the degradation of the specimen, and hence a sharp increase in the accessibility of the bulk of the cellulose nitrate to the denitrating agent.

Thus, by monitoring the molecular-structural inhomogeneity of cellulose nitrates, it will evidently be possible to estimate directly the role of the diffusional component in the analysis of the kinetics of the inhomogeneous cellulose nitration reaction.

VII. Conclusion

The inhomogeneity of the nitration of cellulose affects significantly the properties of the resulting cellulose nitrates directly via their molecular-structural inhomogeneity. In the synthesis of new cellulose nitrate materials with more stringent requirements as regards homogeneity (for example biological membranes, detectors of ionising radiations, enamels, varnishes, etc.), it becomes possible to alter in a planned manner the conditions in the synthesis by taking into account the results of the analysis of the inhomogeneity of the cellulose nitrates obtained. The molecular-structural inhomogeneity must also be monitored when new selective reagents are used in the nitration of cellulose and in carrying out homogeneous transesterification or nucleophilic substitution reactions, whereupon it is possible to increase the selectivity of substitution in specific positions in the glucopyranose ring; the latter factor makes it possible to obtain new cellulose derivatives which cannot be synthesised directly from cellulose itself.

The theoretical ideas concerning the kinetics of macromolecular reactions have been mainly developed for homogeneous conditions[92,117–119] and all investigators agree unanimously that the development of approaches to the description of the kinetics of heterogeneous reactions closest to the real technological processes is an extremely complex task. The studies in the field of the kinetics of inhomogeneous processes, vigorously prosecuted in recent years,[120] involve the reactions of polymers.[120,121] The creation of models of this kind requires a detailed analysis of the changes in the structures of the reaction products, analogous to that proposed for the cellulose nitration reactions.

The applicability of the approaches developed for the analysis of the molecular-structural inhomogeneity of cellulose nitrates to other cellulose derivatives must be pointed out yet again. This applies primarily to the acetates and ethers for which adequate NMR and IR spectroscopic data are at present available.

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Scanning tunnelling and atomic force microscopy in the electrochemistry of surfaces

A I Danilov

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Abstract. The theoretical foundations, principle of operation, constructional features, and the latest advances in scanning tunnelling and atomic force microscopy in situ are examined in relation to electrochemical studies on the surfaces of metallic electrodes, and adsorption and electrocrystallisation processes. The bibliography includes 172 references.

I. Introduction

No one is surprised nowadays by communications concerning the observation of the morphology of surfaces at atomic resolution, although the scanning tunnelling microscope (STM) was invented by Binnig and Rohrer only just over 10 years ago.[1] At that time, it was difficult to believe that the observation of the atomic structure of a surface in vacuo or in air was realistic. Nowadays electrochemists are no longer satisfied with observations ex situ but prefer to use the STM or the atomic force microscope (AFM) for the investigation of the state of the electrode surface in situ during the polarisation process.

The term scanning probe microscopy (SPM), which combines tunnelling and atomic force microscopies because these methods have much in common and are frequently used simultaneously, has been established in the English language literature. Scanning probe microscopy is developing rapidly at the present time, an enormous number of publications concerning its use in electrochemical experiments have appeared, and the degree of sophistication of the research has greatly increased—from the demonstration of the possibilities of the instrument, investigators have gone on to a serious analysis of the results and a realistic study of the electrode surface and the mechanisms of the processes occurring on it. These factors have stimulated the writing of the present review. The principles of SPM and the traditional designs of the instruments are examined very briefly, as there are already many excellent review articles and monographs on this topic in the literature,[1–11] and attention is concentrated on the latest results of electrochemical studies and the prospects for the development of this unique method.

A I Danilov Laboratory for the Structure of Surface Layers, Institute of Physical Chemistry, Russian Academy of Sciences, Leninskii prosp. 31, 117915 Moscow, Russian Federation. Fax (7-095) 952 53 08. Tel. (7-095) 955 44 55

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II. Theoretical foundations of scanning probe microscopy

1. Principle of the operation of the tunnelling and atomic force microscopes

A real possibility of the tunnelling of an electron through a barrier, the height of which greatly exceeds its energy, is known to exist. If two conductors (electrodes), separated by a dielectric (vacuum, gas, or liquid), are brought together to a sufficiently short distance s and a potential U_t is established between them, then a tunnelling current I_t arises in the circuit, is proportional to the applied potential, and depends exponentially on the distance between the electrodes:

$$I_t = KU_t \exp(-A\sqrt{V_t}s), \quad (1)$$

where K is a constant, V_t the height of the potential barrier (for $s > 2$ nm, the height of the barrier is virtually equal to the electron work function), and $A \approx 10$ nm^{-1} eV$^{-1/2}$ is the proportionality coefficient. This is the Fowler–Nordheim equation, which is valid for planar electrodes and low potentials ($U_t \ll 1$ V). In real experiments such conditions are not always observed, but the exponential dependence of the tunnelling current on distance is retained (see, for example, Behm et al.[2] and Christensen[8]).

Simple calculation shows that, in order to record a tunnelling current of the order of magnitude of a nanoampere, it is necessary to bring the probe electrode to a distance of several angstroms from the surface investigated (for metals, $V_t \approx 5$ eV, and a tunnelling current of 1 nA is observed for $s \approx 0.6$ nm when $U_t \approx 1$ eV).[7]

Theoretically everything is fairly simple and it only remains to solve the problem of how the system is to be constructed.

The concept of the STM was proposed by Binnig and Rohrer in 1979, and in 1981 the first clear cut dependence of the tunnelling current on the distance between the specimen and the point of the probe, characteristic of tunnelling, was recorded. Topographical images of the $GaIrSn_4$ surface with multiatomic steps were soon obtained.[1]

The simplest tunnelling microscope (Fig. 1) consists of a piezoceramic scanner *1* (a tripod or sectioned tube, the geometrical dimensions of which vary in the XYZ directions following the application of an electric potential to the corresponding section) with a tunnelling probe *2* (a sharp needle made from tungsten, a platinum–iridium alloy, carbon, or another material), electronic circuits *4* for the maintenance of the potential and the tunnelling current in the test specimen *3* and the probe, and a recording and controlling computer system *5*.

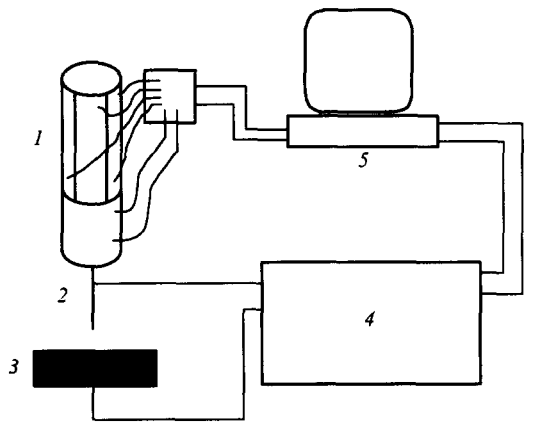


Figure 1. Block diagram of the tunnelling microscope (here and henceforth the explanations are given in the text).

Different designs of piezoscanners make it possible to move the point of the probe to distances ranging from fractions of an angstrom to several tens of micrometers. After the probe has approached the surface to a distance of several angstroms (the moving devices for the solution of this problem will be examined below), the tunnelling current assumes values of the order of magnitude of a nanoampere, and the electronic circuit with a feedback loop makes it possible to stabilise the current by varying the potential on the Z-section of the piezoscanner, i.e. by raising and lowering the probe (Fig. 2*a*) over the surface of the specimen (we recall that the tunnelling current depends greatly on the gap between the electrodes). The galvanostat works similarly, but here the potential on the electrochemical cell is varied in order to maintain a constant current in the working electrode circuit.

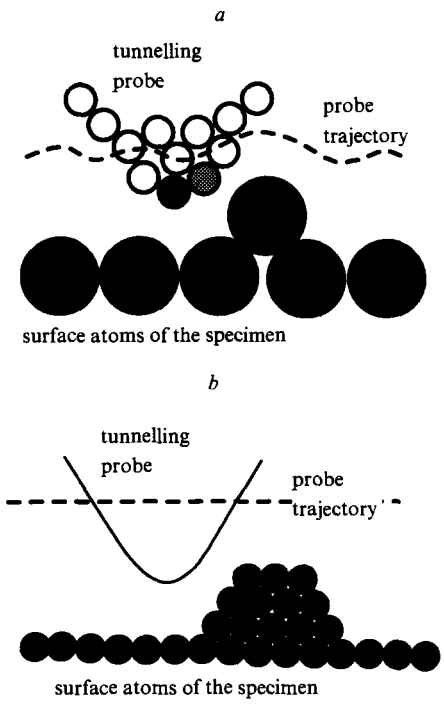


Figure 2. Principal regimes in the operation of the STM: (*a*) maintenance of a constant tunnelling current; (*b*) maintenance of a constant height of the probe over the specimen.

By applying to the X-section of the piezoscanner a potential varying linearly with time, it is possible to move the probe over the surface along a straight line (a ceramic unit, the length of which depends linearly on the applied potential, is used for piezoscanners). By recording the potential on the Z-section of the piezotube which is varied by the feedback loop, one obtains the surface relief along the scanning line. Strictly speaking, the electronic state of the surface and not its relief is recorded, but in most cases these relations are similar on specimens with a homogeneous composition. Thus, by varying the potential on the XY-sections and by measuring the displacements of the probe in the vertical direction, it is possible to scan a section of the surface and to obtain its topographic image. The correct employment of such images requires a careful calibration of the piezoscanners on objects with a known topography.

If the potential on the Z-section of the tube is fixed and the tunnelling current is measured with the probe moving above the specimen, it is possible to record the image of the surface more rapidly (Fig. 2*b*), but there is then an increase in the probability of 'sticking' because the feedback loop does not in this case control the current. This regime is suitable for the investigation of atomically smooth sections of the specimen and makes it possible not only to increase the scanning rate but also to improve the quality of the image by reducing the level of interference.

The sharpness of the probe is important—ideally there should be one atom at its end. Initially investigators wasted much time and effort on the preparation of very sharp needles by electrochemical or gas-phase etching. However, the exponential dependence of the tunnelling current on distance eliminated many problems—nowadays the majority of commercial STM employ mechanically sharpened probes or simply probes sliced at an angle. Under these conditions, some of the surface atoms of the probe are closer to the test surface than others and play the role of the sharp point. Naturally, it is best to have a sharp etched needle, since otherwise in recording the image of a rough surface one may obtain artefacts as a result of the alternate operation of several sections of a blunt needle which are at different times closer to surface projections. For example, in the situation illustrated schematically in Fig. 2*a* a lateral atom, closer to the projection, 'operates' instead of the lowest atom of the probe.

The next step in the development of SPM was the creation of the atomic force microscope.[12] The exponential dependence of the tunnelling current on the distance between the electrodes is of decisive importance for the attainment of the atomic resolution in the STM, whereas in the AFM a similar importance attaches to the pronounced dependence of the force F of the interaction between bodies on the distance between them R,

$$F(R) = \frac{C_1}{R^{13}} - \frac{C_2}{R^7}, \qquad (2)$$

where C_1 and C_2 are constants. The first term in the equation for the Lennard-Jones potential describes the short-range repulsion forces between the electron clouds of the atoms brought into contact, while the second term describes the attraction forces acting over relatively large distances. One of the bodies involved is the probe (the needle *1* fixed on a flat spring *2*), while the other is the test surface *3* (Fig. 3).

The problem of bringing the probe to the required distance from the steps of the specimen and scanning over the latter is solved, as in tunnelling microscopy, with the aid of the piezoceramic XYZ-translator *6*, while the vertical movements of the needle are recorded either with the aid of an optical system [in this case a laser beam is reflected from the mirror *4*, fixed on the spring *2*, and falls on the photodiode *5* (Fig. 3*a*)] or with the aid of the tunnelling probe *7* mounted over the spring *2* (Fig. 3*b*). The second variant requires a more complex control system and is used fairly rarely.

The AFM can operate in two main regimes.

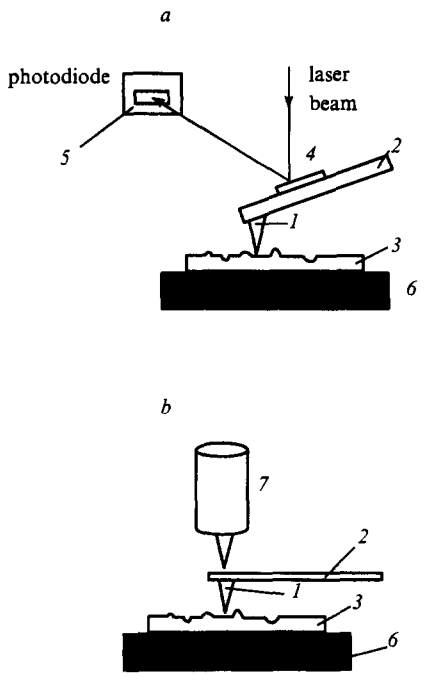


Figure 3. Principle of the operation of the atomic force microscope.

1. Contact-free interaction — the forces of attraction of the probe to the test surface are greater than the repulsion forces [see Eqn (2)]. With the aid of yet another piezocrystal, vibrations are induced in the needle at a frequency ν, which is close to the resonance frequency of the spring ν_r, and with an amplitude of about 2 nm (evidently the distance R between the needle and the specimen must be greater). In this case, the attraction force is determined[8] from the equation

$$\frac{dF(R)}{dR} = \frac{2k\Delta\nu}{\nu_r}, \qquad (3)$$

where $\Delta\nu = \nu - \nu_r$ is the change in the vibration frequency induced by the attraction of the probe to the surface and k is the elastic constant of the spring. The quantity $\Delta\nu$ is determined from the change in the vibration amplitude during the scanning by the needle over the surface of the specimen and the image is formed as the dependence of the force on the XY coordinate of the probe on the plane. Owing to the high vibration amplitudes, the needles must be kept at a considerable distance between the probe and the surface, which lowers the lateral resolution.

2. Contact interaction — repulsion forces predominate over short distances. In the simplest case, the probe acts as a gramophone needle and its vibrations in the vertical direction reflect the surface relief. In another variant of this method, the needle and the spring vibrate at a frequency of several hundreds of Hz with an amplitude of 0.5–2 nm (the needle is periodically in contact with the specimen and accurate values of the vibration parameters are selected for a specific rigidity of the spring). The decrease in the vibration amplitude of the needle as a result of the interaction of the probe with a rough surface is proportional to the height of the rugosities on the latter. During scanning along the XY coordinates, the specimen is moved upwards and downwards with the aid of a piezotranslator (in order to maintain a constant vibration amplitude) and the surface relief is thus recorded.

Atomic force and tunnelling microscopies are undergoing active development; compound devices in which an STM, an AFM, an electron microscope, and instruments for optical studies on surfaces are combined have been built.[13–17] Modifications of the AFM which make it possible to investigate the electrical and mechanical properties of the surface, have appeared,[14,16] but a detailed consideration of all these methods and designs is impossible within the framework of this review.

2. Tunnelling microscopy

As already stated, the tunnelling current is proportional to the potential between the electrodes U_t and depends exponentially on the height of the potential tunnelling barrier and on the distance between the probe and the test surface s. The propor-tionality coefficient K in Eqn (1) is determined mainly by the local density of the electronic states of the needle $[D_t(E_{F,t})]$ and the specimen $[D_s(E_{F,s})]$ at the Fermi level.[8] In the case of the clean uniform surfaces of metals, these quantities are independent and the use of Eqn (1) is fully justified. However, when an adsorbate or formations comprising foreign phases are present on the specimen, the density of the electronic states D_s can no longer be regarded as constant and the tunnelling current depends on the electron work function at the given point on the surface.

In the scanning of an electronically nonuniform surface of a specimen (for example, one with inclusions of foreign atoms) in the constant current regime, the variation of the height of the needle over the plane of the specimen no longer reflects the topography of the surface: a hump is observed over atoms with a low electron work function, whereas hollows are seen over atoms with an increased work function. Thus a problem of separation of the electronic and topographic effects arises in the analysis of the image.

This problem may be solved by means of scanning tunnelling spectroscopy (STS), the essential feature of which involves the measurement of the dependence of the tunnelling current I_t on the potential between the electrodes U_t for a fixed position of the probe above the surface.[2,6,8,18–21] In a modification of the regime involving a constant height of the probe (when a low variable potential is applied to the Z-section of the piezoscanner), it is possible to determine the function $I_t(s)$ for a constant value of U_t and fixed XY coordinates, but with the height of the probe over the surface of the specimen being varied within certain limits. In practice, one usually measures the differential signal dI_t/dU_t or dI_t/ds and then the electron work function at the given point on the surface is determined from the dependence of dI_t/dU_t on U_t (or of dI_t/ds on s). By carrying out such measurements at different points, one obtains a distribution map for the inclusions (the adsorbate, oxides, or other nonuniformities) on the surface of the specimen.

III. Design of the tunnelling and atomic force microscopes

We shall now consider the principal units of the tunnelling and atomic force microscopes. Since foreign commercial microscopes are as a rule not available to Russian investigators because of their high price and the lack of the necessary service arrangements, many investigators have attempted to construct such instruments independently and have achieved considerable success. The information presented here may therefore prove useful to those chemists who recognise the need for the employment of SPM in their research but have not yet gained sufficient experience for the independent construction of an instrument. Furthermore, the knowledge of the design of the apparatus enables beginners in the use of SPM to avoid artefacts in their investigations and in the treatment of the results.

1. The piezoscanner and tunnelling probe

The piezoscanner is the heart of the tunnelling and atomic force microscopes. This device actually makes it possible to move the probe to the required point over the test object and to carry out the measurements necessary to obtain information about the topography or electronic state of the surface.

A tripod (three linked, mutually perpendicular piezoceramic plates), on which a tungsten or platinum needle was mounted, was employed initially for this purpose. By varying the potential of the corresponding plates of the tripod, it is possible to move the probe along three coordinates and to analyse the surface. Recently, however, the tripod has virtually ceased to be used and has been replaced by the piezotube.[22] After special treatment of the piezoceramic (annealing and polarisation in an electric field in order to create the necessary orientation of the domains) and sectioning, such a tube (Fig. 4) makes it possible to scan a section of the surface and ensures the Z-translation of the probe over a range of several micrometers.

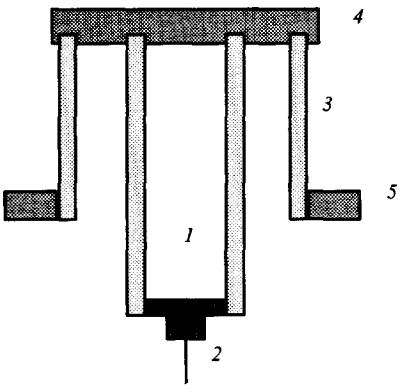


Figure 4. Schematic representation of the piezoscanner: (*1*) inner piezotube with a capacity for XYZ-movements; (*2*) tunnelling probe (needle with holder); (*3*) outer piezotube for the Z-movements and thermocompensation; (*4*) and (5) supports.

The tubular piezoscanner has many advantages over the tripod. It is more compact and more rigid, which means that it has a higher resonance frequency (in the development of the design of the STM, one must endeavour to achieve the highest possible resonance frequency of the scanner and the lowest possible resonance frequencies of the mechanical parts of the instrument in order to reduce the harmful effect of vibrations and acoustic interference). Furthermore, the use of two piezoceramic tubes of different diameter (Fig. 4) makes it possible to extend the scanning range and to reduce appreciably the effect of thermal drift on the measuring process as a consequence of thermocompensation along the Z coordinate.

The range of the movements of the scanner is determined by the nature, structure, and geometrical dimensions of the piezoceramic. For example, the thinner the walls of the tube, the greater the strength of the electric field which can be achieved within the ceramic and the larger the movements of the probe at the end of the tube which can be ensured in scanning the test surface.

The attachment of the probe to the scanner (screw, chuck, magnetic, and other needle holders are used) must ensure the necessary rigidity and at the same time make it easy to replace the needle under operating conditions. Furthermore, this unit must have the smallest possible weight because an increase in the mass of the scanner lowers its resonance frequency. The needle itself must also be fairly rigid and therefore must not be too thin and long.

Needles made of platinum–rhodium or platinum–iridium wire (iridium content 10%–30%) 0.2–1.0 mm in diameter have been most popular recently. In contrast to the tungsten needles, they are hardly oxidised in air at room temperature, are stable in corrosive media (acids and alkalis), and do not introduce impurities into the solution in the course of the experiment.

The platinum–iridium needles are sharpened by electrochemical etching in a 3 M NaCN + 1 M NaOH solution[23] or in a mixture of saturated $CaCl_2$ solution, concentrated HCl, and water in proportions of 60:4:36 by volume[24] at a constant or variable potential $U = 10 - 40$ V. A loop of platinum wire with an electrolyte film is usually employed as the counterelectrode in the cell (Fig. 5*a*).

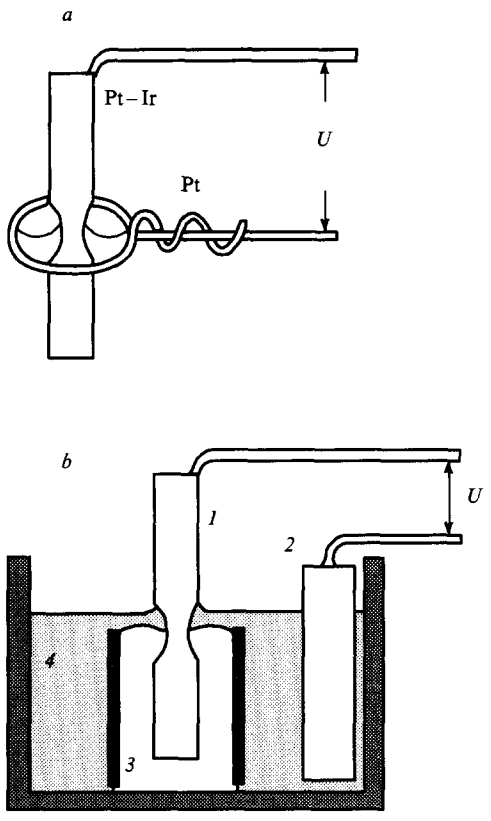


Figure 5. Electrochemical sharpening of the needles: (*a*) etching by means of a wire loop with an electrolyte film; (*b*) etching by immersion in a vessel with electrolyte.

The platinum–iridium alloy dissolves in the meniscus, while the part of the wire (about 1 cm long) below the film of solution serves as a weight which ensures the rupture of the wire when it becomes sufficiently thin. Tungsten needles are etched similarly in 2 M NaOH solution at a constant or variable potential of 1–15 V.[7,8]

The method described is not always convenient. When thick probes are employed, the etching time is several minutes and the electrolyte film can be disrupted as a result of the vigorous gas evolution. In such cases (Fig. 5*b*), the wire *1* from which the needle is to be prepared is lowered vertically into the vessel with the etch solution *4* and the auxiliary electrode *2* to a depth of about 1 cm. The immersed part of the wire is either insulated to prevent its dissolution or an air-filled glass capillary *3* is employed.[25] It is noteworthy that the upper part of the wire also has a sharp end if the current is interrupted immediately after the breaking away of the lower part.

Satisfactory results in the sharpening of platinum or platinum–iridium needles by treatment in a mixture of $CaCl_2$, water, and acetone followed by micropolishing in aqueous sulfuric acid solution have been obtained.[26] The authors were able to avoid the use of toxic cyanide solutions and to obtain smooth readily reproducible needles with a radius of curvature less than 10 nm.

Fairly numerous studies have been devoted to the technology of the preparation of sharp needles and these have been reviewed.[27]

In an experiment in solution, the Faraday current I_F due to the electrochemical reaction on the surface of the needle passes through the latter in addition to the tunnelling current. Reliable information about the topography of the working electrode can then be obtained only subject to the condition $I_F \ll I_t$. This is achieved in two ways: either the probe potential is maintained in the region corresponding to the minimum Faraday current or virtually the entire surface is insulated by a nonconducting material allowing only the minimum possible section on the very end of the needle to remain 'operational'. Glass or polymers are used as insulators; insulation with the aid of the thermoplastic material Apiezon wax is fairly popular.[3]

One of the main problems in the insulation of needles is to ensure that the area of the active surface of the probe does not exceed 1 μm^{-2}, which corresponds to $I_F < 0.1$ nA. It is sometimes simpler to cover the entire surface of the needle with the insulator and then 'expose' its end by means of heat treatment, the application of a powerful electric field, ionic etching, or in some other way.

A novel method for the insulation of needles has been proposed by Mao et al.[28] They use a polymer, deposited from solution by means of an electric current, as the insulating coating. In order to make sure that the insulator on the end of the needle is not too thick (otherwise the problem of the electrical and diffusional screening of the section of the working electrode underneath the probe arises in the course of the STM experiment), electrophoresis is carried out on the needle the end of which is immersed in a drop of mercury. The needle is slowly withdrawn from the drop and at the instant of rupture of the electrical contact between the needle and mercury the coating deposition current is automatically switched off.

The method for the preparation of insulated platinum–iridium needles proposed by Bach et al.[29,30] is the simplest and most convenient. A mechanically or electrochemically sharpened needle is immersed in a solution of polyacrylic acid partly neutralised by a base (Glassophor ZQ 84-3225, produced by the BASF Company, Germany) and electrophoresis is carried out with a platinum cathode at a potential of 25–70 V. The decomposition of water on the anode leads to the acidification of the near-electrode space, as a result of which the polymer passes to a sparingly soluble form and is deposited on the platinum–iridium needle as a film. Further polymerisation, designed to strengthen the coating, is achieved by means of heat treatment ($\sim$200 °C for several minutes), whereupon the chemical stability of the polymer increases and the very end of the needle is exposed as a result of thermocontraction.

With the aid of needles insulated in this way, it has been possible to determine the structures of atomic adsorbed layers of copper on gold.[30] This fact indicates the high quality of the probe and the absence of impurities from the test solution. Stationary Faraday currents of the probe in 0.2 M KCl + 0.01 M $K_3Fe(CN)_6$ solution do not exceed 0.2 nA, which corresponds to an area of the active surface of the needle equal to the area of a circle with a radius less than 0.1 μm.[30] The 0.2 M KCl + 0.01 M $K_3Fe(CN)_6$ solution is frequently used to characterise microelectrodes by means of cyclic voltammetry or stationary methods.[31]

2. The polarisation circuit

When STM is used to investigate the behaviour of electrochemical systems, studies in which the measurements are performed with monitoring of the potential of the working electrode are of greatest interest. In this case, the probe is the fourth electrode in the cell and its potential is specified (measured) relative to the working electrode or the reference electrode. The usual potentiostat and a three-electrode cell were used initially[32–34] for the polarisation of the working electrode, the probe potential being determined from the tunnelling potential between the specimen and the probe:

$$E_t = E_s + U_t, \tag{4}$$

where E_t and E_s are the potentials of the probe and the specimen respectively.

Recently, however, virtually all investigators have used a bipotentiostat, similar to that employed for the polarisation of a disc electrode with a ring.[35] It permits the independent monitoring of the potential of the specimen and the probe relative to the reference electrode (from which the tunnelling potential is equal to the difference between the above potentials).[36–40] The bipotentiostat differs from the usual potentiostat in that, to obtain an image in the STM, it is necessary to ensure the operation of the feedback loop which maintains a constant tunnelling current, i.e. the cell polarisation circuit and the circuit for the control of the Z-movement of the piezoscanner must be adjusted for mutual consistency.

There is one circuit, with optical decoupling, which makes it possible to record the image at high Faraday currents without insulating the needle.[41] A similar circuit has been used[42] to investigate the initial stages in the deposition of copper on pyrographite. After each scan along the X coordinate, the needle is raised, the feedback loop is switched off, and the Faraday current due to the electrochemical reduction of oxygen on the probe is measured (in the quoted instance, $I_F \approx 40$ nA, tunnelling current $I_t \approx 0$). The current I_F is subtracted from the overall current of the needle, lowered to place it in its working state, the appropriate potential being applied from a digital-analogue converter to a summator, and the feedback loop is switched on again to maintain a constant tunnelling current $I_t \approx 4$ nA. Thus, after each scan the Faraday current is corrected, which makes it possible to record the image of the surface. The usual potentiostat-galvanostats with a three-electrode signal are used for atomic force microscopy.

3. Design of the moving device

Piezoscanners usually have a range of Z-displacements of the order of magnitude of 1 μm, so that the maintenance of a constant tunnelling current requires that the probe be brought to a distance $s < 1$ μm from the test surface without sticking the needle into the specimen. This problem is solved in different ways in various designs of the STM.[3,43–48] We shall consider some of them.

a. Mechanical moving devices

The microscrews employed initially in optical apparatus were some of the first to be used. Differential screws combined with a reduction gear ensure fairly small translational displacements of the order of several micrometers of linear movement per turn of the screw. Here it is necessary to solve the problem of play and of the stability of the position of the moved piezoscanner after the attainment of the specified point. Repeated scanning for a long time is sometimes needed for the analysis of the surface in experiments employing the STM. The stability of the position of the piezoscanner is adversely influenced by thermal drift and the relaxation of the mechanical stresses arising as the moving system actually moves.

Computer-controlled step motors are usually employed to automate the moving device — they make it possible to rotate the shaft of the screw by hundredths of a turn with a high accuracy.

b. Piezoelectric moving systems

The range of variation of the geometrical dimensions of the piezo-ceramic tube does not usually exceed several micrometers and the moving device must ensure the movement of the scanner by a fraction of a millimetre. The gap between the specimen and the probe can be set more accurately by hand in the preparation of the experiment, but the probability of random touching increases under these conditions.

The question arises how to increase the range of movement. Imagine the movement of a caterpillar. It gets hold of a leaf with its rear legs, lifts its front legs, and stretches. It then fixes the front legs on the leaf, raises its rear legs, and draws them forward, contracting its body.

The piezotranslator can work similarly. It is only necessary to find a way of fixing a particular end between the expansion/contraction stages.

The piezoelectric 'creeping worm' motor (Inchworm, Burleigh Instruments, Inc.), which ensures the movement of the piezoscanner by several millimetres with a minimum step of 1 nm and a rate up to 0.5 mm s^{-1}, may serve as an example of the mechanical fixing in the majority of commercial STM.[3] Fig. 6 presents a simplified diagram of this motor. The lower part of the motor contains the piezoceramic tube *1*, attached by the holder *5*, with upper (*2*) and lower (*3*) piezofixing devices. The slider *4* with the piezoscanner (not shown in the diagram) is located within the tube.

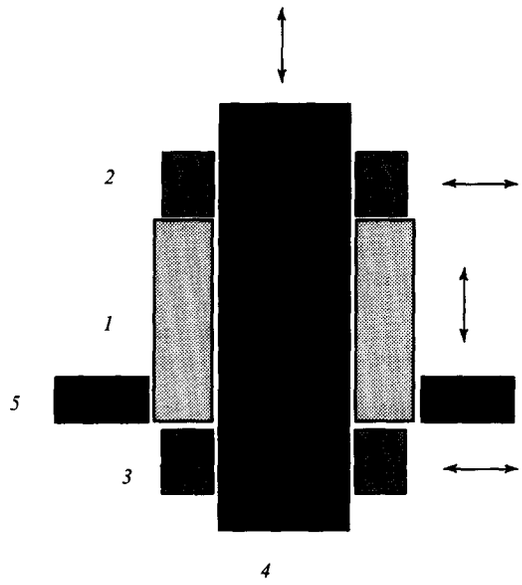


Figure 6. Design of the Inchworm piezoelectric motor. The arrows indicate the directions of the possible movements of the motor components.

In the static state, the fixing devices *2* and *3* grasp the slider from two sides by application of the appropriate pressure. In order to move the slider downwards, the fixing device *2* is released, the pressure on tube *1* is increased, and the latter becomes longer; the fixing device *2* is then applied again, while the fixing device *3* is released, whereupon the pressure on the tube is smoothly reduced. The tube contracts and pulls the slider with the piezoscanner. Thus the slider is alternately 'grasped' by the fixing devices and moves over a distance of up to 2 μm in one step. A very high precision in the treatment of the surfaces and the selection of the appropriate materials, which do not respond to changes in atmospheric humidity and exhibit a high resistance to wear and a low sliding friction, is necessary to ensure the stable operation of the motor.

A motor of simpler design may be made by employing magnetic or electromagnetic fixing devices, but here too it is necessary to overcome numerous difficulties to ensure smooth movement and the stability of the working position.

A somewhat different principle has been applied by Wildoer et al.[43] The slider is held in the resting position not by piezoelectric fixing devices but by flat springs adjusted in such a way that a slow increase in the length of the tube leads to a movement of the slider together with its free end by the frictional force, and a sharp contraction of the tube results in sliding. By applying a sawtooth potential to the piezotube, it is possible to move the slider over considerable distances.

The quality of the treatment and the selection of the materials are also very important in this design—the authors employed stainless steel coated with titanium carbonitride in order to diminish the coefficient of friction and to increase the resistance to wear of the slider and the flat springs.

4. Vibro- and sono-insulation

In order to obtain a high-quality image, it is necessary to achieve a low level of interference from electromagnetic, acoustic, and mechanical influences.[3,8] For this purpose, the measuring block of the STM is mounted on a fairly massive vibroinsulating platform. Spring or rubber suspensions, Viton ring washers,[49] or simply a half-deflated automobile inner tube provide effective protection against mechanical vibrations. In order to reduce the harmful effect of acoustic vibrations, use is made of metallic or glass jackets with sound-absorbing coatings. The earthed metallic jacket at the same time shields the measuring system from electromagnetic influences, but in this case visual monitoring of the state of the electrochemical cell is difficult.

The atomic force microscope is more stable towards low-frequency vibrations than the tunnelling microscope because the resonance frequencies of the springs usually exceed 10 kHz for the AFM whereas the typical vibrations of buildings have frequencies of the order of 20 Hz and an amplitude of about 1 μm. Since the amplitude of the induced vibration, A, is given by

$$A = A_0 \frac{\nu^2}{\nu_0^2}, \tag{5}$$

such vibrations at the resonance frequency induce vibrations with an amplitude of only 0.004 nm. This simple calculation[8] shows that, in contrast to the STM, the atomic force microscope hardly requires special vibroprotection in order to achieve atomic resolution.

5. Treatment of the image

When the test surface is scanned by the tunnelling probe, the primary image is usually produced in the form of a map of the distribution of the measured parameter (tunnelling current, height of the relief, etc.) on the scanning plane. Modern computers ensure a fairly high resolution and a wide colour range for a clear representation of the information obtained as a result of such scanning. There are numerous graphic programs which make it possible to edit the image and view the surface in two and three dimensions, but in work with the STM a special program is needed which combines at least the control of the movement of the probe towards the surface, the monitoring of the electrochemical behaviour of the system, the production of the image, and its primary processing.

We shall deal briefly with the processing of the images, concentrating attention on the risk of artefacts. The principal rule required to avoid such errors is that one should endeavour to obtain a high-quality image without resorting to methods for its improvement by means of computer programs. If all the precautions needed to reduce the level of interference have been taken and the image still remains subject to noise, it is necessary to understand the cause of such noise. It may be that it is a characteristic property of the system investigated and not an induced interference. For example, the presence of halides in the electrolyte is usually accompanied by an increase in the noise in the image because of the increase in the mobility of surface atoms.[50–52]

Digital filtration of images helps in many instances to increase the contrast in the image (or, conversely, to reduce it) for the subsequent analysis of the topography of the surface, but this method must be used with very great caution since, with the aid of Fourier transformations for example, it is possible to see a periodic structure in cases where it has never existed.

There are also computer program methods for the elimination of image defects[5,53] associated with the drift of the system and the nonparallel arrangement of the scanning and specimen planes,[54,55] the nonlinearity of the movement of the tunnelling probe in the scanning of the surface,[56] etc.

IV. Applications of scanning probe microscopy in electrochemistry

Scanning probe microscopy has provided unique possibilities for the investigation of the atomic structure of the electrode and has made it possible to see what happens on the surface when the components of the solution are adsorbed and when the electrode potential is altered. Investigators have become able not only to visualise the mechanism of the electrode process from coulometric, voltammetric, and optical data, as well as data obtained by structural methods, but have also acquired the capacity to 'see' how the atoms and molecules of the adsorbate are arranged, on which active centre the electrode reaction begins and proceeds at a high rate, what happens to the surface in adsorption–desorption processes, etc. So far, the STM is not able to provide answers to questions such as how the elementary step in the electrode process occurs, how the reaction is influenced by the scanning probe, and whether or not the processes occurring on the surface monitored by the probe and on other sections of the electrode are identical. However, there are no grounds for doubting that in the immediate future answers to these questions will be obtained with the aid of the combined use of STM, AFM, and optical and structural methods. However, even now, in the early stages of the development of scanning probe microscopy, many important results requiring comprehensive consideration have been obtained. We shall examine the latest results in this field.

1. Direct observation of the atomic structure of the electrode surface in solution

Even before the STM era, cyclic voltammetry and structural methods made it possible to establish that a change in the potential of the platinum electrode leads to the reconstruction of the surface layers, which is accelerated by oxygen adsorption-desorption processes. The reconstruction of the Pt(111) surface in sulfuric acid has been investigated by the STM method in situ.[57–60] It was established that when the potential is cycled in the range 0.10–0.65 V relative to the normal hydrogen electrode (NHE), the surface of platinum is stable as a function of time and extensive terraces with a monatomic height (0.23 nm) can be seen on it, while cyclic voltammetry (CVA) reveals a high degree of perfection of the Pt(111) single crystal [the shape of the curve resembles a butterfly, there are no distinct peaks corresponding to weakly and strongly bound hydrogen characteristic of a polycrystalline material, and at 0.45 V a sharp peak is observed and is caused, according to STM data obtained in situ, by an order–disorder transition in the monolayer of adsorbed bisulfate having a $(\sqrt{3} \times \sqrt{7})$ structure†].[60] If the potential is displaced to the hydrogen adsorption and evolution region, the CVA curve changes irreversibly and begins to resemble the curve characteristic of polycrystalline platinum,[57–60] while on the STM image a 'noise' appears. Further cycling in the range 0.05–1.5 V leads to an increase in the 'noise' on the image, although after five cycles the monatomic steps can still be seen and their distribution in space does not change.[60] The authors concluded that the adsorption–desorption of oxygen is accompanied by a rearrangement of the surface layers of platinum with the formation of randomly oriented islands 3–5 nm in diameter and with a height corresponding to 1–2 atoms: the adsorbed oxygen is incorporated in the surface layer and displaces some of the platinum atoms, which do not return to their former sites after the desorption of oxygen. It is not surprising that the rearranged surface gives rise to a CVA curve characteristic of a polycrystalline material.

The surfaces of platinum single crystals have been studied in detail[61] by the CVA and STM methods. It was established that the degree of ideality of the surfaces of the single crystals is greatly influenced by the preliminary treatment of the platinum before the electrochemical experiment and by the adsorption of oxygen during the recording of the CVA curve (thus the stage where the platinum heated in a hydrogen flame is cooled in water containing dissolved oxygen may 'spoil' the surface).

The Pt(111) surface, which is relatively insensitive (after heat treatment) to the presence of oxygen in the cooling water and is stable during cycling in the hydrogen and double layer regions, is rapidly spoiled when the potential shifts to +1.4 V (NHE): peaks due to weakly and strongly bound hydrogen appear on the CVA curve, the sharp peak at 0.45 V vanishes, and the STM images reveal a transformation of the atomically smooth terraces into grainy surfaces,[61] while low energy electron diffraction data indicate the loss of long-range order and the presence of a large number of randomly distributed surface defects,[62,63] which agrees well with the results of other studies.[57–60]

A surface of the Pt(100) single crystal has a lower reticular density and exhibits a greater tendency to undergo reconstructions.[64] A freshly polished Pt(100) face contains a large number of defects, which can be 'healed' by annealing at about 1000 °C with subsequent cooling in an oxygen-free atmosphere (cooling in iodine vapour, which is adsorbed on the platinum surface and prevents the influence of oxygen, yields the best results). According to STM and voltammetric data, the Pt(100) surface exhibits a high degree of ideality. The adsorption of oxygen on cooling or at high anodic potentials in solution leads to the appearance of a large number of linear surface defects along continuous rows of atoms: the STM image shows clearly a network of linear defects with rectangular cells, and in addition terraces are clearly seen.[61]

Rougher surfaces can also be observed with the aid of the STM. Polycrystalline platinum has been selected as the object of study.[65–68] After mechanical polishing, washing, and prolonged annealing, the platinum surface is entirely suitable for the investigation of oxidation processes, the electrodeposition of metals, the synthesis of conducting polymers, the mobility of atoms, etc. and even atomic resolution can be achieved on individual sections of the surface.

Gold single crystals have been studied in fair detail.[7,69–82] After treatment in a flame and cooling in pure water, the surface of Au(111) consisted of extensive atomically smooth terraces separated by monatomic steps.[7] The topography of the Au(100) surface was characterised by the presence of a large number of islands with a monatomic height. According to Nichols et al.,[69] the structural rearrangement of the denser hexagonal (5×20) lattice, formed on treatment of Au(100) in a flame, into the less dense cubic (1×1) surface, liberates approximately 20% of the surface atoms. These in fact form the above islands by surface diffusion.

The influence of the adsorption of anions and oxygen on the topography of Au(100) has been investigated.[69] The Au(100) surface is stable in 1 M H_2SO_4 solution at a potential of +0.4 V relative to the saturated calomel electrode, but the displacement of the potential into the +1.0 V region leads to the disappearance of the islands. A similar picture is observed in 50 mM H_2SO_4 + 5 mM HCl solution: the islands dissolve at +0.7 V. The polarisation of Au(100) at +1.25 V in 50 mM $HClO_4$ + 1 mM $Cu(ClO_4)_2$ solution leads to the appearance of a rough surface in which the height of the rugosities is ~1 nm as a result of the formation of oxides. But after the displacement of the potential into the double layer region, the surface is smoothed out — both the rugosities and the islands with a monatomic

† The $(\sqrt{3} \times \sqrt{7})$ structure corresponds to the sulfate superlattice in which the distances between the nodes are greater by factors of $\sqrt{3}$ and $\sqrt{7}$ than the distances between the atoms of the Pt(111) substrate.

height vanish. The authors explain this phenomenon by the increase in the mobility of the gold atoms following the adsorption of anions and the desorption of oxygen.

More vigorous oxidation of Au(111) (a film sputtered onto mica) in perchloric acid occurs when the electrode potential is cycled in the range 0.7–2.0 V relative to a quasi-equilibrium $Ag/AgClO_4$ electrode.[70,71] At potentials of 1.25 and 1.45 V, the CVA curve shows anodic peaks corresponding to the formation of gold oxide, whilst during the reverse scan the oxide is reduced at 1.05 V. At the anodic limit in the cycling of the potential of $E_a = 1.7$ V, small pits arise on the gold surface and rapidly disappear. At $E_a = 1.7$ V, the pits attain dimensions of the order of 4 nm and only vanish after 10 min. After intense oxidation ($E_a = 2.0$ V), many large pits are formed, the boundary of the terrace becomes curved, and the picture then remains unaltered until the introduction of 0.05 mM HCl into the solution. After this, the steps in the terrace become straightened in 15 min.[70] These findings confirm yet again that the fairly high mobility of the surface gold atoms increases still further in the presence of halides.[72] In contrast to gold, the defects on the surface of platinum, arising as a result of the adsorption–desorption of oxygen at high anodic potentials, are not healed during the experiment.[57–63]

The atomic structure of the unreconstructed Au(100) surface has been observed with the aid of the STM in situ.[73–74] The results of studies on the processes involved in the rearrangement of the Au(111), Au(110), and Au(100) surfaces as well as high-index gold faces by means of STM and AFM have been described.[75–82] Scanning probe microscopy has been used to investigate the state of the surfaces of silver,[83–87] copper,[88] carbon glass,[89] highly ordered pyrographite,[90,91] and other electrode materials, but their detailed consideration is outside the scope of the present review.

2. The study of adsorbed atomic layers

Adsorption with charge transfer, leading to the formation of adsorbed atomic layers at potentials more positive than the phase deposition potential [in the English language literature, the term underpotential deposition (UPD) has become established], has become the object of vigorous study during the last 20 years. There are several reasons for this. The structure and properties of adsorbed atomic layers differ from those of bulk-phase deposits; noble metals modified by adsorbed atoms possess unique catalytic properties (increased activity and selectivity, high resistance to catalyst poisons); the formation of adsorbed atomic layers is the first stage in the bulk-phase deposition of metals, the formation of nuclei on them being of fundamental interest in the study of the processes involved in nucleation and the growth of nuclei.

Voltammetry combined with coulometry and vacuum structural methods have been used traditionally to investigate the UPD. The development of SPM has led to new possibilities for monitoring in situ the state of the surface during the adsorption–desorption of atoms.

The deposition of copper on gold is one of the processes that has been investigated in greatest detail. A gold film 100 nm thick with the (111) texture, sputtered onto glass, was used as a support.[92] The reference electrode was a copper wire and the state of the surface was monitored with the aid of the AFM with atomic resolution.

The hexagonal structure of the Au(111) substrate with atomic distances of 0.29 nm is clearly observed at potentials more positive than the copper adsorption potential in sulfate (0.1 M H_2SO_4 + 1 mM $CuSO_4$) and perchlorate [0.1 M $HClO_4$ + 1 mM $Cu(ClO_4)_2$] solutions. Although the sulfate is adsorbed strongly at these potentials (+0.7 V relative to the copper reference electrode), its influence on the structure of the image was not observed. The authors explain this finding by the fact that the needle of the AFM displaces the adsorbed sulfate atoms during the scanning of the surface. A compressed hexagonal close-packed (HCP) Cu(111) copper layer with atomic distances of 0.26 nm (the atomic radii of Cu and Au are 0.175 and 0.142 nm respectively), rotated by 30° relative to the gold lattice, is observed at a cathodic overpotential of 0.05–0.10 V in both solutions after the deposition of several copper monolayers. Copper dissolves layer-by-layer and at +0.7 V the gold support without visible structural changes is observed, which indicates, according to the authors,[92] the complete reversibility of the adsorption–desorption process. This claim appears unduly dogmatic, since experiments in which AFM and STM are employed are carried out as a rule on the smoothest sections of the surface (otherwise atomic resolution cannot be achieved), while the reconstruction processes, induced for example by surface alloy formation, occur most vigorously on defects (dislocations, grain boundaries, etc.).[93]

An hexagonal close-packed copper monolayer with interatomic distances of 0.29 nm, rotated by 30° relative to the substrate, is observed in perchlorate solution at +0.11 V (the potential of the desorption peak on the CVA curve is +0.33 V), while the $(\sqrt{3} \times \sqrt{3})R30°$ open structure with interatomic distances of 0.49 nm is observed in sulfuric acid solution at +0.1 V. The same structure has been observed in situ with the aid of the STM in other investigations.[52,73,94,95] Similar results have been obtained in the analysis of the diffraction of low energy electrons.[96] Auger spectroscopy[97] of electrodes removed from the solution indicates the coadsorption of the sulfate. The adsorption of the sulfate on Au(111) in sulfuric acid solution has been investigated by IR spectroscopy and by means of STM in situ.[98] It has been shown that the SO_4^{2-} anion forms a $(\sqrt{3} \times \sqrt{7})$ superlattice with a degree of occupation of 0.2.

The $(\sqrt{3} \times \sqrt{3})R30°$ structure of the adsorbed copper atoms should correspond to a degree of filling of the monolayer of 1/3. In a sulfate electrolyte, there are two sharp desorption peaks on the CVA curve,[52,99] at +0.05 and +0.21 V, their areas being 0.15 and 0.30 mC cm^{-2} respectively, while the theoretical charge necessary for the adsorption of a monolayer (1×1) is 0.44 mC cm^{-2} (on the assumption of two-electron transfer), i.e. according to the coulometric data 2/3 of a monolayer is adsorbed at 0.1–0.15 V. Among the studies known to the authors, integration of the more anodic adsorption peak yielded a degree of occupation of 0.38 only in the study of Haiss et al.[95] This may be associated with the insufficiently low rate of scanning of the potential, since Shi and Lipkowski[99] maintained the electrode at the required potential for up to 10 min in order to obtain the equilibrium degree of adsorption. Furthermore, for determination of the degree of coverage it is better to employ the anodic branch of the CVA curve so as to eliminate the influence of the diffusion from the dilute solution on the adsorption kinetics.

Detailed thermodynamic analysis of the CVA curve showed[99,100] that the maximum coadsorption of the sulfate (one SO_4^{2-} ion on two adsorbed Cu atoms) occurs for degrees of coverage of the substrate by copper of $\theta = 0.25 - 0.7$ The $(\sqrt{3} \times \sqrt{3})R30°$ structure observed with the aid of STM and AFM corresponds to the adsorbed sulfate ions and not to copper atoms. Gordon et al.,[101] who investigated the adsorption of copper on gold by microgravimetry (quartz microbalance), EXAFS spectroscopy, the GIXS method (grazing incidence X-ray scattering or, more briefly, 'surface X-ray scattering'), which makes it possible to identify the surface structure from X-ray scattering data, and electrochemical methods, arrived at similar conclusions. The degree of charge transfer in the adsorption of copper is close to 2 and depends little on the potential. These results agree well with the multistage adsorption model,[102,103] according to which the adsorbed copper atoms substituted the SO_4^{2-} ions on the gold surface, arranged in such a way that the sulfur atom is located at the copper adsorption site, whilst three oxygen atoms are linked to three neighbouring gold atoms (Fig. 7).

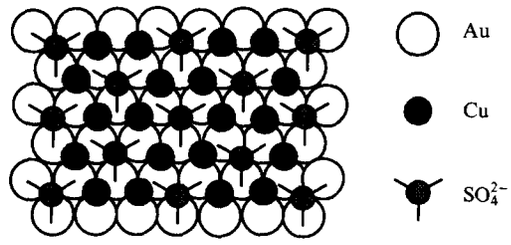


Figure 7. Schematic illustration of the structure of the adsorbate on Au(111) in sulfuric acid solution.

Several interesting features of the Au(111)/Cu/SO_4^{2-} system are noteworthy. Within the limits of a single atomically smooth Au(111) terrace, the sections of the $(\sqrt{3} \times \sqrt{3})R30°$ structure are separated by a phase boundary (the neighbouring rows of adsorbed sulfide ions are displaced to the 1/2 sites) — the situation is analogous to the formation of twinned crystals. At a potential of +0.2 V, the adsorbed copper atoms are partly desorbed [bands of the $(\sqrt{3} \times \sqrt{3})R30°$ lattice 5 – 10 nm wide and several nanometers long are observed].[52] The boundary of the $(\sqrt{3} \times \sqrt{3})R30°$ layer has been detected also in another study.[92] At +0.25 V, the lattice disappears completely, but the atomic resolution for the Au(111) surface cannot be achieved until the complete removal of the adsorbed atoms. At low coverages, the adsorbed copper atoms and sulfate ions apparently possess a high mobility (two-dimensional gas)[52,99] and their movement makes it impossible to obtain a clear-cut STM image.

When the electrolyte contains chloride ions (they can diffuse through the salt bridge when a calomel or a silver/silver chloride reference electrode is employed), the (5 × 5) lattice with interatomic distances of 0.37 nm is observed in addition to the $(\sqrt{3} \times \sqrt{3})R30°$ structure.[73] The STM yields an image comprising approximately ten $(\sqrt{3} \times \sqrt{3})R30°$ and (5 × 5) domains on a (22 × 22) nm section of the surface.[95] According to a study[104] of the coadsorption of copper atoms and halide ions on Au(111) and Pt(111) from 50 mM H_2SO_4 + 1 mM $CuSO_4$ + 0.1 mM KX (X = Cl^-, Br^-, I^-) solutions on gold at a potential of 285 mV (NHE), in the presence of chloride the STM records the (5 × 5) structure. In the bromide solution, the interatomic distances are increased by 6% [the (4 × 4) lattice relative to Au(111)], while in the presence of iodide a further increase in the adsorbate lattice parameter is noted — the (3 × 3) structure is observed [the same structure has been seen[105] on Au(111) in a study of the coadsorption of iodine and silver]. Coulometry yields a degree of coverage of the surface by adsorbed copper atoms (on the assumption of a two-electron transfer) equal to 0.4 of a monolayer regardless of the nature of the halide. According to the authors, the STM yields an image of the lattices of the chlorine, bromine, and iodine adsorbed on a layer of preadsorbed copper atoms, because an increase in the distances between the adsorbed atoms is correlated with the dimensions of the halides. It has been suggested that the adsorbed copper is partly discharged and stabilised by the anions.

Many fewer studies have been devoted to the UPD of copper on platinum.[104,106,107] This is apparently associated with the experimental difficulties in the preparation of platinum single crystals with a high degree of ideality and of clear-cut images of the surface with atomic resolution.

The first publication on the study of the UPD of copper on platinum with the aid of the STM in situ did not appear until 1991.[106] The substrate consisted of a Pt(111) single crystal treated in a burner flame; a 0.05 M H_2SO_4 + 5 mM $CuSO_4$ solution and a hydrogen reference electrode were used to prevent the contamination of the electrolyte with traces of chloride.

When the electrode potential is cycled in the range 0.5 – 0.8 V (NHE) at the rate 1 mV s^{-1}, a CVA curve with two sharp desorption peaks at potentials of 0.67 and 0.69 V and a half-width of about 5 mV is recorded. The overall charge in the desorption of adsorbed copper atoms is 460 μC cm^{-2} (this is twice as great as for the adsorbed hydrogen atoms in sulfuric acid); integration of the more anodic peak yields 270 μC cm^{-2}, which corresponds to approximately 60% coverage of the platinum surface by the adsorbed copper. A clear-cut image of the hexagonal $(\sqrt{3} \times \sqrt{3})R30°$ adsorbate structure with distances between the projections of about 0.5 nm was obtained at a potential of 0.68 V. The authors[106] believe that this is the lattice of adsorbed copper atoms and the discrepancy between the coulometric and STM data [we recall that a degree of monolayer coverage of 1/3, i.e. 160 μC cm^{-2}, and not the experimentally observed 270 μC cm^{-2} should correspond to the $(\sqrt{3} \times \sqrt{3})R30°$ superlattice] is explained by the effects due to the charging of the electrical double layer on desorption of the sulfate and bisulfate anions. However, such a large difference between the charges (110 μC cm^{-2}) can be hardly due to a non-Faraday process. Apparently, as in the case of the UPD of copper on Au(111),[52,73,92,95,100–103] the STM yields an image of the structure of the adsorbed sulfate.

At a potential of 0.8 V, the STM yields, with atomic resolution, the image of a nonperiodic structure in which the height of the projections is 0.04 – 0.06 nm and the average distance between them is 0.5 – 0.6 nm. It was not possible to obtain the image of the hexagonal Pt(111) lattice. On consecutive recording of several images of the same section of the surface, it was found that the disposition of the projections and hollows varies with time; this is probably associated with the mobility of the adsorbed sulfate and bisulfate ions.[106] The influence of organic additives on the UPD of copper on platinum has also been investigated in another study[107] with the aid of STM in situ, but it was not possible to record the structure of the adsorbate with a lateral (side) atomic resolution.

A study has been made[104] of the sorption of copper on platinum in the presence of halides from 50 mM H_2SO_4 + 1 mM $CuSO_4$ + 0.1 mM KX solutions, where $X^- = Br^-$ or I^-. An image of platinum with atomic resolution was obtained initially in sulfuric acid solutions at 380 mV (NHE) and the interatomic distances and the orientation of the substrate were determined. After this, in the solution with added KI the $(\sqrt{3} \times \sqrt{3})R30°$ structure was observed at the same potential for several hours. This superlattice was not observed in ex situ studies after the removal of the electrode from the cell; it apparently exists only in solution. The same structure has been observed in a solution with added KBr at a potential of 400 mV. In both cases, a copper monolayer (1 × 1) is deposited on the platinum surface according to coulometric data. The authors believe that the recorded $(\sqrt{3} \times \sqrt{3})R30°$ structure corresponds to a second layer of the superlattice consisting of iodide or bromide ions adsorbed on the copper monolayer [the $(\sqrt{3} \times \sqrt{3})R30°$ iodine lattice on Pt(111) in perchloric acid solution with added iodine has been observed by Yau et al.[108]].

The adsorption of lead atoms on silver single crystals may serve as an example of yet another system which has been studied in detail by means of electrochemical and structural methods and also in situ with the aid of STM.

Several absorption – desorption peaks in the UPD region have been observed on the CVA curve for the Ag(*hkl*)/Pb^{2+} system, which indicates the stepwise formation of dimeric monolayers with different superlattice structures depending on the crystallo-graphic orientation of the substrate and the electrode potential.[109] The use of the STM with lateral atomic resolution in situ demonstrated the formation on Ag(111) of a compressed HCP Pb monolayer, rotated by 4.5° relative to the lattice of the support, with distances between the nearest neighbours of 0.34 nm in the region of potentials more positive than the equilibrium value by 0 – 100 mV.[110]

A completely different picture is observed on Ag(100) in the same potential range. At 50 mV, the application of the STM in situ

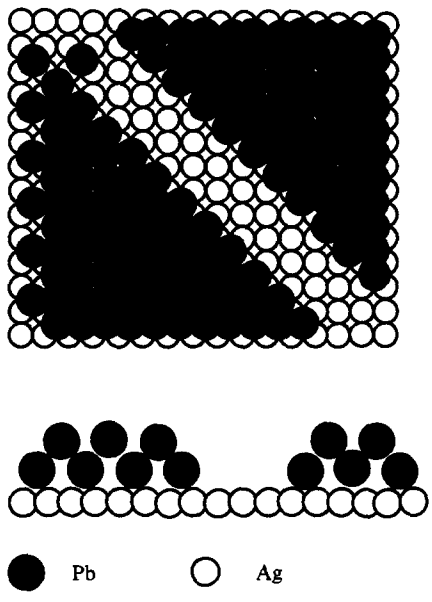


Figure 8. Schematic illustration of the two-layer $c(2 \times 2)$Pb–$c(2 \times 2)$Pb adsorption lattice with a twin boundary between the domains.

demonstrated the presence of a square lead superlattice with a relatively low reticular density. The symmetry of the superstructure and the distances between the first (0.40 nm) and second (0.59 nm) nearest neighbours are satisfactorily consistent with the 'Ag(100) upper layer–$c(2 \times 2)$–$c(2 \times 2)$Pb' double layer superlattice (Fig. 8), as postulated previously.[111] However, measurements of the degree of surface coverage, Monte Carlo mathematical modelling, and tunnelling microscope data indicate that the adsorbed lead atoms form ordered domains separated by boundaries (the chess board effect).[109]

At relatively high anodic potentials (more positive than the equilibrium value by 120–200 mV), the structure of the first Ag(100)–$c(2 \times 2)$Pb adsorbed layer cannot be observed with the aid of the STM. This can be explained by the high mobility of the adsorbed lead atoms at low and moderate surface coverages (the exchange current of the adsorbed lead atoms increases sharply at low surface coverages[112]). The Ag(100)–$c(2 \times 2)$Pb structure corresponds to $\theta = 0.5$ (each adsorbed atom occupies two adsorption sites in the square lattice), which also agrees well with the results of mathematical modelling for an energy of interaction between nearest neighbours of 2.5×10^{-21} J atom^{-1}.[113]

The structural transformation of the square Ag(100)–$c(2 \times 2)$–$c(2 \times 2)$Pb bilayer into a compressed HCP monolayer has been observed in situ with the aid of STM with the potential being varied from 50 mV to zero. It was postulated that this process begins at the boundaries of the ordered domains of the bilayer, the relative compression of the adsorption layer agreeing well with STM and X-ray scattering data for a hexagonal close-packed layer of adsorbed lead atoms on Ag(111).[109]

Thus, regardless of the crystallographic orientation of the silver substrate, the adsorbed lead atoms form an HCP Pb(111) monolayer. This unexpected result emphasises yet again the unique possibilities of the use of the STM in situ for the investigation of electrode processes.

In the Au(*hkl*)/Ag^+ system, there is a strong adsorbate–substrate interaction and the lattice parameters differ only slightly (0.2884 nm for gold and 0.2890 nm for silver), which makes it possible to expect the operation of the Frank–Van der Merwe mechanism, i.e. the formation of dimeric nuclei and subsequent layer-by-layer growth of the deposit. The silver adsorption–desorption process on gold depends greatly on the crystallographic orientation of the substrate. The degree of surface coverage by the adsorbed atoms was determined[109] from the anodic desorption curves after brief (not longer than 2 min) polarisation of the electrode in dilute (10^{-5}–10^{-3} M $AgClO_4$) solutions at the equilibrium silver deposition potential. The formation of noncompressed silver monolayers with an orientation epitaxial relative to the substrate was observed with the aid of the scanning tunnelling microscope.[109,114–119] In experiments with prolonged (of the order of 40 min) maintenance of the electrode at potentials close to the equilibrium value (0–15 mV), evidence for the formation of the Au–Ag alloy, beginning on the surface defects and the boundaries of the projections, was obtained.[119]

The UPD of silver on Au(111) in a sulfate solution has been investigated.[120] The $(\sqrt{3} \times \sqrt{3})R30°$ structure was observed for this system for the first time with the aid of the STM. According to coulometric data, this lattice corresponds to 1/3 of the silver monolayer. The authors attribute the STM image to the silver superlattice, but in this case the microscope can record both adsorbed silver atoms and sulfate anions (the probable structure of the adsorbate is illustrated schematically in Fig. 9). The results of a detailed study of this system with the aid of in situ and ex situ methods have been published.[121]

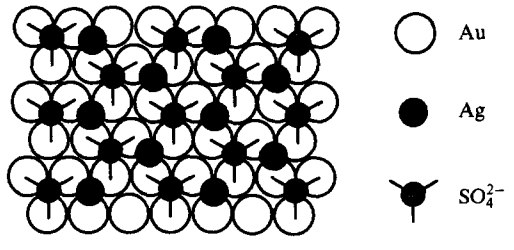


Figure 9. Schematic illustration of the $(Ag\sqrt{3} \times \sqrt{3})R30°$ adsorption lattice on Au(111).

The influence of the nature of the anion on the UPD of silver and mercury on Au(111) has been studied[117,122,123] with the aid of atomic force microscopy. It was shown that the mercury monolayers have an hexagonal structure with an interatomic distance of 0.58 nm (the crystal lattice parameter of solid mercury at low temperatures is 0.31 nm) in sulfate, nitrate, and perchlorate electrolytes. The adsorbed silver atoms are extremely sensitive to the size of the anion: the packing density of the adsorbate increases in the sequence sulfate (44%) < nitrate (56%) < perchlorate (64%) < acetate (100%, HCP).

The structure of the surface of gold modified by adsorbed atoms and its influence on the catalytic properties of gold have been investigated.[124–126] The structure of the bismuth monolayer on Au(111) depends on the applied potential: at potentials of 10–190 mV (more positive than the bulk-phase deposition potential), a rectangular $(p \times \sqrt{3})$ lattice, compressed along one of the axes and with an interatomic distance of 0.34 nm and a degree of surface coverage of about 60%, is formed. At potentials of 200–280 mV, there is a stable (2×2) phase with the angle $\theta = 0.25$ and a lattice parameter of 0.57 nm. The catalytic activity of the (2×2) structure in the oxidation of hydrogen peroxide is higher, since in this case the gold and bismuth atoms are accessible to the H_2O_2 molecules (Fig. 10). For the denser monolayer, only bismuth atoms are accessible, whilst for zero surface coverage only gold atoms are accessible. The maximum activity is observed when the Au and Bi atoms act jointly [124,125] When Au(111) is modified by adsorbed lead atoms, the potential at which the surface is coated by islands of the Pb(1×1) HCP phase corresponds to the highest catalytic activity,[126,127] whereas the clean surface of gold and the complete lead monolayer on Au(111) are catalytically inactive. The increased activity of the heterometallic centres is apparently associated with spatial effects

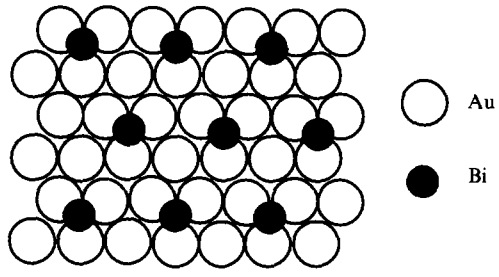


Figure 10. Schematic illustration of the Bi(2 × 2) adsorption lattice on Au(111).

and the different adsorption capacities of the adsorbed atoms and the surface atoms of the support in relation to oxygen and hydrogen atoms.

The examples of studies on the structures of adsorbed atomic layers examined here demonstrate convincingly that tunnelling and atomic force microscopes are powerful instruments for the study of adsorption processes. However, scanning probe microscopy cannot as yet do without the employment of traditional electrochemical methods (cyclic voltammetry, coulometry, etc.), in which the necessary requirements as regards purity in the experiments and in the preparation of the objects of study are met. Only comprehensive combined investigations make it possible to reach conclusions, with a high degree of reliability, about the mechanism of the adsorption process and the influence of various factors on the latter.

3. Scanning microscopy of the initial stages of the electrodeposition of metals

Scanning probe microscopy proved extremely useful for the investigation in situ of the initial stages of the electrocrystallisation and corrosion of metals, because the size of the nuclei of the new phase does not as a rule exceed several tens of atoms.[128,129] There are numerous publications devoted to the use of SPM for the observation of processes involving the phase deposition of metals from model and industrial electrolytes under potentiostatic, galvanostatic, and pulsed electrolytic conditions.[2,3,5,7,11,32–34,42,73,91,109,130–155] The influence of organic additives on the mechanism of electrocrystallisation has been studied in a series of investigations.[152–155] An increasing number of publications have been appearing on the use of SPM for the study of the structure and mechanism of formation of passive films in anodisation and also of the initial stages of corrosion processes.[156–166]

Despite the diversity of the systems investigated and the characteristic features of each of them, the following general conclusions can be made: (1) nucleus formation always begins on the active centres of the substrate, which consist of the projections on the boundaries of the terraces and of crystal lattice defects (as a rule, dislocations); (2) the nuclei of the new phase are formed later on the flat terraces, where the number of defects is small, and then on the defects themselves; (3) in the vast majority of studies, it has been concluded that the height of the nuclei is several times smaller than their transverse dimensions, which indicates a high energy of interaction of the atoms of the deposited metal with the atoms of the substrate.

We shall consider certain examples of the investigation of the initial stages of electrocrystallisation by use of the STM in situ. Generalised results of the study of the 'adsorption layer–phase' transition on the surface of gold in 10^{-5} M $AgClO_4$ solutions have been published.[109] The processes, involving the formation of a monolayer of adsorbed atoms and of the three-dimensional silver phase, are controlled by diffusion under these conditions and are slow. A special polarisation procedure, in which the electrode is maintained at specific potentials, was used to achieve the deposition of the required number of silver monolayers on gold. The number of monolayers was monitored coulometrically by the successive etching of the deposit. The formation of three-dimensional silver crystals was not observed microscopically up to the deposition of 40 monolayers. The mechanism of the layer-by-layer deposition of silver was supported by the formation of the lead UPD on such a silver deposit. Cyclic voltammetry in a lead-containing solution yields adsorption–desorption curves typical of the Ag(*hkl*)/Pb^{2+} systems, which are characteristic of the deposition of two or more silver monolayers on Au(*hkl*). Scanning tunnelling microscopy also indicates the layer-by-layer epitaxial growth of the silver deposit on Au(*hkl*). The uniform distribution of the deposit on the surface of the substrate is further confirmed by data obtained by scanning Auger spectrometry.[114–116]

In the deposition of fewer than two silver monolayers, slow alloy formation between the gold atoms of the surface layer and the silver atoms of the deposit is observed. In this case, CVA in solution with added lead gives rise to a curve with features characteristic of two systems: Ag(*hkl*)/Pb^{2+} and Au(*hkl*)/Pb^{2+}.

The observed layer-by-layer growth of the silver deposit on gold can occur in different ways depending on the degree of ideality of the substrate and on the overpotential.

1. The monolayer growth of a single nucleus on a surface free from screw dislocations at relatively low overpotentials (the growth of a new two-dimensional nucleus begins after the layer of silver has spread over the entire surface).

2. The formation of several nuclei on a surface free from screw dislocations at relatively high overpotentials and the subsequent growth of a packet of layers (polynuclear multilayer growth).

3. Multilayer spiral growth on the surface screw dislocations at low overpotentials.

In the study of the 'adsorption layer–phase' transition in more concentrated solutions (10^{-1} M $AgClO_4$), a time dependence of the current (current transients) with two characteristic sections was observed. For short times, the descending part of the transient corresponds to the formation of several monolayers of the deposit. The subsequent increase in the current is associated with the change in the nature of the deposition and the formation of three-dimensional multilayer growth packets. The dependence of the stationary current on the overpotential is evidence in support of the multilayer growth on the screw dislocations on the silver layers inherited from the gold substrate.[109]

The study of the phase deposition of lead on silver single crystals at potentials more negative than the equilibrium value showed that, regardless of the crystallographic orientation of the substrate, the lead films and three-dimensional crystallites have the (111) texture.[110,111,130–133] This means that the compressed two-dimensional HCP layer of adsorbed lead atoms constitutes the base for the subsequent epitaxial three-dimensional formation and growth of the bulk phase of lead. The influence of this sublayer on the nucleation process and the growth kinetics has been analysed on the basis of the atomistic theory of nucleation.[134]

Parallel monatomic steps have also been observed[135] in situ with the aid of STM in the three-dimensional growth of a lead film. According to the authors, these were generated by a screw dislocation (the image of an 80 × 80 nm section of the surface clearly shows five growth steps). The specific boundary energy of a monatomic step was estimated[135] from the average distance between the steps and the overpotential employed. It proved to be 3×10^{-14} J cm^{-1}.

Measurements of the tunnelling current under the conditions of a constant height of the probe above the electrode surface showed that the effective heights of the tunnelling barrier differ from the pure Ag(100) and Ag(111) substrates, whereas in the presence on the latter of a HCP monolayer of adsorbed lead atoms they are the same and are virtually equal to the height of the barrier for the Pb(111) bulk phase. For the Ag(100)–$c(2 \times 2)$–$c(2 \times 2)$Pb bilayer superlattice, which exists at potentials of

40 – 100 mV (more positive than the equilibrium value), the height of the tunnelling barrier is appreciably lower.[109]

These results demonstrate unambiguously that the Stranskii – Krastanov mechanism operates in the Ag(*hkl*)/Pb^{2+} system: a three-dimensional lead phase is formed on a silver substrate modified by a two-dimensional layer of adsorbed atoms.[110,130,131]

Electrolytes with organic additives are employed in the majority of technological processes to ensure the necessary decorative, protecting, and physicochemical properties of the galvanic coatings. The mechanism of the effect of the additives has always interested specialists and the introduction of SPM made it possible to obtain unique new information about this problem.

The influence of benzotriazole (BTA) on the nucleation and growth of copper crystals on platinum in sulfuric acid and perchlorate electrolytes has been investigated under potentiostatic and galvanostatic conditions.[152] The density of the nuclei was determined with the aid of a Fourier transformation of the profile of the surface of the deposit, and by assuming that the characteristic frequency of the rugosities of the profile is inversely proportional to the average width of the nucleus. It was shown that in the presence of BTA the faceting of the deposit is suppressed (the crystallites have a nearly hemispherical form) and the deposition overpotential increases appreciably, but the number of nuclei hardly changes.

Crystal Violet (CV) and benzotriazole derivatives were selected in other studies[153–155] as additives to sulfuric acid and perchlorate copper-plating electrolytes. The substrate was gold film sputtered onto glass and annealed in a burner flame in order to obtain the (111) texture. It was established that, in solutions without additives at overpotentials of 200 – 400 mV, instantaneous nucleation and three-dimensional growth of crystallites 1 – 10 nm high take place. The introduction of 10 mg $litre^{-1}$ of CV into the 0.1 M H_2SO_4 + 0.05 mM $CuSO_4$ solution suppresses the tangential growth of the crystals — their height does not exceed 1 nm. However, in a solution with 0.1 M H_2SO_4 + 1 mM $CuSO_4$ this additive hardly affects the morphology of the copper crystals.

Regardless of the presence of additives in the solution, the nucleation of the copper crystals takes place on defects; the nuclei are not formed on the flat defect-free terraces. The authors explain this finding by the greater size of the organic molecules, which cannot block tightly the steps and defects on the substrate, allowing access by the adsorbed copper atoms and ions to the nucleation and growth sites.

The influence of organic additives is manifested at later stages. In pure H_2SO_4 + $CuSO_4$ solution, copper crystallites have flat upper faces and stepped edges. In the presence of the benzotriazole derivative BT-A in 50 μM $CuSO_4$, a quasi-two-dimensional growth of the deposit takes place in the electrolyte, whilst in 1 mM $CuSO_4$ both planar and three-dimensional copper crystals are formed.

The addition of another benzotriazole derivative (BT-B) at a concentration of 10 mg $litre^{-1}$ has a more pronounced inhibiting effect. Regardless of the copper sulfate concentration, the tangential growth of the crystals is suppressed and their height does not exceed 1.5 nm.

An AFM with a wide-field (8 μm × 8 μm) piezoscanner was used to observe thicker deposits. In the deposition of copper from a 120 g $litre^{-1}$ $CuSO_4$ + 0.5 M H_2SO_4 solution at −74 mV, a thick deposit, in which the height of the rugosities is ~500 nm, is formed. In the presence of CV, the height of the crystallites reaches 10 nm [the thickness of the monatomic copper(111) layer is 0.209 nm], whilst in the presence of 10 mg $litre^{-1}$ of BT-B the lateral growth of layers with a thickness up to 1.5 nm (4 – 7 monolayers) takes place. These layers then grow together and the sites where this has taken place become the active centres for the nucleation of a new upper monolayer of copper. The authors attribute this sharp decrease in the thickness of the growing layer to the influence of the substrate. We may recall that the interatomic distances in the Cu(111) and Au(111) lattices are 0.256 and 0.289 nm respectively, while the UPD layer has a lattice parameter characteristic of the substrate. Furthermore the energy of the Cu – Au interaction is greater than that of the Cu – Cu interaction, which is indicated by the occurrence of the UPD and the formation of an alloy. The monolayer growth of copper on the extended UPD layer is apparently energetically unfavourable and the spreading of the packet of layers is accompanied by the relaxation of stresses.

The planar organic molecules of the additives are apparently more strongly adsorbed on the top of the growing layer than on the growth steps by virtue of steric factors. In this case, the inhibition of the vertical growth should be manifested to a greater extent than that of the lateral growth. The defects arising in the growing together of the lower layers may serve as the active centres for the nucleation of the new layer. Yet another factor promoting the lateral growth in the presence of additives is the overall inhibition of the process (the discharge of the ions and their incorporation into the lattice), which leads to the formation of less defective layers and hence to a decrease in the number of active centres for secondary nucleation. The principal conclusion reached by Nichols et al.[154] reduces to the statement that the form of the crystallites in electrodeposition is determined by the ratio of the rates of the secondary nucleation and the lateral growth, and that surface-active additives may alter this ratio.

An example of the use of SPM for the monitoring of the technological copper plating of printing plates is provided by another study of Nichols et al.[155] The atomic force microscope was used at the stage involving the preparation of the surface before chemical copper plating and the generation of the adhesion layer, and the STM was employed to investigate the initial stages of the electrocrystallisation of copper from industrial electrolytes with organic additives. Thus the STM has already ceased to be an instrument for purely theoretical research and is being used more frequently as an element of technological monitoring.

V. Prospects for the development of scanning probe microscopy

Naturally, the examples of the employment of SPM examined in the previous sections naturally did not exhaust all the possibilities of this method in relation to electrochemistry. Studies involving tunnelling and atomic force microscopy in biology and bioelectrochemistry,[5] organic electrochemistry, and the electrochemistry of semiconductors and conducting polymers have not been dealt with in this review, and certain studies on the corrosion of metals and alloys have only been touched upon — these require special consideration because the number of publications on these problems have been increasing every year and it is impossible to analyse them within the framework of a single article.

In concluding the survey of the latest advances in the use of SPM in the electrochemistry of surfaces and in the electrocrystallisation of metals, it is desirable to consider the problems and prospects for the development of this method. The inconsistency between the electrochemical parameters averaged over the entire electrode surface (the current – potential – time relations) and the local visual information about the structure of a small section of the electrode and the processes occurring on it (one cannot be certain that the processes under the probe and at a distance from it take place at the same rate) can apparently be regarded as the principal problem of the use of the STM in situ. The size of the tunnelling probe is so great compared with the distance between the latter and the test surface that diffusional and electrical shielding[93] or stimulation[145] [observed in the study of the deposition of copper on Cu(110) with the aid of the AFM] effects inevitably arise. In each specific case, investigators have endeavoured to take this influence into account by selecting

experimental conditions such that it can be neglected. However, they have not always been able to ensure an unambiguous interpretation of the results. The appearance in recent years of wide-field piezoscanners, capable of recording the image of a surface whose size runs into tens and even hundreds of micrometres, has made it possible to scan virtually the entire microelectrode surface with the exception of the edges (in this case, the working feedback loop would stick the probe into the dielectric material), but a satisfactory resolution is so far virtually unattainable over large areas.

The electrical conductivity of the object is not of fundamental importance for atomic force microscopy, so that the employment of the AFM for the analysis of the entire microelectrode surface might eliminate the problem of the correlation between electrochemical data and the topography (here it is necessary to take into account the possible activation of the surface by the probe[145]). The present authors are unaware of any publications of this kind, but the logic of the development of events suggests that they are to be expected in the immediate future.

Yet another problem is the recognition of the image. Scanning probe microscopy yields a picture of the surface, but it is by no means always clear what it represents. The studies on the copper UPD process on gold and platinum examined above may serve as an example. The question arises how one can distinguish an adsorbed copper atom from a sulfate ion. Tunnelling spectroscopy should apparently be relevant here, but the employment of STS in electrochemical systems has significant characteristic features. It has been shown[167] that the change in the electron work function on passing from one metal to another is compensated by the corresponding change in the Galvani potential, so that the rate of the electrode reaction (and also possibly the rate of the tunnelling of electrons to the probe) is independent of the electron work function and is determined solely by the electrode potential. In this case, the use of STS in solutions on metallic electrodes is impossible from the standpoint of the modern theory of the elementary step. However, measurements of the dependence of the tunnelling current on the height of the probe over the Ag(111) and Ag(100) substrates and the calculations of the effective tunnelling barriers have shown[109] that, for an identical potential of +300 mV relative to the Pb^{2+}/Pb electrode, these values are 0.35 ± 0.01 and 0.31 ± 0.01 eV respectively. In the presence of a lead monolayer on the surface of a silver single crystal, the height of the barrier is 0.17 ± 0.01 eV regardless of the potential (0 – 50 mV) and the crystallographic orientation of the substrate. Unfortunately, the potentials of the tunnelling probe in the measurement of the tunnelling barriers are not quoted in the communication of Staikov et al.[109] Such information might throw light on the situation. The resolution of this contradiction apparently requires careful theoretical and experimental studies on the application of STS in situ.

In discussing the prospects for the development of SPM, one can postulate that the range of objects and the different aspects of such investigations should greatly expand and that the method will be used with increasing frequency for the solution of technological problems. To a large extent, this concerns the problems of nanotechnology, which began to develop actively after the invention of the STM. The possibility of observing atomic structures led to the wish to modify the surface at the atomic level.[5,11] Investigators learnt how to draw letters and symbols with a line having a width of several nanometres, and studies on the construction of the nanoelements of integrated circuits, memory devices, elements for quantum electronics, etc. are being vigorously prosecuted. It appears that electrochemistry will not be neglected either. There have already been publications on the local (in the nanometre range) deposition and dissolution of metals, the study of electrode reactions on the surfaces of semiconductors[11] with the aid of the SPM, and the preparation of multilayer coatings with a monatomic thickness of the layers (sandwich heterostructures[109]). The development of tunnelling and atomic force microscopy has led to the development of a series of related methods,[4–6] and so called scanning electrochemical microscopy is extremely promising.[168–170] The essential feature of the method is that it employs as the probe a disc ultramicroelectrode 0.1 – 25 μm in diameter with insulated lateral surfaces on which a potential is maintained, thereby ensuring the occurrence of an electrochemical reaction — for example the oxidation of Cu^+ or the reduction of Cu^{2+} in the investigation of the dissolution of copper on the main electrode. The probe moves over the test surface and the distribution of the active dissolution centres can be inferred from the probe current.

The use of a probe as an auxiliary electrode permits selective deposition, the etching of metals and semiconductors in electrolytes with a low scattering capacity and in polymer films with ionic conductivity, and electropolymerisation. The resolution ensured by the method depends on the size of the probe, the distance between the microelectrode and the specimen, the electrolyte composition, and the electrolysis conditions and can reach 100 nm.[170] Satisfactory results have been obtained when probes consisting of very sharp noninsulated needles were employed.

A probe can be used as a reference electrode and the distribution of the surface potential can be monitored, for example, in the study of corrosion processes.[171,172] The method is called scanning potentiometry and has a very low resolution.

Yet another promising aspect of the development of SPM involves the creation of combined instruments, in which tunnelling and atomic force microscopy as well as its variations are combined with other in situ methods (optical, acoustic, microgravimetric, etc.). Such studies are already being carried out[13–17] and the first results give rise to the hope for their successful development.

Binnig and Rohrer, the inventors of the STM, entitled their Nobel lecture in 1986 'Scanning Tunnelling Microscopy — From Birth to Youth'. Likewise one may say that the youth of scanning tunnelling microscopy has now ended and that it is now an entirely serious method which has justified the boldest hopes concerning it. Scanning probe microscopy is entering the period of maturity and is used very productively in most diverse fields of science and technology. However, its main attainments still remain in the future.

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Mechanoemission and mechanochemistry of molecular organic crystals

E A Varentsov, Yu A Khrustalev

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Abstract. Data on the emission phenomena and chemical processes occurring in molecular organic crystals capable of rapid exothermic decomposition when subjected to mechanical influences are surveyed. The influence of the nature, composition, and pressure of the gaseous medium on the probability of initiation of the mechanical decomposition of single crystals is examined. The existing concepts concerning the initiation of fast reactions in organic crystals are analysed. A general scheme is proposed for the electrophysical phenomena and chemical reactions occurring when solids are subjected to mechanical influences. The bibliography includes 132 references.

I. Introduction

The study of the physical phenomena and chemical reactions occurring in solids subjected to mechanical influences may play a notable role in the search for nontraditional ways of carrying out technological processes and in the selection of new methods for controlling the activation of chemicals and materials.

The mechanical stresses acting from outside on a solid can lead to irreversible consequences when they have attained certain values: plastic deformation of the crystal lattice and decomposition of the crystal.

In the course of the decomposition of solids, chemical bonds are broken and active centres are formed, whereupon streams of electrons and ions and electromagnetic radiation are generated. These include X-rays with a wide spectral range[1-7] and various electrophysical phenomena due to the formation on the fresh surfaces of an uncompensated charge that relaxes relatively slowly and persists for a fairly long time (up to several hours in the case of dielectric materials). Naturally, the physicochemical properties of the solid (especially its conductivity) influence the intensity and kinetics of the electrophysical phenomena. Such influence is most marked in the case of dielectric materials. The forms of radiation noted above may be combined under the term cold plasma.[8] The idea of the transition of a substance to a plasma state when a solid is subjected to mechanical influences was first proposed by Thiessen.[9,10] Subsequent experimental studies confirmed the validity of this hypothesis.[1-7]

The emission phenomena and chemical reactions observed when solids are subjected to mechanical influences are summarised in the generalised scheme in Fig. 1.

Fig. 2 presents a scheme of the possible consequences of subjecting polymers to mechanical stresses. The mechanical degradation of polymer macromolecules is also accompanied by the rupture of chemical bonds: reactive free radicals (paramagnetic centres) and low-molecular-mass compounds (fragments of macromolecules down to the monomer) are generated. The mechanochemical transformations in polymers have been considered in detail in a number of studies.[1,3,6] A number of electrophysical phenomena are observed on formation of the disintegration surfaces in polymers (as in dielectrics): the appearance of an excess electrical charge, the emission of electrons, gas discharges, luminescence, and other types of emission (IR, radio waves). The characteristic features of their manifestation have been treated systematically in a number of studies.[1-4,6,7]

For a long time, the objects in the study of the mechanoemission and mechanochemistry of solids have been mainly ionic and homopolar crystals as well as polymers (see, for example, Refs 1-4, 6, and 11-13). When these substances are disintegrated, the rupture of chemical bonds is an obligatory consequence.

The structure of the molecular crystals of organic substances has a number of features, which is reflected in their properties. The structural unit in the crystal lattices of organic substances is the molecule, the atoms of which are linked by strong covalent bonds. Only weak van der Waals interactions exist or hydrogen bonds are formed between the molecules. Such a structure of molecular crystals determines many of their physical and mechanical properties: the high electrical resistivity ($10^{15}-10^{18}$ Ωm), the low melting point (down to ~600 K), and the poor mechanical strength and hardness.

Molecular organic crystals have found extensive practical applications and the study of the variation of their electrophysical and physicochemical properties when the crystals are subjected to mechanical influences is therefore a problem of current interest.

The mechanoemission phenomena and chemical reactions in molecular organic dielectric materials, which disintegrate rapidly when subjected to mechanical forces, are described in the present review. The authors have devoted special attention to the

E A Varentsov Moscow Engineering and Physical Institute, Kashirskoe shosse 31, 115409 Moscow, Russian Federation. Fax (7-095) 324 87 66
Yu A Khrustalev Laboratory for the Physical Chemistry of Modified Surfaces, Institute of Physical Chemistry, Russian Academy of Sciences, Leninskii prosp. 31, 117915 Moscow, Russian Federation.
Fax (7-095) 952 53 08

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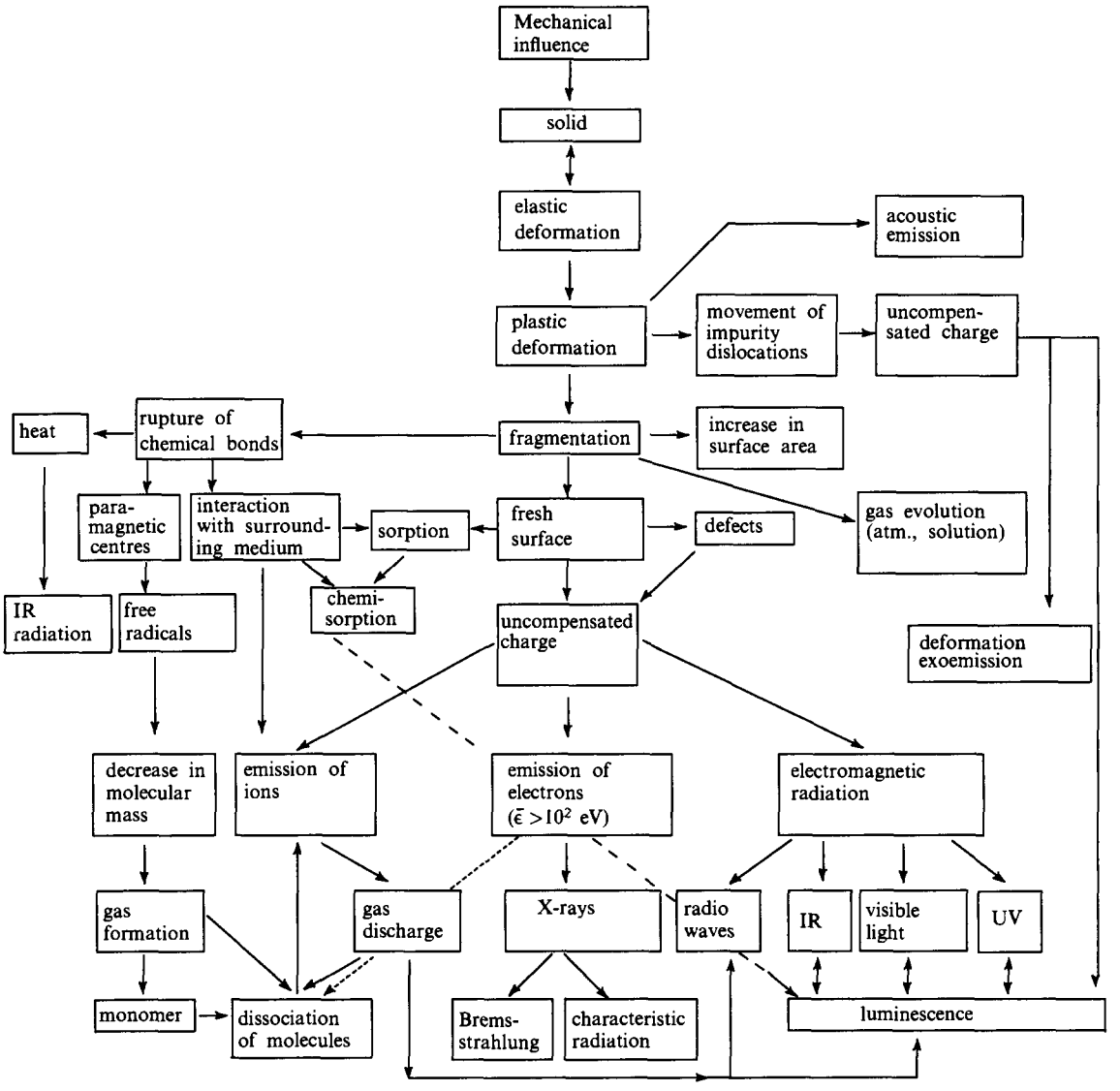


Figure 1. Generalised scheme of the emission phenomena and chemical reactions occurring when solids are subjected to an external mechanical influence.

electrophysical phenomena accompanying the appearance of new disintegration surfaces. These phenomena may induce mechano-chemical reactions in the molecular organic substances. The mechanoemission phenomena accompanied by the rupture of bonds of different nature are in our view not only responsible for the chemical reactivity of the fresh surface but also activate the gaseous medium in its vicinity.

II. Electrophysical phenomena

1. Charges on the fresh cleavage surfaces of ionic crystals

In the disintegration of dielectric solids, uncompensated charges having different signs appear on the walls of the developing crack. The very strong electric fields arising under these conditions are the cause of various emission phenomena leading also to chemical changes in the test substance.

The study of the electric fields on the freshly formed surface and especially in a developing crack is fairly complex owing to the rapid relaxation of the excess charge in the initial instant of the lifetime of the fresh surface and the small size of the electrically active regions. Thus the nonstationary electric field in the cleavage crack (the rate of propagation of which is several hundreds of metres per second) in the case of alkali metal halides (a lithium fluoride single crystal) does not exceed 20% of the initial value ($\sim 60\ \mu Cm^{-2}$) after only 10–20 s.[14]

In real crystals, defects are always present as a consequence of their deviation from the ideal periodicity. One distinguishes point defects (impurity atoms or ions, vacancies, atoms or ions of the test substance itself localised in the intestices, etc.), linear defects (dislocations — breakdown in the regular arrangement of atomic planes, in particular of boundaries between regions with different orientations of the crystal structure) and bulk-phase defects (accumulation of vacancies, pores, gas bubbles, etc.). The defectiveness of the crystal lattice as well as the process involving the rupture of an ionic bond (i.e. the very chemical nature of the ionic crystal) are responsible for the nonuniformity of the distribution of electrons between cations and anions. It must be emphasised that the electrically active structure of real crystals has been pre-programmed, i.e. specified, by the nature and characteristic features of the growth of the nuclei of the future crystals with particular defects,[15] while the process involving the disintegration of crystalline substances itself leads to the additional formation of new charged defects on the fresh cleavage surface.

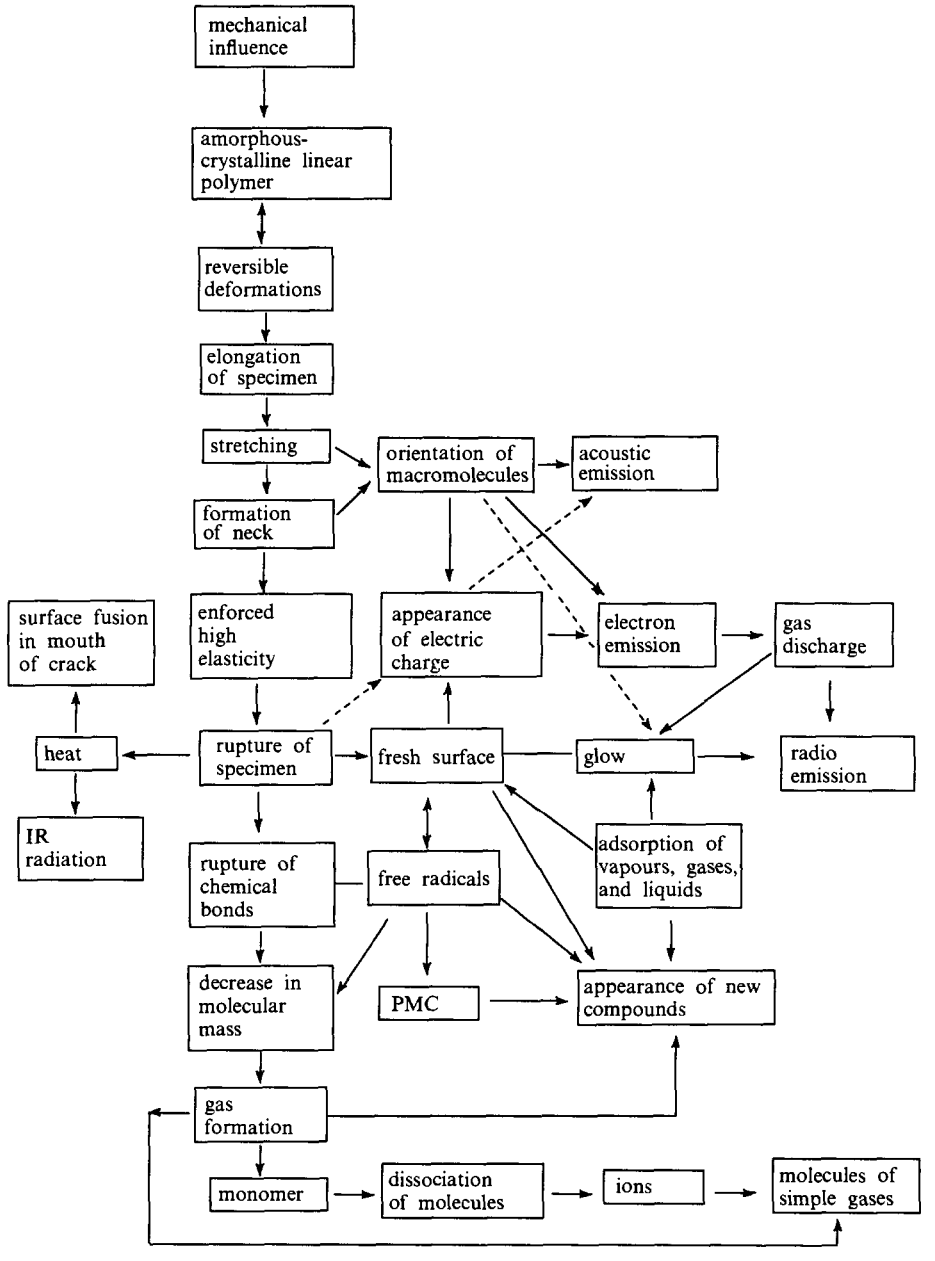


Figure 2. Scheme of possible mechanoemission phenomena and mechanochemical reactions occurring when polymers are subjected to external stresses.

The defective sites constitute electrically active centres and uncompensated ruptured chemical bonds on the disintegration surface of the crystal. Such active centres are frequently detected by the decoration method, where a decorating substance is deposited from the vapour (or liquid) phase (such substances are usually gold, silver chloride, anthraquinone, latexes, etc.). The nuclei are then formed and grow predominantly on the negatively charged section of the surface. The decoration patterns — the topographies of the surfaces and, in particular, of the cleavage surfaces with point defects and their accumulations — are investigated by optical and electron microscope methods.[15] In the case of ionic single crystals, the density of the charged active centres usually attains values of $10^{10} - 5 \times 10^{11}$ cm^{-2}. The results of the study of the electrical nonuniformity (defectiveness) of the cleavage surfaces of various solids by the decoration method have been surveyed in a monograph.[15]

Distler et al.[15] actually observed by the decoration method the electrical breakdowns between positively and negatively charged microregions on the fresh cleavage surface of a quenched sodium chloride crystal for a field strength of $\sim 10^8$ V m^{-1} (see also Deryagin et al.[1]). The decorating gold particles were condensed at the instant of the disintegration of the specimen, i.e. during the growth of the main crack. It has been noted that the charging of the cleavage surface in lithium fluoride does not influence greatly the crack propagation velocity.[16] It is believed[17] that the rate of movement of the main crack can be regulated up to its arrest with the aid of externally applied electric fields.

It has been established by modern physical research methods that the growth of the main crack in ionic crystals, in particular in alkali metal halides, proceeds nonuniformly — in jumps.[17-20] It has been claimed[20] that the power of the emission of the charged particles from the mouth of the crack exceeds by 6 - 10 orders of magnitude the power of the emission of particles from the edges of the crack. It is of interest that the low-temperature chemical reactions occurring on brittle disintegration of solid systems are also of the pulsating type.[21]

Scanning of the surface by means of a special probe electrode using the familiar vibrating capacitor principle may serve as another method for the determination of the electrical surface microrelief, for example of the mirror cleavage plane of the crystal.

Distler et al.[15] concentrated attention on the study of the point defects inducing the appearance of charged microregions on the cleavage surface, i.e. after the fragmentation of the specimen. Among the models of the mechanisms of the generation of a charge in the crack on plastic deformation and disintegration of ionic (in particular, alkali metal halide) crystals, the dislocation model proposed by Molotskii has come to be most widely used.[22] The dominant role of the dislocation mechanism in the charging of a freshly formed disintegration surface in alkali metal halides has been demonstrated.[23] The relaxation of the charge makes it possible to account for the mechanochemical dissociation of the walls of the crack (for example the emission of lithium ions from lithium fluoride).[23,24] The dislocation concept has been supported also by other workers.[18,25,26] Other defects can likewise promote the formation of a charge on the fresh cleavage surface of an ionic crystal.

A possible mechanism for the appearance of deformation luminescence and electron emission in alkali metal halides has been provided[25] by the intersection of dislocations in the course of the plastic deformation of the specimens, where there is a probability of electronic transitions which result in the appearance of electron and hole centres. The recombination of these active centres leads to the emission of electrons and photons. The movement of the dislocations at low rates of deformation (down to 10^{-5} s^{-1}) in a single slip of annealed lithium fluoride specimens leads to the accumulations of charges on the surface of the specimen up to electrical breakdown.[26]

2. Uncompensated charges on the cleavage surfaces of organic crystals

It has been established experimentally at the optical level by the method involving decoration with anthraquinone[27] that electrically charged regions, differing in the sign and magnitude of the potential, are present on the cleavage surfaces of cyclotrimethylenetrinitramine (C3MNA) and trinitrophenylmethylnitramine (3NPNA) crystals. Since the decoration was carried out several minutes after the breakdown of the crystals, the observed mosaic microrelief of the electrically active regions reflects only partially the distribution of the charge density of the electric fields on the fresh cleavage surface and in essence represents the residual charge distribution pattern despite the strong dielectric properties of the test crystals.

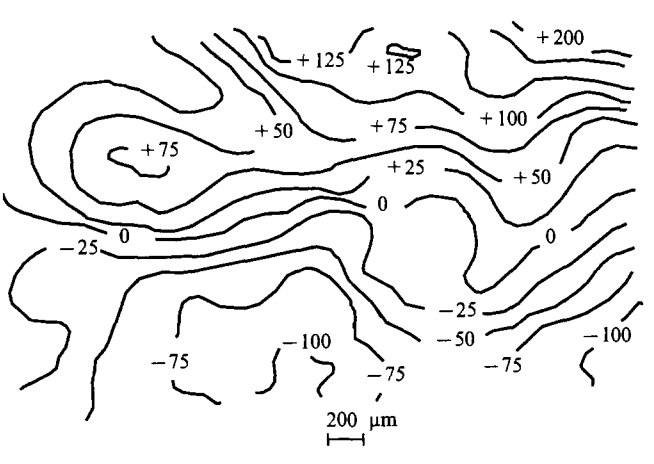


Figure 3. Electric relief of the local fields on the cleavage surfaces of a C3MNA crystal.[27]

The nature of the distribution of the electrical charges on the cleavage surfaces of the same crystals has been investigated by the scanning probe method based on the dynamic capacitor principle.[27] Topograms with a linear resolution of ~ 50 μm obtained (Fig. 3) show that the positive and negative potentials of individual sections of the cleavage surface may reach 10^3 V.

The considerable external similarity between the topograms of the electrical microrelief and the geometrical relief of the breakdown surface, which can be observed visually under a microscope with a magnification by a factor of 50–100, is noteworthy.[27] Polishing of the cleavage surface of the crystal by a solvent, which to a large extent removes the microrugosities, entails the virtually complete disappearance of the electrical microrelief. Rubbing of the solvent-etched surface with a cotton cloth again induced the appearance of an electrical potential up to 10^3 V. The subsequent relaxation of the potential depends significantly on the pressure (the rate of relaxation diminishes on rarefaction) and the humidity (Fig. 4).

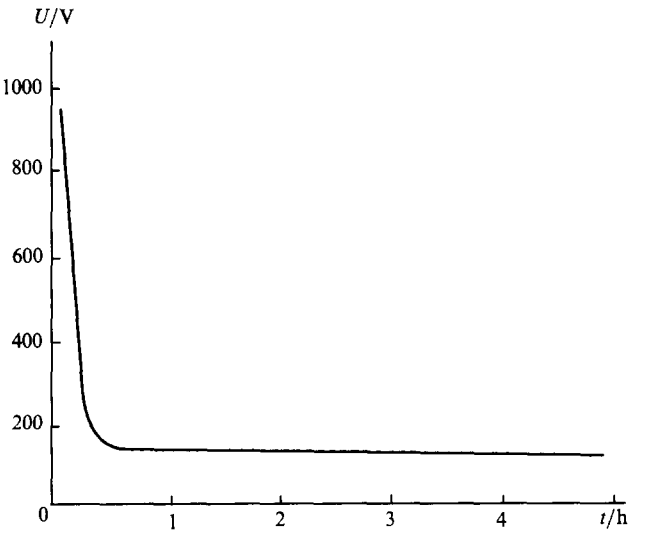


Figure 4. Relaxation of the potential (U) on the surface of a C3MNA crystal after polishing and rubbing against a fabric.[27]

3. Different ways leading to the formation of the electrical microrelief on the breakdown surfaces of organic crystals

The formation of an electrical microrelief on the breakdown surface of an organic crystal may be a consequence of a change in the geometry of the defective surface—the appearance on it of dislocations.

It has been demonstrated experimentally that the cleavage surfaces in the test crystals contain numerous steps and other imperfections.[27] These substances have dipole moments of 3–5 D.[28,29] The microrugosities may generate, in the direction of the measuring electrode, fields of different sign and potential depending on the orientation of the molecular dipoles on the cleavage steps. An experimental test on flat and point electric field sources showed that the dependence of the electrical output signal on the distance between the sources and the electrode (r) is close to exponential for $r > 0.2$ mm.[27]

The presence of steps on the cleavage surface of a sodium chloride single crystal as well as the appearance of new planes, uncharacteristic of the cubic form of the crystals, in particular the [111] plane, has been established.[30]

Thus the microrugosities on the cleavage surface of the crystal investigated may influence significantly the magnitude of the potential determined by the scanning probe method. Consequently the topography of the electrical surface microrelief

represents an electrical map of its geometry. This is also indicated by the disappearance of electric fields after the surface has been etched with a solvent.

The dislocations on the cleavage surface, giving rise to steps, are electrically charged. They distort the pattern of the electron distribution in the crystal lattice. The accumulation of electrons on the cleavage surface become the cause of the appearance of a potential at the fresh surface, where their density is three orders of magnitude higher than for the main bulk of the crystal which has been little deformed.[27]

Experiments have shown[27] that the external pressure and concentration of water vapour play a notable role in the relaxation of charges on the cleavage surface. This is evidently associated with the adsorption and desorption processes on the fresh cleavage surface, which alter the electrical relief.

It is difficult to say which of the mechanisms examined above is decisive because they are manifested simultaneously.

4. Electron emission and electromagnetic radiation emitted from the fresh cleavage surface

When organic molecular crystals of pentaerythritol tetranitrate (PETN), C3MNA, cyclotetramethylenetetranitramine (C4MNA), and 3NPNA were cleaved in a vacuum chamber at a residual pressure of $10^{-3}-10^{-5}$ Pa, the emission of electrons from the cleavage surface was recorded.[31-35] The maximum emission intensity was recorded immediately after the disruption of the specimen, decreasing by a factor of 3–6 after 2–5 s.[34,35] Bearing in mind that the delay in the recording of the emission after cleavage in the experiments of different workers[31-35] was 0.05–1 s, it follows that the initial emission intensity should have been several orders of magnitude higher than the observed value, since the rate of its decrease is nearly exponential.

The electron flux depends on the nature of the substance and the crystallographic orientation of the disrupted specimen. For example, a low electron emission has been noted for 3NPNA compared with other crystals (Fig. 5).[34,35] In C3MNA specimens the maximum electron intensity is higher by a factor of three (6×10^3 counts s^{-1} cm^{-2}) on disruption along the (010) plane than along the (001) plane. Several minutes after disruption, the electron flux as a rule exceeded the background value only by a factor of 1.5–2. In parallel experiments, the variation of the emission flux was 20%–30%. An estimate of the energy of the electrons, by the method involving tunneling through barriers, showed that it can reach values in the range 10^3-10^4 eV for organic molecular crystals.[34,35]

The intensity of the electron emission from PETN decreases by approximately two orders of magnitude 5×10^{-2} s after disruption of the specimen (Fig. 6).[31,32] Unfortunately the method used to disrupt the specimens (crushing of the crystal between two planes) precluded the recording of the emission directly from the fresh surface.

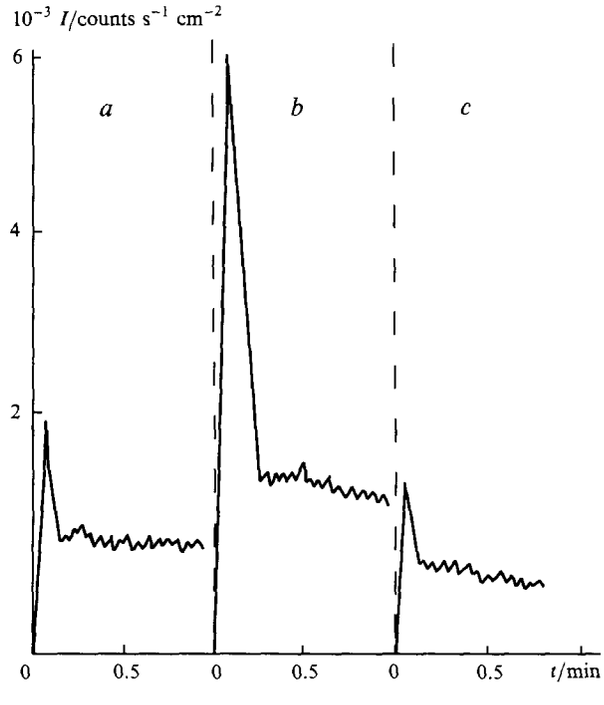


Figure 5. Kinetics of the decrease in the intensity of the emission of high-energy electrons from fresh cleavage surfaces of various crystals:[34] (*a*) C3MNA, (001) plane; (*b*) C3MNA, (010) plane; (*c*) 3NPNA (010) plane.

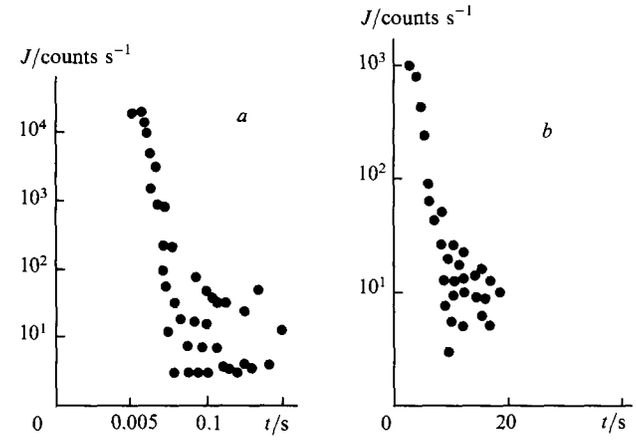


Figure 6. Decrease in the intensity of the emission of electrons (*a*) and protons (*b*) on fragmentation of PETN crystals.[31]

The proton flux was also recorded simultaneously with the electron flux,[31] but its magnitude proved to be an order of magnitude less (Fig. 6). The formation of protons is probably not always related directly to the disruption of the organic crystal, i.e. is not a result of the appearance and development of the cracks leading to the disruption of the specimen. It may be that in effect analogous to that described by Gai et al.[36] was observed in the experiment: the electrons emitted from the breakdown surface of the specimen bombard the metallic surfaces between which the crystal was contained or the metallic surfaces of the vacuum chamber, inducing the dissociative ionisation of the water molecules adsorbed on them to yield protons.

On cleavage of crystals of organic substances in the dark in the immediate vicinity of a highly sensitive photographic film in air, a compact group of individual spots exposed on the film was observed, indicating a nonuniform nature of the emission from the fresh cleavage surface.[34] Since the specimens were disrupted in air, the exposed spots reflected the pattern of the local electric gas discharges in the vicinity of the charged regions of the fresh surface. Furthermore the glow may be due to the interaction of the molecules and ions of the gaseous medium on an initial excited nonequilibrium potential surface.[37,38] The radio emission pulse in the centimetre range recorded on disruption of the crystals in air, confirms the probability of the gas-discharge processes.[34] Nor can one rule out also the possibility that the photographic film is exposed by X-rays, which was observed when crystals of organic substances were cleaved. Apparently this emission represents bremsstrahlung.[35] It is to be expected that the interaction of electromagnetic radiation arising over a wide spectral range (optical, X-ray, etc.) on disruption of a freshly formed surface may be an additional cause of electron emission.

The recording and study of the electromagnetic radiation arising on disruption of rocks and crystals have been examined in a monograph.[39]

We suggest that the very strong electric fields in the developing crack 'accelerate' free electrons, imparting energies up to 10^2-10^4 eV to the latter. Such electrons have in fact been recorded in experiments on the disruption of organic substances.[34,35] The elucidation of the cause of the appearance of the energy necessary to expel an electron from the surface of the crystal remains perhaps the main question to which so far there has been no unambiguous answer.

There exist a series of approaches which explain the appearance of the additional energy in an electron (present at a local level in the vicinity of the surface of the solid) needed to exceed the electronic work function. For example, Krylova[40,41] noted the following possibilities: the utilisation of the high-energy component in the Maxwell distribution, the Auger effect in the electron–hole recombination, the acceleration of the electrons by the internal electric field of the surface layer of the dielectric material. (For further details concerning the acceleration of electrons in internal fields, see Deryagin et al[1]). The energy promoting the expulsion of an electron, for example on photostimulation, can be induced by an external photoeffect.

If the molecule is a component of a condensed phase containing identical molecules, then additional forces begin to operate, which alter the ionisation energy to a considerable extent. In the case of organic crystals, this is the polarisation energy in the crystal (it may be compared with the solvation energy of ions in solution).[42] It has been shown by UV photoelectron spectroscopy that the ionisation potential for different crystalline organic substances is lower by 1.1–3.0 eV than the ionisation potential in the gas phase.[42]

The application of the band theory to the description of electronic processes is justified both experimentally and theoretically for many solids. It constitutes the basis of a qualitative description of the rules governing charge transfer in readily conducting materials, semiconductors with a high mobility of carriers, and dielectric materials of the ionic crystal type. However, the employment of methods of band theory for the description of the physical processes in molecular crystals, a characteristic feature of which is the small overlap of the electronic wave functions and the low mobility of the charge carriers, is by no means always valid.[43,44] For example, in anthracene and naphthalene the temperature dependence of the electron transfer process is consistent with band theory but not in all the crystallographic directions.[44] Band theory describes adequately the properties of organic crystals such as charge-transfer complexes and radical-ion salts with high electrical conductivities in the dark.[42]

It is noteworthy that the nature of the transfer of charge carriers in organic crystals is determined by the presence of capture and scattering centres, the role of which may be assumed by the crystal lattice defects.[45] For this reason, various mechanical, thermal, and radiation influences, altering the concentration and nature of the defects and their distribution, change within certain limits the electrophysical properties of the molecular crystals and thus promote or hinder the charge transfer processes, which is probably a preliminary stage in the appearance of electron emission on disruption.

III. The formation of free radicals

It was noted above that the mechanical disruption of polymers entails the rupture of interatomic bonds with formation of free radicals.[3,6,11–13,46,47] The cleavage and dispersion of crystalline substances with covalent polar bonds leads to the appearance of unsaturated bonds (free radicals).[48–52] The appearance of free radicals on disruption of the cohesion of crystals of organic substances was believed for a long time to be impossible, since it had been postulated that this entails the rupture of only weak van der Waals bonds, the energy of which are lower by one–two orders of magnitude than that of covalent bonds.[53]

An attempt was made[54] to investigate the destruction of PETN during the insertion of a chisel into the crystal under high vacuum conditions at room temperature. Unfortunately, the authors[54] did not present concrete results on the measurement of the mass spectra and merely published their conclusion that the $\dot{C}H_2-O-NO_2$ radicals are formed on rupture of the carbon–carbon bonds and are decomposed further to NO and CO. The claim that the mass spectra of the PETN decomposition products which they obtained on mechanical disruption differ from the mass spectrum of the thermal degradation products is in our view rather unconvincing. The point is that the qualitative and quantitative compositions of the gases evolved on thermal decomposition of unstable substances such as PETN, C3MNA, C4MNA, and 3NPNA depend to a large extent on the temperature range, the heating rate, the external pressure, the amount of impurities, the phase state, and other parameters.[55–60] The absence of thermostatic control or cooling in the experiment[54] on mechanical degradation also do not constitute evidence that thermal degradation did not occur.

Owens and Sharma[61] investigated the changes occurring in trinitrotoluene (TNT) and C3MNA crystals acted upon by weak shock waves. Studies by the EPR method did not permit definite conclusions, since it was not possible to assign the signal due to the paramagnetic centres. Changes in the spectrum of C3MNA subjected to the action of shock waves were detected by X-ray photoelectron spectroscopy. The decrease in the peak with an energy of 407.5 eV, corresponding to the nitrogen atom of the NO_2 group, relative to the 402 eV peak, corresponding to the ring nitrogen atom, showed that ~14% of the N–N bonds in the test substance were ruptured. Such an effect was not observed for the control specimens which had not been subjected to the action of shock waves, i.e. the effect was not induced by the X-rays with an energy of 1.2536×10^3 eV employed in the technique. In the TNT specimens subjected to the action of shock waves, a shift of the 405 eV peaks towards lower energies was observed, which can be accounted for, according to the authors,[61] by the displacement of the hydrogen atom of the $-CH_3$ or $-\rangle CH$ group towards the oxygen atom of an adjoining group.

Analysis of the products obtained under the influence of weak shock waves and the products of the low-temperature decomposition enabled the authors[61] to conclude that different mechanisms operate in the decomposition of the molecules of the initial substance and that high-temperature heating centres probably arise on exposure to shock waves. However, treatment with shock waves involves a series of significant differences from the mechanical treatment.[62] Whereas in the mechanical treatment the time elapsed from the start of the decomposition process to the instant of attainment of the maximum pressure (pulsed influences, impact) or, conversely, the time required for the decrease in the pressure from the maximum value to the end of the removal of the stress (pulsed removal of the stress) is $10^{-3}-10^{-4}$ s, on exposure to shock waves (pressure of 1 – 10 GPa) the time is 10^{-6} s. The passage of the narrow 'peak' pressure front through the bulk of the substance at a rate exceeding the rate of propagation of acoustic waves in the given medium is characteristic of a shock wave.[62] Thus, strictly speaking, treatment with shock waves constitutes a physical process, different from the mechanical process.

When triaminotrinitrobenzene (TATNB) was subjected to shock waves[63] and mechanical[64] influences, the formation of free radicals was observed.

The generation of radicals in arylindanedione dimers (ADD) has been recorded by the EPR method in studies[65,66] involving the shear deformation under a high pressure on Bridgman anvils. The release of pressure led to a rapid and irreversible decrease in the concentration of the paramagnetic centres in the polycrystalline specimen approximately by an order of magnitude. The use of a high-pressure chamber for the recording of radicals under the

conditions of a high hydrostatic pressure led to a completely different result. It was found that radicals are not generated under these conditions.[65,66] Consequently, on rupture of the bonds in ADD, radicals are formed only at high pressure when shear deformation takes place. The kinetic features of the mechanically induced dissociation of molecules under the conditions of shear deformation were established: the pressure dependence of the rate of application of the shear deformation and of the shear angle.[65,66] It was concluded[66] that the rupture of the bonds between the monomers in the dimer, leading to the formation of free radicals, occurs on brittle disruption of the crystalline ADD specimen on newly formed surfaces.

It was established[67] that the fraction of the energy consumed on rupture of the chemical bond in ADD on shear deformation at high pressures does not exceed 1%. On the other hand, most of the mechanical energy (~90%) is dissipated as heat. These data confirmed the above criticism of the study[54] in which a difference was noted between the mass spectra obtained for PETN subjected to mechanical influences and those of the thermal degradation products. Evidently, in the experiments carried out in the above study,[54] the insertion of the chisel into the crystal resulted in the transformation of a large proportion of the mechanical energy into thermal energy. Later it was found[68] that radicals were generated as a result of the mechanostimulated dissociation of the ADD molecules.

It has been established by the EPR technique[35,69] that the dispersion of the PETN, C3MNA, and C4MNA in a vibromill with glass spheres at a frequency of 50 Hz and at the temperature of liquid nitrogen in a helium atmosphere leads to the formation of paramagnetic centres, which were identified as $\dot{N}O_2$ radicals (Fig. 7, Tables 1 and 2). Evidently these radicals are products of the nonthermal decomposition of the test substances. The number of the free radicals is of the order of 10^{16} g^{-1} or 10^{12} cm^{-2}. Thus we observed[69] a fundamentally different pattern in the decomposition of the PETN crystals on disruption from that put forward by Fox and Soria-Ruiz.[54]

Fairly reliable results, indicating the abstraction of the NO_2 group from the PETN molecule, have been obtained by the EPR method, which records the paramagnetic centres directly, in combination with a low temperature (77 K) and thermostatic control. However, the accumulation of 'paired' radicals was not detected.[69] This can be accounted for by their high instability and

Table 1. Parameters of the g-tensor of the NO_2 molecules at 77 K.[35]

Matrix	g_{xx}	g_{yy}	g_{zz}	g_{av}
Ice[a]	2.0066	1.9920	2.0022	2.0003
Argon[a]	2.0037	1.9900	2.0037	1.9991
PETN	2.0065	1.9915	2.0025	2.002±0.0005
C4MNA	2.0065	1.9925	2.0035	2.008±0.0005
C3MNA	2.006	1.992	2.003	2.000±0.001

[a] Values taken from Atkins and Symons.[70]

Table 2. HFS parameters (G) of the EPR signal of the $\dot{N}O_2$ radical at 77 K.[35]

Matrix	$-B_{xx}$	$-B_{yy}$	$-B_{zz}$	A_{iso}[b]
Ice[a]	6.28	2.24	13.33	56.88
Argon[a]	−3.6	7.2	3.6	54.2
PETN	4	7	11	55
C4MNA	5	7	12	56 (±1)
C3MNA	4	8	12	56

[a] Values taken from Atkins and Symons.[70]
[b] $A_{iso} \approx \frac{1}{3}(A_{xx} + A_{yy} + A_{zz})$.

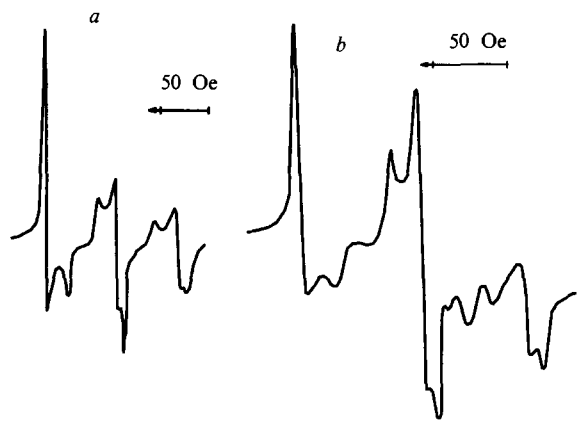


Figure 7. The EPR signals of the $\dot{N}O_2$ radicals in matrices comprising ground PETN (*a*)[69] and C4MNA (*b*)[35] at 77 K.

their rapid destruction even at 77 K or by the very great width of their signal, which is difficult to observe owing to the triplet of the anisotropic lines due to the NO_2 species. When C3MNA and C4MNA crystals dispersed at 77 K were heated to 293 K, we observed a decrease in the concentration of the $\dot{N}O_2$ radicals almost to the level of the sensitivity of the EPR apparatus, while heating of the ground PETN crystals even to 373 K did not lead to the complete destruction of the paramagnetic centres.[69] This means that the destruction of the $\dot{N}O_2$ radicals on raising the temperature is not associated with the dimerisation reaction $2\,\dot{N}O_2 \rightarrow N_2O_4$ and is induced by their interaction with the products of the decomposition of the 'paired' radicals and the occurrence of the oxidation-reduction reactions

$$\dot{N}O_2 + \dot{R} \rightarrow CO_2 + CO + H_2O + N_2.$$

Neither nitrogen dioxide nor its dimer were detected in the mass spectrum of the gases evolved after heating to 298 K; the PETN dispersed at 77 K.[35] Only peaks corresponding to the products of the decomposition of the PETN molecule were detected: H_2O, CO, CO_2, N_2. The peak observed at $m/e = 30$ may belong to NO as a side product of the degradation reaction, formed in small amounts when NO_2 and the 'paired' radicals interact. Most of the $\dot{N}O_2$ radicals and the products of their reactions with the unstable fragments of the initial molecules may remain trapped in the matrix of the crystalline test substance, which is indicated by the retention of 30% of the paramagnetic centres in the PETN heated to 373 K.

It has been suggested[35,69] that degradation of the PETN molecules with elimination of the NO_2 groups takes place as a result of the action of different types of radiation (electron emission, X-ray and optical radiations, etc.), arising on disruption of the crystal. The fact that an anomalously high radiation yield has been observed in mechanically activated solids may confirm the validity of this hypothesis.

Delpuech and Cherville[71,72] investigated the electronic structures of a series of organic compounds capable of undergoing a rapid exothermic decomposition and the changes in these substances occurring when they are subjected to pulsed mechanical influences. The stable ground state, the structural features of which determine the absorption and distribution of energy, as well as various unstable states arising as a result of impact stresses were examined. Characteristics such as the radiochemical yield of the $\dot{N}O_2$ radicals (G_R) and the primary radiochemical yield of the excited molecules (G_o) have been compared for three groups of organic substances—nitramines, aromatic nitrocompounds, and nitric acid esters. Here G_R corresponds to the number of NO_2 species for each 100 eV of the absorbed radiation energy determined by the EPR method at 77 K and G_o is the number of excited NO_2 molecules in the specified energy range for each 100 eV of the radiation energy.

Table 3. The radiochemical yields of NO_2 molecules and the yields of excited molecules.[71,72]

Nitro-compound	G_R	G_o(calc.)	G_o(expt)	
		G_o(calc.) [C3MNA]	G_o(expt)[C3MNA]	
			methanol[a]	acetonitrile[a]
PETN	3.80	0.87	0.60	—
C3MNA	0.9	1	1	1
C4MNA				
(δ-modification)	—	1.02	—	—
(β-modification)	0.8	1.03	1.08	1.17
(α-modification)	—	1.03	—	—
EDNA	0.3	1.06	1.08	—
3NPNA	0.006	1.55	1.58	1.45
TNA	$<10^{-3}$	1.56	1.83	1.82
TATNB	0.01	2.01	—	2.15
TNB	$<10^{-3}$	2.09	2.25	2.18

[a] solvent.

The primary radiochemical yield was determined by UV spectroscopy (in the range 195–360 nm) and theoretically by means of the semiempirical CNDO/2 computational method. The advantage of the theoretical calculation was that the quantity G_o for the molecules of organic substances was calculated in relation to the crystalline state (Table 3).

As a rule, substances with a higher probability of the initiation of rapid exothermic decomposition when subjected to a pulsed influence (impact) have a higher value of G_R and a lower value of G_o. This means that the exothermic reaction can be more readily induced by means of a mechanical influence in organic compounds with a low radiation stability.

For their calculations, Delpuech and Cherville[71,72] selected only organic substances whose structures had been reliably demonstrated. The distribution of the electric charge densities, obtained by the semiempirical INDO method, is presented in Table 4, which indicates the asymmetry of the charge per unit bond length $\Delta c^0/l$ for the most polarised $R-NO_2$ bonds as well as the ionisation energies.[71,72] Evidently the asymmetry of the charge distribution varies in the range 0.5–1.1 for all $R-NO_2$ bonds. The nitramine $N-NO_2$ bonds and the ester $O-NO_2$ bonds are more polarised than the $C-NO_2$ bonds, which are stabilised as a result of resonance with the bonds in the benzene ring. Comparison of the data in Table 4 for substances with related functional groups showed that the parameter $\Delta c^0/l$ is insufficient for predicting the probability of the initiation of the rapid exothermic decomposition. Hence one may conclude that the genesis of the decomposition of the molecules of the test substances cannot be adequately assessed solely on the basis of the structural parameters of the stable ground state. The authors[71,72] suggested that the distribution of the energy absorbed when the substances are subjected to a mechanical influence reflects more fully the variation of the parameter $\Delta c^0/l$ in different excited states.

Calculations have also been made for the excited states with the aid of quantum-chemical methods.[71,72] It was found that the classification of nitramines in terms of the asymmetry of the charge per unit $N-NO_2$ bond length in the excited state is identical to the classification in terms of the probability of the initiation of the decomposition for substances subjected to a pulsed stress. The results of the above studies[71,72] made it possible to differentiate two main criteria for the assessment of the behaviour of nitramines and aromatic nitro-compounds when reactions in the latter are initiated by means of pulsed mechanical influences — the electronic structure in the ground state and the way in which the absorbed energy is distributed.

Table 4. The ionisation potentials and maximum charge asymmetries in the ground states of nitramines and aromatic nitro-compounds.[71,72]

Substance	Ionisation potential/eV	Bond	Charge asymmetry	Charge asymmetry per unit bond length
C3MNA	14.83	N_1-NO_2	1.044	0.764
C4MNA (δ-modification)	13.49	N_8-NO_2	0.937	0.673
C4MNA (β-modification)	13.80	N_2-NO_2	0.889	0.650
C4MNA (α-modification)	13.62	N_1-NO_2	0.902	0.662
3NPNA	12.98	$N-NO_2$	0.841	0.624
		C_2-NO_2	0.608	0.409
EDNA	13.76	$N-NO_2$	0.880	0.676
TNA	12.90	C_6-NO_2	0.673	0.461
TNB	13.64	C_5-NO_2	0.575	0.391
TATNB	11.98	C_1-NO_2	0.820	0.579
PETN[a]	—	—	—	0.645

[a] nitric acid ester.

IV. The influence of the gaseous medium on the initiation of fast exothermic decomposition reactions

If it is assumed that the occurrence of mechanochemical reactions is in some way related to the appearance of a gas discharge in the developing crack, one may expect that the composition and pressure of the gaseous medium are capable of influencing significantly the initiation of reactions involving the fast exothermic decomposition of organic molecular crystals subjected to mechanical influences.

The influence of air and pure oxygen and nitrogen pressures (in the range $10^{-3}-10^{-5}$ Pa) as well as the pressures of argon and helium (with different concentrations of air in the latter as an impurity) on the probability of the initiation of the decomposition of C3MNA, C4MNA, PETN, TNPA, and BP [benzoylhydroperoxide?] has been investigated.[33,35,73–75] The tests were carried out under the conditions of pulsed stresses (over a period of $\sim 10^{-3}$ s) and pulsed relaxation of stresses (over a period of $\sim 10^{-4}$ s). The experimental results showed that changes in the initiation probability W are not observed in the air pressure range 10^2-10^5 Pa (Fig. 8), an appreciable decrease in W was noted in the air pressure range 0.1–1 Pa, while at a pressure of 10^{-2} Pa the probability W was close to zero. This behaviour is qualitatively the same for all the substances investigated, although it is less

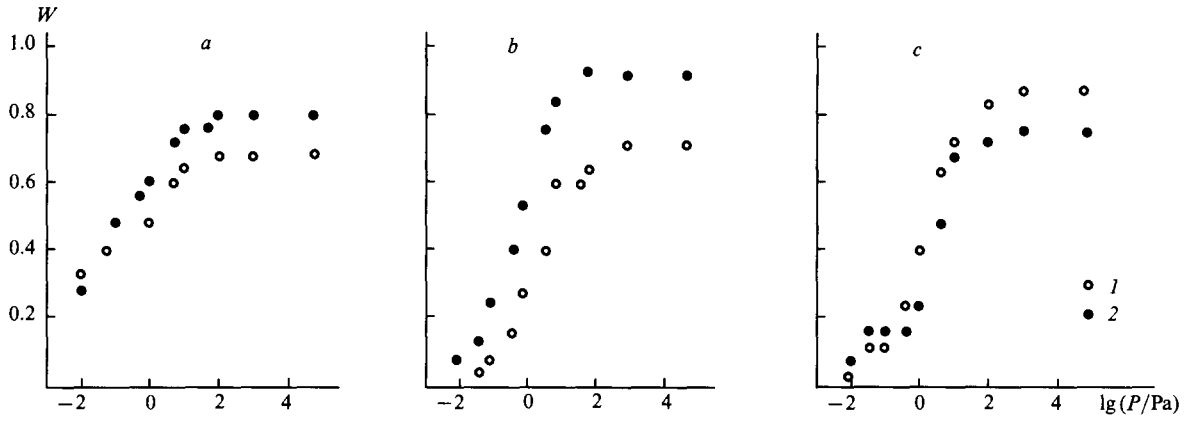


Figure 8. Dependence of the probability of initiation of the rapid exothermic decomposition of BP (*a*), C3MNA (*b*), and C4MNA (*c*) on air pressure[35,75] for a pulsed application of a stress (*1*) and for a pulsed removal of a stress (*2*).

marked in BP. For both types of influences (pulsed stresses and pulsed removal of stresses), the dependences of the probability of initiation of the decomposition on air pressure are identical.

When the experiments were carried out in pure oxygen and nitrogen, it was observed that W in oxygen depends to a considerable degree on the gas pressure in the range $1-10^3$ Pa and that the pressure range is higher in oxygen than in nitrogen (Fig. 9). Tests in argon and helium with air partial pressures in the range $10^{-1}-10^3$ Pa showed that the probability of the initiation of the fast exothermic decomposition of organic molecular crystals is appreciably lower than under an air, oxygen, or nitrogen atmosphere. The concentration of air exerts a marked influence on the mechanochemical decomposition of the test substances. It has been noted that, for equal pressures of atmospheric oxygen, the probabilities W were appreciably lower when, after evacuation, the chamber was filled with an inert gas up to a total pressure of 10^5 Pa. Argon suppressed the initiation process more than helium.

The creation of a vacuum in the system used to subject specimens to various influences (gas rarefaction less than 1 Pa) is a common procedure designed to prevent gas-discharge processes.[76] In terms of this aspect, the experimental results of our investigations[33,35,73-75] constitute evidence indicating that the gas discharge in the developing crack is an important step in the initiation of fast reactions involving the exothermic decomposition of organic substances subjected to mechanical influences. It has been stated[73] that it is incorrect to compare the experimental results of tests of the given substances in gaseous media with Paschen's curve, since Paschen's law is valid only for a discharge in a constant electric field at gas pressures exceeding 10 Pa and for a distance between the electrodes greater than 10^{-3} m.[8,77] The electric discharges in the developing crack arise in the gas flow in a highly nonuniform electric field with 'pulsed' switching on for very short distances between the walls of the crack (micrometres and fractions of a micrometre). Paschen's curve establishes the relation only between the threshold breakdown potential and the product of the gas pressure and the interelectrode distance but yields no information whatever about the nature and intensity of the gas-discharge process.[8,77]

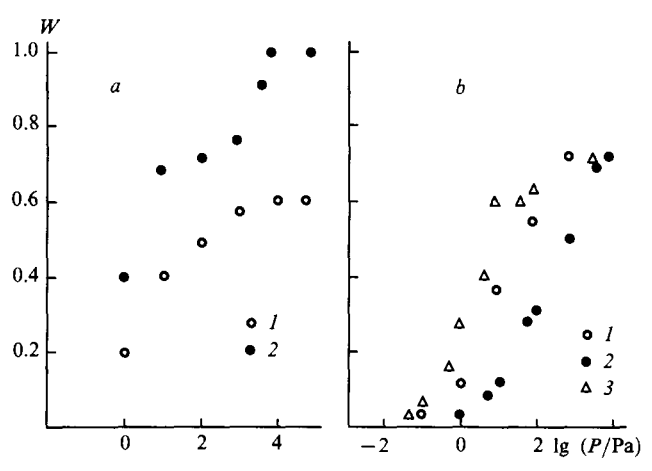


Figure 9. The influence of the nature of the gaseous medium on the probability of the initiation of the fast exothermic decomposition of C3MNA:[74] (*a*) pressure of pure nitrogen (*1*) and pure oxygen (*2*); (*b*) influence of the partial pressure of the air impurity in helium (*1*) and argon (*3*) [the data in vacuo (*2*) are given for comparison].

V. Initiation of fast reactions occurring as an explosion

In order to analyse the relation between the mechanochemical processes and the mechanical emission phenomena and in order to determine the role of the latter in the processes leading to the initiation of fast exothermic reactions, it is necessary to examine the existing concepts concerning the initiation of mechanochemical reactions in organic solids.

The thermal theories of the initiation of fast exothermic reactions have until recently gained the greatest currency in our country in relation to typical organic explosives. In our view, the following conclusions must be regarded as the greatest achievement of the thermal theories applied to typical explosives.

1. The essential preliminary step in the initiation of the decomposition reactions is fragmentation (cohesive or adhesive).

2. The initiation of a chemical reaction when the system is subjected to a mechanical influence is regarded as a multicentre process.

3. The initiation microcentres are localised in the fragmentation zone. These theories are based on the idea that local heating centres (the so called 'hot spots' arise in the solid subjected to mechanical influences). After the attainment of critical parameters (size, temperature, induction period), the surrounding condensed phase is ignited from these 'hot spots'. Next the decomposition reactions proceeds in the form of accelerating combustion and deformation.[78-86] Various mechanisms for the generation of 'hot spots' have been proposed — viscous heating during the rapid flow of the solid under pressure, adiabatic compression of gaseous inclusions, dry friction of the solid impurities. However, they did not receive subsequently a satisfactory experimental and theoretical confirmation. Among the thermal theories, the initiation theory indicating that brittle fragmentation of the organic substance in the condensed phase causes the formation of the heat centre received the greatest

recognition.[78,81,83–86] The following simplifications and assumptions were used in this theory: a solid crystalline substance is regarded as a continuous isotropic medium with certain generalised characteristics, to which the laws of the theory of the resistance of materials are applicable; the decomposition of the substance in the 'hot spot' is merely a solid-phase chemical reaction; the chemical reactions of the 'hot spots' obey the Arrhenius law of kinetics.

Thus the thermal theories do not consider the fragmentation of organic crystals at the atomic-molecular level and do not take into account the fact that, during the application of stresses to specimens, their mechanical properties may vary within fairly wide limits depending on the defectiveness of the crystals, the chemical purity, the crystalline modifications, the crystal habit, etc. The electrophysical phenomena and the physicochemical transformations of the organic substances accompanying the fragmentation of the crystals remain outside the scope of the thermal theories.

Plastic deformation is a preparatory stage in the formation of cracks along local zones (slip bands).[87,88] All these features render the laws of the classical theory of the resistance of materials relatively unsuitable in the present situation.

In our view, the thermal theories do not take into account the primary initiation of chemical reactions proper, i.e. the question of the way in which the mechanical influence on the organic crystal causes chemical changes and reactions. Furthermore, they do not provide a satisfactory basis for the appearance of high-temperature heating centres on fragmentation of solids, although they do describe qualitatively the process involving the propagation of reactions in the thermal regime (combustion, transition to detonation).

The theory of 'short-lived active centres', arising on the freshly formed decomposition surface of the solid, has been proposed.[49,89] It identifies the relaxation processes with the spontaneous destruction of these centres (radicals, broken bonds) in vacuo and with the destruction as a result of interaction with molecules of the surrounding gas in a chemically reactive medium. The theory of 'active centres' describes quite satisfactorily the mechanochemical processes occurring in homopolar crystals, where the rupture of covalent bonds is an obligatory consequence of the mechanical fragmentation.

It is necessary to turn attention to the fact that in this model an important role is assigned to the gaseous medium and its composition and pressures determine to a large extent the course of the chemical reaction on the fresh disintegration surface. However, this model does not consider the possibility of the activation of the gaseous medium itself during the appearance and development of cracks, whereupon the emission of electrons and radiation in various parts of the spectrum and a gas discharge with formation of excited molecules, ions, and atoms are observed.

Benderskii and coworkers[90–94] used the model of the self-activated solid matrix for low-temperature chemical processes. Self-activation occurs as a result of the chemical reaction and the operation of mechanical stresses in frozen reactants. The theoretical ideas concerning the phenomenon of the low-temperature detonation of mixtures of chlorine and hydrocarbons subjected to preliminary irradiation are described in these communications. It is suggested that the mechanical energy accumulating in the solid creates directly conditions for the acceleration of chemical processes, reducing the activation energy. This model of the occurrence of fast low-temperature reactions in a solid is based on the classical kinetic Arrhenius theory. However, it has been established[95] experimentally that the application of a stress to the specimen under the conditions of compression from all sides up to a pressure of 0.6 Pa hinders the cryochemical reactions in the solid matrix subjected to preliminary activation by photo- and gamma-irradiation, which is inconsistent with the concept of the direct influence of mechanical energy of the deformed specimen on the chemical process.

Ideas concerning the nature of the spontaneously developing high-speed autowave regimes of cryochemical reactions have been put forward.[95–100] It is suggested that, after a solid specimen subjected to preliminary irradiation is exposed to a mechanical influence, a narrow zone with a well developed network of freshly formed cracks arises and spreads. Chemical reactions creating conditions for the subsequent intense crack formation in the neighbouring zone of the matrix take place on the surface of these cracks or in its vicinity. As a result of the movement of the zone with a well developed network of fresh cracks through the solid specimen, the seemingly layer-by-layer dispersion of the substance in the travelling field of mechanical stresses takes place. The proposed model includes a sequence of feedback-controlled processes accompanied by the transformation of mechanical energy into chemical energy, i.e. the chemical reaction leads to a further brittle fragmentation of the specimen due to the density or temperature gradients giving rise to the stresses fragmenting the specimen.†

A proportion of the energy of the exothermic process, as it were, accumulates in the matrix in the form of mechanical deformations, while the unreacted portion of the specimen passes at the same instant to a nonequilibrium stressed state. The mechanical energy is then transformed into chemical energy via the brittle fragmentation stage, i.e. reactions on the fragmentation surfaces and in their vicinity are initiated. Preliminary irradiation creates two types of 'active centres' — both physical and chemical in the frozen matrix. The physical centres are local 'perturbations' of the mechanical stresses (associated with the appearance in the crystal lattice of decomposition products which entail an increase in the concentration of crystal defects) and also the centres for the initiation of new phases. The chemical 'active centres' are radicals or fragments of the initial molecules. In the proposed model,[95] the high-speed cryochemical reactions are formally similar to detonation in its classical hydrodynamic sense, although the physical nature of these two phenomena is undoubtedly different. In the irradiated matrix comprising the frozen reactants, the mechanical fragmentation is a kind of trigger which induces the appearance and development of the autowave regime in the chemical reaction.

Solid-phase chemical reactions without the formation of gaseous products over a period shorter than 10^{-7} s (on Bridgman anvils at high pressures with shear deformation), accompanied by the appearance and propagation of a powerful detonation wave, have been described.[101] Explosive decomposition and synthesis have been observed on Bridgman anvils in the study of the monoaxial compression of various substances.[102–104] These chemical reactions are accounted for by the direct transformation of the accumulated mechanical energy into chemical energy without heating.

The theory of the 'magma-plasma' ('tribo-plasma'), in which the fragmentation zone in the solid is represented as the centre of a special plasma has been proposed to account for the set of mechanoemission phenomena from the standpoint of a single general model.[6,9,10] The existence of the plasma state has been confirmed by the broad spectrum of the electron and electromagnetic emissions characteristic of the state. In the region of such high-energy states, there is a possibility of various chemical reactions which cannot be achieved during normal heating.

In relation to substances capable of rapid exothermic decomposition when acted upon by mechanical influences, we proposed a plasmochemical concept,[74] in which it is possible to differentiate two most important aspects. The first is the activation of fresh surface as a result of the fragmentation of the solid and the second is the activation of the gaseous medium in the vicinity of the fresh surface under the influence of mechanoemission phenomena.

† The autowave mechanism of the self-activation of the cryopolymerisation process has been described in a review.[99]

The brittle fragmentation of crystalline bodies, occurring in the form of crack formation, is a result of a complex interaction of the crystal lattice defects, in the first place dislocations.[87] The excited fresh surface with a high concentration of crystal lattice defects has a mosaic electric field microrelief.[15] The electrons emitted from the new surface fall on the opposite wall of the crack during its development and can induce various kinds of radiation damage, the degradation of molecules with formation of fragments and radicals, ionisation, the excitation of the molecules of the organic substance, and the appearance of secondary emissions.[1] The secondary electromagnetic and electron emissions are also capable of inducing further radiation processes in the substance. The activation of the gas phase as a result of ionisation, dissociation and excitation of atoms and molecules, reactions involving the sticking of electrons, etc. under the influence of electrons and electromagnetic waves leads to the formation of species with a high reactivity.[8,105]

The activated gaseous plasma may interact with the fresh surface, which should lead to a further decomposition of the molecules of the organic phase and to various chemical reactions on the walls of the crack. Since the decomposition of the molecules of the organic substances investigated is accompanied by the evolution of energy, this process develops and leads to the formation of a certain critical centre, in the region of which further chemical decomposition may be described within the framework of the thermal theory.[82]

Relaxation phenomena with different mechanisms must necessarily occur at all stages in the development of the process under consideration. In the gaseous plasma, the active species interact with other molecules and atoms, which leads to the transfer of the charge, excitation energy, vibrational energies, etc.[8,105] During the formation of the critical thermal centre, there is a possibility of thermal relaxation due to thermal conduction and convection.

A scheme reflecting the general features of the high speed reactions occurring when solids are subjected to mechanical influences has been put forward.[35] This scheme is applicable to the reactions occurring on Bridgman anvils, in a roller apparatus with pulsed application and removal of stresses, and also to a low-temperature explosion, etc. Plastic deformation (induced by mechanical forces), combined with a high pressure leads to the formation of a fresh surface with a high concentration of crystal defects. Under the influence of various types of emission, accompanying this process, there is a possibility of the appearance on the surface and in the near-surface layer of the substance of local zones with a postcritical density of active species. Such active species may be radicals, ions, point defects, etc. The initiation of reactions in these local zones leads subsequently to their propagation throughout the bulk of the specimen, i.e. the microregion of the explosive reaction arises from the microcentres. The propagation of the reaction through the substance is determined by factors such as its chemical nature and its structural characteristics and takes place in a thermal regime[82] or in the form of an autowave process.[95]

VI. Conclusion

In our view, high-speed chemical reactions in a solid matrix (in particular, during the initiation of the explosion) proceed in three stages, which differ fundamentally in their physicochemical nature.

The first stage is the appearance of active species under the influence of a set of mechanoemission phenomena. The application of the rules of radiation chemistry and photochemistry, taking into account the pulsed regime in the process involving the decomposition of organic molecular crystals or other substances, is valid in this case.

The second stage involves the interaction of active species with 'inactive' atoms and molecules, where the energy is supplied not in the form of heat but via electron, ion, and photon impacts and via interaction with electronically excited atoms and molecules (plasma) with imposition of electric fields generated on the fresh fragmentation surface.

The third stage involves the propagation of the decomposition reactions of organic substances throughout the bulk phase.

A thermodynamically nonequilibrium system, containing highly reactive species (electrons, ions, radicals, etc.) and arising when solids are subjected to a mechanical influence, promotes a course of the processes which is significantly different from that in the usual thermochemistry.[106-108] The characteristic features of these processes are as follows:[106-108] high local bulk-phase and surface energy densities; non-equilibrium conditions (non-Maxwell and non-Boltzmann distribution with respect to the energy of translational motion and the population of the quantum levels for the species comprising the system); the mutual approach and overlap of the characteristic times for the physical phenomena and chemical processes; the leading role in the chemical processes of electrons, ions, excited molecules, and radicals, which do not play a significant role in traditional kinetics; the multipath nature of the processes in the reacting system.

The traditional kinetic energy of chemical reactions and the theory of rate processes are inapplicable in this case. The translational, rotational, and vibrational energies of the molecules and atoms may differ greatly and the system components may have different temperatures. There is actually a possibility of the case where the concept of "temperature" is altogether inapplicable to high-speed chemical reactions. Classical chemical kinetics do not apply in this case and the expression for the chemical reaction rate constants loses its significance.[108]

The fraction of the substance participating in the second stage of the initiation of the explosion depends on the overall area of the fragmentation surface in the specimen. Under the conditions of the intense formation of cracks and rapid dispersion, a considerable proportion of the substance participates in chemical reactions the kinetics of which differ from 'Arrhenius' kinetics. This also explains the unusual, atypical products of the mechanical and chemical reactions which have been frequently observed experimentally.

The third stage in the initiation of the explosion is the propagation of the decomposition reactions throughout the bulk of the substance. Depending on the conditions, this stage can proceed in a thermal regime and can be described satisfactorily by Arrhenius kinetics or it can proceed in the form of an autowave process of the kind observed in low-temperature explosions.[95-100]

For a long time, investigators avoided mentioning certain reliable experimental data in considering various models, since such data had no acceptable explanation. For example, investigators carrying out experiments on the initiation of the explosion in typical explosives know that particles of solid impurities significantly increase the probability of the initiation of the decomposition process (sensitivity) when the system is subjected to mechanical influences. Metallic surfaces in contact with the specimen act slowly when the extent of their treatment is reduced, i.e. with increase in microroughness.[35,109] The current initiation theories cannot explain satisfactorily these seemingly simple phenomena. The concept of the three-stage development of the explosive decomposition of organic substances proposed by the present author readily accounts for the relations indicated. The particles of solid impurities and the microrugosities on flat solid surfaces are factors intensifying the crack formation process, which stimulates in its turn an appreciable increase in the area of the fragmentation surface in the specimen and the occurrence of chemical reactions in the zone of such cracks in the second stage of the initiation of the explosion.

In our view the separation of these three stages of high-speed chemical reactions, differing fundamentally in their nature and occurring when the system is subjected to mechanical influences, may help to eliminate the disagreements arising among

investigators when an attempt is made to extend laws valid for one stage to the entire set of mechanochemical reactions in the given substance.

The chemical reactions occurring when inorganic crystals are subjected to mechanical influences have their characteristic features. Thus it has been found[110] that the mechanical fragmentation of a number of sodium salts leads to the formation of gaseous products different from those produced on thermal decomposition. The differences between the gaseous products detected have been explained by the appearance in the cracks at the top of the specimens of short-lived highly excited ions and radicals, which give rise to low-molecular-weight products on recombination.

The breakdown of stoichiometry on the cleavage plane of a LiF crystal has been noted.[111] The surface undergoes metallisation after fragmentation under these conditions as a consequence of the formation of σ-centres near a dislocation step at a distance not exceeding the critical Auger ionisation radius of the dislocation electron. The acceptor σ-centres may form with the polymer [in particular with poly(vinyl chloride)] surface chemical (irreversibly bound) charge-transfer complexes.[112]

The influence of the concentration of point defects (F-centres) on the adhesion of metals (gold, silver, and copper) for a bulk density of F-centres of 2×10^{16} cm^{-3} and a surface density of $\sim 10^{13}$ cm^{-2} has been observed in LiF crystals.[113] The adhesive interaction has been explained by the formation of the Li^0–metal bond.

The appearance of defects of the type of F-centres on the fresh cleavage surface of an ionic crystal has been established.[114]

The emission of negatively charged (O^-, O^{2-}) and positively charged (Cu^{2+}) species has been observed on cleavage of superconductors.[115] The authors explain this effect by the electron–hole recombination involving the surface active centres with participation of copper ions and neutral oxygen diffusing from the bulk of the $YBa_2Cu_3O_{7-x}$ ceramic during vacuum annealing. The active centres were excited both mechanically (cleavage *in vacuo*) and by the ionisation irradiation of the specimens.

The exciton and dislocation processes occurring on mechanochemical dissociation of ionic crystals have been examined.[116]

The appearance of an excess charge on the surfaces of dielectric materials freshly formed on mechanical fragmentation is a consequence of the appearance of additional defects. As already stated, the charge density on a fresh cleavage surface of a crystal may attain values corresponding to electrical breakdown (10^8–10^9 V m^{-1}).[15] Vorob'ev et al.[117] observed the formation of extended dislocations in alkali metal halide crystals after these had been acted upon by a powerful electric field ($\sim 10^8$ V m^{-1}), which is due to the mechanical stresses already existing in the specimen and which become manifest following the application of an electric field (both pulsed and constant potentials were applied). Zuev et al.[118] demonstrated the aggregation of impurity–vacancy pairs with dislocations in a sodium chloride crystal doped with Ca^{2+} ions, the aggregation being stimulated by an electric field.

Okuyama et al.[119] investigated mass-spectrometrically the desorption of the K^+ and Na^+ ions and of cluster ions from the surfaces of potassium and sodium chloride crystals in a strong electric field.

The results of Laptenkov et al.[120] indicate the possibility, in principle, of regulating with the aid of strong electric fields the kinetics of the chemical reactions in ammonium perchlorate occurring with participation of dislocations. The effect of the electric field on the thermal decomposition of ammonium perchlorate single crystals was explained within the framework of the dislocation model of the development of reactions centres. The increase in the rate of growth of these centres following the application of an electric field may be caused by the Coulombic interaction of the external electric field and the edge-type charged dislocations, which move and multiply under the influence of the mechanical stresses in the crystal during the evolution of the gaseous ammonium perchlorate decomposition products.

The electric field causes the ageing of solid dielectric materials[121] and the initiation of ionic polymerisation processes.[122] It has been shown[123] that prolonged pulsed application of a $5 \times 10^7 - 10^8$ V m^{-1} electric field to solid polymers (polystyrene, organic glass) induces the accumulation in the material of bulk-phase charges (fields up to 1.7×10^7 V m^{-1}). At the same time, microcracks are initiated and develop, which leads to the formation of either a fragmentation zone, comparable in size to the interelectrode distance (1–2 mm), or of a tree-shaped dendrite channel.

Polyethylene films maintained in a 2×10^7 V m^{-1} field for 5–60 h undergo the degradation of macromolecular chains.[124] The appearance of oxygen-containing groups (C=O) in polyethylene following the application of an electric field has been described.[125] Under the influence of a strong electric field, free radicals of two types are formed in polyethylene prior to electrical breakdown. They accelerate the fragmentation of the polymeric dielectric material.[126] According to Gezalov and Kerimov,[126] the appearance of radicals is a consequence of the local heating of the specimen and also of the development of ionisation processes in the polymer.

Zakrevskii and Slutsker[127] discussed the initial stages of the fragmentation of polymers under the influence of mechanical stresses and an electric field. The mechanisms of the rupture of macromolecules in these fields, including the ionisation of the macromolecules as a result of tunnelling electron transfer and subsequent decomposition of the positively charged macroions, are considered. The authors conclude that the mechanical and electric fields exert a 'cross' influence. In their view, the application of an electric field to a mechanically stressed polymer should accelerate the stage involving the tunnelling ionisation of the macromolecules, while the mechanical stress should accelerate the stage involving the fluctuation decomposition of macroions in the electric field. However, in real cases the external field employed should not influence appreciably the tunnelling effect. The mechanical strength (longevity) is reduced in the electric field, whilst the electrical strength is reduced under the influence of the mechanical stress.[127]

The study of the dynamics of the release of a charge carrier from a dipole trap (an analogue of the elementary step in a chemical reaction) in a polymer matrix under the influence of an electric field has been investigated by the Monte Carlo method.[128] The authors suggest a series of experiments to test this calculation.

The emission of negatively and positively charged species from inorganic and organic solids has been investigated[129] in the corrosion of metals and in the exposure of polymers of different nature to thermal influences ('cooling to cryogenic temperatures–heating' cycles). Krylova[129] believes that, regardless of the method of excitation, the emission of charged species is induced by the same phenomena, which are analogous to the Auger relaxation and Auger recombination processes in atomic and ionic collisions on surfaces known in emission electronics. The energy evolved in these exothermic processes is the cause of the low-temperature 'pre-threshold' emission of charged (as well as neutral) species. In other words, the rupture of chemical bonds during corrosion (electrochemical formation of metal ions) and also in the cryolysis of polymers leads to the separation of the charges formed, and their subsequent recombination is accompanied by the evolution of the energy required for the emission of the charge. This approach follows from the development of the physicochemical concept of exoemission.[40]

It has been shown[130,131] that exoemission is a sensitive method for the monitoring of the initial stages in the fragmentation of polymeric materials subjected to mechanical (and radiation) influences as well as cooling–heating cycles. It has

been established[36,132] that the electrons emitted when solids (dielectric materials, metals, and polymers) are subjected to mechanical influences are capable of inducing the dissociative ionisation of the water molecules adsorbed on the surfaces.

The studies mentioned above demonstrate unambiguously an interrelation between the mechanoemission phenomena and the mechanochemical processes. It is at least incorrect to ignore the influence of electroemission phenomena on the chemical processes and reactions occurring when solids are subjected to a mechanical influence.

The principal fluxes of electrons, ions, and other charged and high-energy species, and of electromagnetic radiation are observed during the short period of the movement of the main crack in the solid specimen ($\sim$1 μs) and it is not always possible to record them experimentally. Nevertheless they undoubtedly affect the structural changes and chemical interactions in the vicinity of the charged fresh fragmentation surface. The presence of an excess charge on the cleavage planes of solids, especially dielectric materials, should affect the chemical reactions occurring on application of mechanical stresses. (The appearance of an excess charge on the fragmentation surface of a solid has been explained by its increased defectiveness and the deviation from stoichiometry.) It appears therefore that, in considering the mechanochemical reactions in solids, it is essential to take into account also the electroemission phenomena. The question arises whether they are of decisive importance. The answer to this question should be sought in each specific case when a particular solid is subjected to a mechanical stress, taking into account the experimental conditions.

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Synthesis of nucleoside 5′-triphosphates labelled with radioactive phosphorus isotopes

Yu S Skoblov, A E Korolev, R N Maslova

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Abstract. The review presents an analysis of the chemical chemicoenzymic, and enzymic methods of synthesis of nucleoside 5′-triphosphates labelled with phosphorus isotopes (^{32}P and ^{33}P) in the α- and γ-positions. The major part of the review is devoted to enzymic methods of synthesis, because they have undoubted advantages. The enzymic reactions are described in detail, the specificity and availability of the enzymes are considered, and data on the radiation stability of certain enzymes are presented. The bibliography includes 29 references.

I. Introduction

Radioactive isotopes have long been used in the study of the structures and functions of nucleic acids. Mainly the ^{14}C carbon atom was used initially. As the technique for the measurement of radioactivity developed and liquid scintillators began to be employed, there was a sharp growth of interest by investigators in tritium-labelled compounds. This was due to the much higher molar radioactivity of such compounds, which made it possible to reduce by two orders of magnitude the amount of specimen required for an adequate test of its radioactive emission.

The phosphorus-32 isotope has also long been used. Compounds labelled with ^{32}P were initially obtained by the ^{31}P$(n,\gamma)^{32}$P reaction involving the irradiation of an inorganic compound, usually an orthophosphate salt, with neutrons, whereupon the molar radioactivity of the product was not higher than that of the tritium-labelled compounds.

Instead of the whole nucleic acid molecules, only their small fragments, obtained by genetic-engineering methods, have become the objects of study during the last few years. This required a transition to the use of picomolar amounts of material, whereas a much higher specific radioactivity is needed for a reliable test of the specimen. From this point of view, the most suitable isotope proved to be phosphorus-32 obtained by the ^{32}S$(n,p)^{32}$P reaction involving the neutron irradiation of elemental sulfur. The specific radioactivity of phosphorus-32 without a carrier (for 100% isotope enrichment) is 9131 Ci mAt^{-1}, i.e. is 300 times greater than for tritium. Apart from this isotope, the phosphorus-33 and sulfur-35 isotopes, which also have a fairly high specific radioactivity (see Table 1), have been used successfully to label nucleic acids.

Nucleic acids labelled with radioactive isotopes of phosphorus (^{32}P and ^{33}P) as well as sulfur (^{35}S) are widely used in molecular-biological research and constitute the cornerstone of the principal methods such as hybridisation on filters, hybridisation in situ, sequencing of DNA, and many others. The choice of the radioactive label is determined mainly by two parameters: the sensitivity of the autoradiographic detection and spatial resolution.[1] These parameters depend in their turn on the β-emission energy of the radioactive isotope and its half-life, which determine the maximum specific radioactivity of the corresponding isotope. Table 1 presents the physical characteristics of the above isotopes.

Table 1. Physical characteristics of the radionuclides.

Physical characteristic	Isotope		
	^{32}P	^{33}P	^{35}S
Half-life/days	14.3	25.4	87.4
Maximum β-emission energy/MeV	1.71	0.20	0.167
Theoretical specific radioactivity of the radionuclide/Ci mAt^{-1}	9 120	5 200	1 488
Maximum specific radioactivity (virtually attainable) of the labelled nucleotides/Ci mmol^{-1})	7 000	4 500	1 500

In the determination of single animal genes by Southern's blot-hybridisation method,[2] the decisive factor is the requirement for the maximum sensitivity of the autoradiographic detection needed for subpicogramme amounts, which may be ensured only by use of the phosphorus-32 isotope, which possess the highest specific radioactivity among the isotopes considered here. On the other hand, in the method for the dideoxynucleotide sequencing of DNA, the requirement for sensitivity may be abandoned in favour of the high resolution of the bands on the autoradiogram,[3] which can best be ensured by labelling nucleic acids with sulfur-35

Yu S Skoblov The Isotope Division, State Scientific Centre of the Russian Federation, Institute of Physics and Power Engineering, pl. Bondarenko 1, 249020 Obninsk, Russian Federation.
Tel. (7-084) 399 57 72
A E Korolev Isotopchim S.A.R.L.B.P., 16 04310 Ganagobie-Peryis, France. Fax (3-379) 268 08 13
R N Maslova Engelhardt Institute of Molecular Biology, Russian Academy of Sciences, ul. Vavilova 32, 117984 Moscow, Russian Federation. Fax (7-095) 135 14 05. Tel. (7-095) 135 15 40

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and also with phosphorus-33, which have a low energy and therefore the path traversed by their β-particles in the gel is short. This applies equally to the method of hybridisation in situ, for which spatial resolution is decisive.

In many instances, phosphorus-33 has an advantage over sulfur-35, because it makes it possible to increase greatly detection sensitivity, whilst only slightly weakening spatial resolution. This has proved particularly important for the method based on the polymerase chain reaction ('cyclic sequencing') which makes it possible to sequence relatively small amounts of the matrix at high temperatures in order to reduce the amount of artefacts in the determination of the structure.[4] The ^{33}P-labelled primer ensures an adequate sensitivity and permits an autoradiographic exposure in the course of one night. This applies also to the method used in the analysis of the polymorphism of single-stranded configurations, in which the requirements for both spatial resolution and for detection sensitivity are fairly stringent.[5] A more detailed justification of the choice of the radioactive isotope for the above research methods has been given in the review by Evans and Read.[1]

One may note yet another advantage of nucleoside 5'-phosphates labelled with phosphorus-33 over the same compounds, labelled with sulfur-35, namely their complete chemical identity with the natural products, which eliminates any artefacts in the enzymic reactions in which labelled nucleoside 5'-triphosphates are employed as substrates. One should note that the majority of the methods impose stringent requirements on the quality of the nucleoside 5'-triphosphates labelled with radioactive phosphorus atoms, especially those with a high molar radioactivity, but it is not always possible to supply these compounds to remote regions in the course of 2–3 days at the appropriate temperatures using dry ice. We therefore thought it useful to survey the known methods of synthesis of these compounds.

The literature on this specific topic is extremely limited, since mainly the outline synthetic schemes are published in the open press without the technological details, which are mostly part of the [classified] know-how. It must be emphasised that even the most thorough and scrupulous copying of the published methods does not always lead to the expected results. In the present review, we attempted to present not only the published synthetic schemes but also to assess their reliability and reproducibility on the basis of the authors' personal experience.

Nucleoside 5'-triphosphates containing the radioactive isotope in the α- or γ-positions in the phosphate groups are usually employed to obtain labelled nucleic acids in vitro. Deoxynucleoside triphosphates with a phosphorus label in the α-positions are used to introduce the label into the 3'-end of DNA with the aid of various DNA polymerases and for the synthesis of a radioactive DNA molecule containing the label in one, two, or all four nucleotides. Adenosine triphosphate with a phosphorus label in the α-position is used to introduce the label into the 5'-ends of DNA and RNA. Scheme 1 presents the formulae of all the nucleoside triphosphates used in molecular-biological research, the synthesis of which is described in the present review.

The synthesis of nucleoside 5'-triphosphates with a phosphorus label in the α- and γ-positions and having a high molar radioactivity (3000–6000 Ci mmol^{-1}) involves a series of specific difficulties.

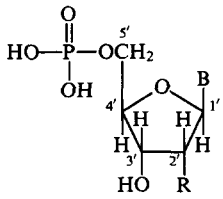
1. The reactions used to obtain the target compounds must not lead to an uncontrolled isotopic dilution of the radioactive phosphorus by the nonradioactive isotope – phosphorus-31.

2. The location of the radioactive atom must be rigorously fixed. The use of methods which might alter the location of the radioactive atom or introduce the label in different positions in an uncontrolled manner is not permissible.

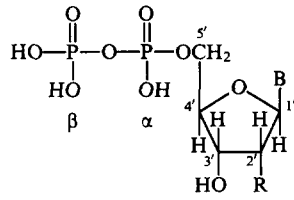
3. The high molar radioactivity of the nucleoside 5'-triphosphates used in molecular biology makes it necessary to carry out the syntheses with amounts of the radioactive isotope of 10^{-9}–10^{-8} mol, which corresponds to a radioactivity of 10–100 mCi (for phosphorus-32).

4. The low concentration of the radioactive substance requires the use of a large excess of the nonradioactive

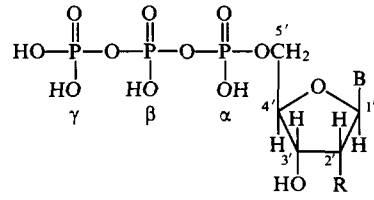
Scheme 1



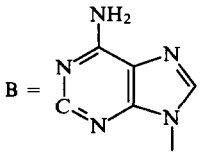
Nucleoside 5'-monophosphates



Nucleoside 5'-diphosphates



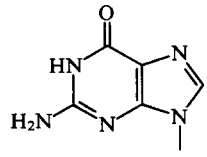
Nucleoside 5'-triphosphates



Adenine

R = OH (AMP, ADP, ATP)

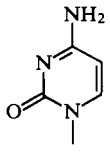
R = H (dAMP, dADP, dATP)



Guanine

R = OH (GMP, GDP, GTP)

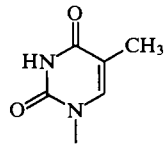
R = H (dGMP, dGDP, dGTP)



Cytosine

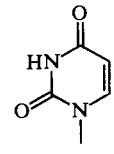
R = OH (CMP, CDP, CTP)

R = H (dCMP, dCDP, dCTP)



Thymine

R = H (TMP, TDP, TTP)



Uracil

R = OH (UMP, UDP, UTP)

components in order to increase the rate and yield of the reaction, which frequently leads to the appearance or side products.

5. For a high bulk-phase radioactivity of the reaction mixture (1 - 10 Ci ml^{-1}), the reaction time must be reduced to a minimum, since considerable amounts of mainly unidentified products, induced by the ionising radiation, accumulate (radiolysis products as well as the products of radical reactions).

6. The purification and especially the analysis of the products are hindered by the small amount of the substance and virtually preclude the use of the classical purification methods applied in organic chemistry (crystallisation, extraction, distillation, filtration, etc.) and analytical methods such as NMR, EPR, and IR spectroscopy, mass spectrometry, and X-ray diffraction.

7. Experiments with radioactive substances make it necessary to ensure the personnel safety, so that all manipulations in the syntheses must be performed observing radiation safety standards, preferably at a distance, in isolated compartments. The available descriptions of the methods of synthesis of nucleotides and nucleoside 5'-triphosphates labelled with radioactive phosphorus atoms are extremely scanty. The starting material in these syntheses is orthophosphoric acid. All the methods can be divided into the following groups:

(a) chemical methods in which chemical reagents are used in all the stages;

(b) chemicoenzymic methods in which enzymic reactions are employed together with chemical ones;

(c) enzymic methods in which all the stages of the synthesis are carried out with the aid of enzymes.

Nucleoside 5'-triphosphates labelled with radioactive phosphorus atoms in the α- or γ-positions are of greatest interest for molecular biology and the present review is devoted to the analysis of the methods of synthesis of these compounds. Most attention has been devoted to enzymic methods of synthesis because at present these procedures are used on an increasingly wide scale for the synthesis of nucleic acid precursors labelled with radioactive isotopes of not only phosphorus and sulfur but also of carbon, as well as tritium-labelled ones.[6]

The majority of studies considered in the present review were carried out using [^{32}P]orthophosphoric acid, but all the methodological procedures presented are valid also for syntheses in which [^{33}P]orthophosphoric acid is used. This is also confirmed by the personal experience of the authors of the review.

II. Synthesis of nucleoside 5'-[γ-$^{32(33)}$P]-triphosphates

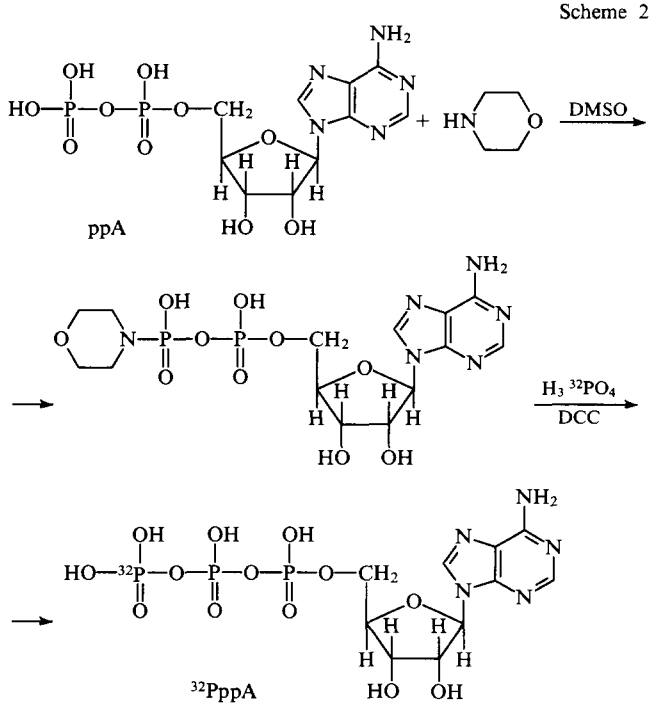
1. Chemical methods

The synthesis of nucleoside 5'-triphosphates labelled with radioactive phosphorus in the γ-position is not a very complex task. Moffat[7] was the first to propose a method of synthesis of [γ-^{32}P]ATP (^{32}PppA) from ADP (ppA) and [^{32}P]orthophosphoric acid ($^{32}P_i$). The reaction, involving the formation of an intermediate morpholide derivative, was used to activate the β-phosphate of ADP (Scheme 2). The reaction with $H_3\,^{32}PO_4$ was carried out in anhydrous dimethyl sulfoxide (DMSO) in the presence of *N,N'*-dicyclohexylcarbodiimide (DCC).

[γ-^{32}P]ATP with a molar radioactivity of 10 mCi $mmol^{-1}$ was obtained by this method in 65% yield. Such a low molar radioactivity of the product was explained by the lack at the time of [^{32}P]orthophosphoric acid with a high molar radioactivity. At the present time the method makes it possible to obtain a product with a high molar radioactivity (up to 1000 Ci $mmol^{-1}$). The main disadvantage of the proposed method is the instability of the intermediate morpholide derivative (it decomposes at room temperature in several hours).

This method was improved by a group of investigators at the All-Union Institute of Molecular Biology (VNII MB) in Novosibirsk,[8] who were able to select conditions for the stable isolation and storage of the intermediate activated ADP

Scheme 2



derivative. It was suggested that 4-(*N,N*-dimethylamino)-pyridine be used to accelerate the second stage — the synthesis of [γ-^{32}P]ATP proper. With the aid of this modification, it is possible to obtain comparatively simply [γ-^{32}P]ATP with any specified molar radioactivity up to the limiting value. The method can be applied successfully also to the synthesis of other nucleoside 5'-triphosphates by employing the corresponding nucleoside 5'-diphosphates.

The reaction is also carried out in anhydrous dimethyl sulfoxide and proceeds fairly rapidly (10 - 20 min), but is frequently accompanied by the accumulation of side products of the type AppppA, AppppA, and other unidentified compounds. This factor not only lowers the yield of the target product but also greatly complicates its isolation. On the other hand, the presence of such impurities in the target product is extremely undesirable, because they possess pronounced sorption properties. For this reason, this method has not come to be widely used in laboratory practice or in industrial manufacture.

2. The chemicoenzymic method

The only chemicoenzymic method of synthesis of [γ-^{33}P]ATP described in the literature involves the formation of acetyl [^{33}P]phosphate from acetic anhydride and [^{33}P]orthophosphoric acid and subsequent phosphorylation of ADP by this reagent with the aid of acetyl kinase.[9]

Bearing in mind the wide variety and reversibility of the enzymic reactions with participation of ATP, several versions similar to that already described could be proposed — for example, the synthesis of [γ-^{32}P]ATP from the ^{32}P-labelled phosphoenol pyruvate with the aid of pyruvate kinase or from labelled creatine phosphate with the aid of creatine kinase. Such reactions would proceed rapidly without the formation of side products and with a satisfactory yield. Nevertheless, the cost of the preparation of labelled precursors from [^{32}P]orthophosphoric acid, i.e. acetyl [^{32}P]phosphate, [^{32}P]phosphoenol pyruvate, or creatine [^{32}P]phosphate, and of their isolation from the reaction mixture before the enzymic stage, renders the synthesis laborious and uncompetitive compared with enzymic methods and it has therefore not come to be widely used.

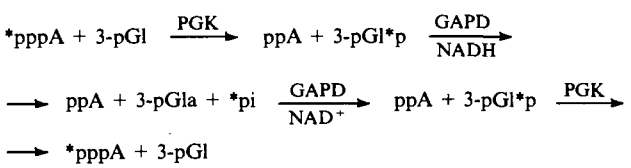
Overall, the chemicoenzymic methods of synthesis of [γ-^{32}P]ATP are nowadays of purely theoretical interest and are not used for preparative purposes.

3. Enzymic methods

The simplest in execution and most effective method of synthesis of nucleoside 5'-triphosphates labelled with ^{32}P (or ^{33}P) in the γ-position proved to be the enzymic method. The initial idea of the method utilised the reversibility of the glycolytic reactions in the reconstructed fragment of the nucleoside chain (Scheme 3).

With the aid of phosphoglycerate kinase (PGK) and glyceraldehydephosphate dehydrogenase (GAPD), ATP was converted into ADP and orthophosphate via the intermediate 1,3-diphosphoglycerate (pGlp) in the presence of 3-phosphoglycerate (3-pGl). The addition of [^{32}P]orthophosphoric acid to the reaction mixture in the last stage inevitably leads to the formation of [γ-^{32}P]ATP owing to the reversibility of the enzymic reaction during the attainment of equilibrium in the system (Scheme 3a).

Scheme 3a



*p = the phosphate group whose exchange is catalysed by the enzymes PGK and GAPD

This method, proposed by Glynn and Chappell,[10] was rapidly incorporated into laboratory practice. The method acquired particular popularity by virtue of the simple and readily reproducible procedure proposed by Maxam and Gilbert[11] for the determination of the DNA sequence. The entire synthesis of [γ-^{32}P]ATP by this method took less than 2 h and the product could be used without isolation for the introduction of the label in the 5'-end of DNA. However, the method does not allow, in principle, the synthesis of [γ-^{32}P]ATP without dilution by the phosphorus-31 isotope and in reality affords the final product in 60%–70% yield and with a molar radioactivity of 1000–1500 Ci mmol^{-1}.

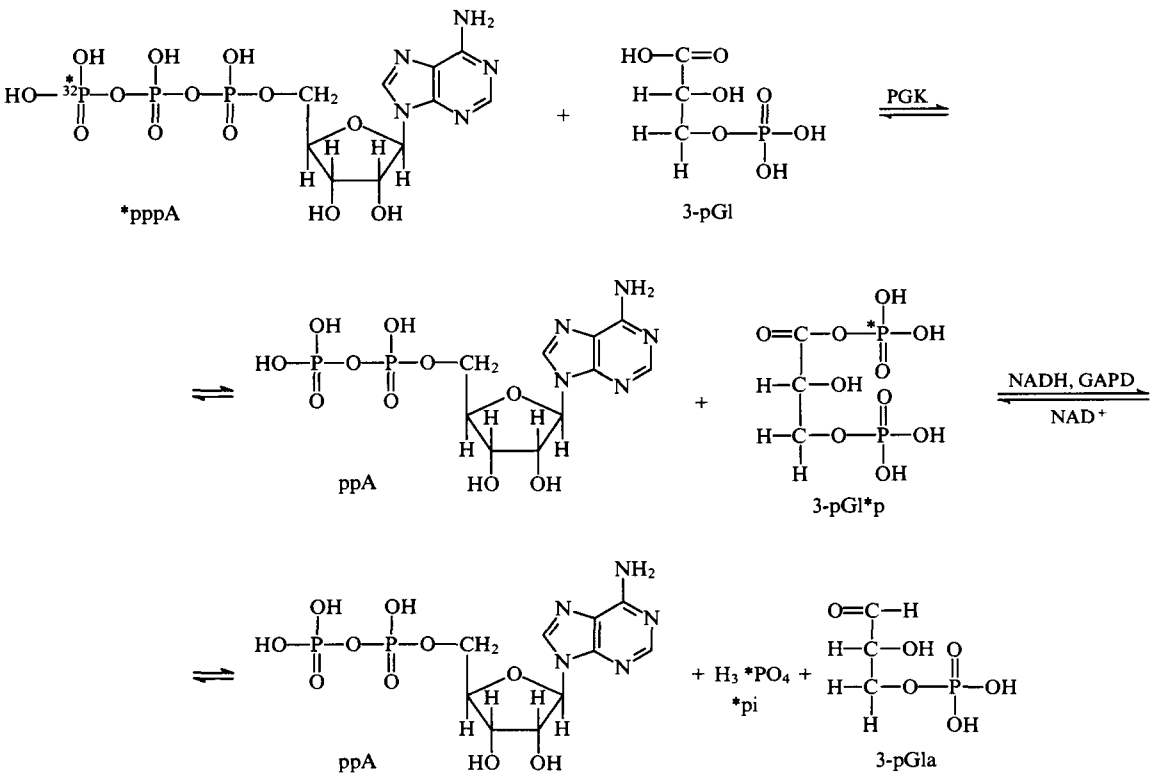
Later Stupar and Leskovac[12] analysed the method of Glynn and Chappell from the standpoint of the optimisation of the reaction yield and the molar radioactivity of the [γ-^{32}P]ATP obtained.

In 1973, Schendel and Wells[13] published a study in which they suggested that the scheme underlying the Glynn–Chappell method be 'inverted' and that the direct synthesis of [γ-^{32}P]ATP from glyceraldehyde-3-phosphate and [^{32}P]orthophosphoric acid be employed. Theoretically, this would make it possible to obtain [γ-^{32}]ATP with the maximum possible molar radioactivity, equal to that of the initial [^{32}P]orthophosphoric acid, i.e. without isotopic dilution. Bearing in mind the instability of glyceraldehyde-3-phosphate, the authors suggested that a stable and commercially available preparation be employed — the diethyl acetal of glyceraldehyde-3-phosphate. Free glyceraldehyde-3-phosphate was then formed in the first stage — the chemical hydrolysis of the diethyl acetal — and this was followed by the enzymic synthesis proper. However, the admixture of inorganic phosphates formed from the unstable glyceraldehyde-3-phosphate in the first stage of the hydrolysis of the diethyl acetal lowers the radioactivity of [γ-^{32}P]ATP sharply and in an uncontrolled manner owing to isotopic dilution. This method has not therefore found extensive application either in laboratory practice or in industry.

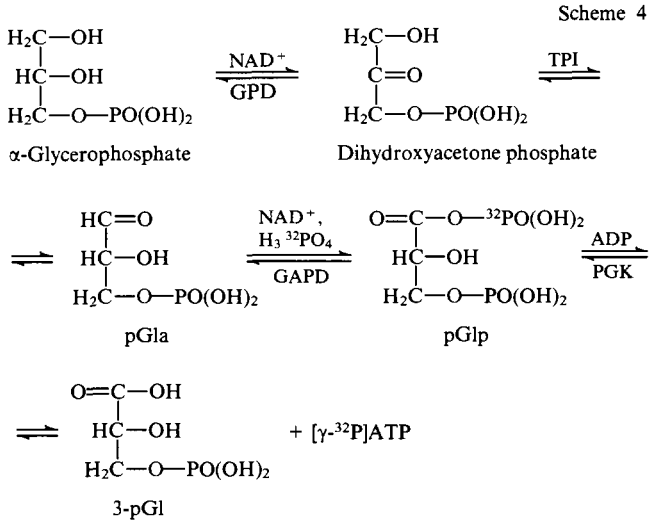
In order to increase the molar radioactivity of the preparation, Walseth and Johnson[14] improved the method further — a fragment of the glycolysis chain was supplemented by three more fragments: glycerophosphate dehydrogenase (GPD), triosephosphate isomerase (TPI), and lactate dehydrogenase (LDH). Glyceraldehyde-3-phosphate was then synthesised from α-glycerophosphate, while LDH was added to the system in order to regenerate the NAD^+ (Scheme 4). Since LDH does not participate directly in the synthesis of [γ-^{32}P]ATP, it is not shown in Scheme 4.

The yield of ATP increased to 90%–98% and, which is most important, the molar radioactivity rose to the limiting values, which were determined by the molar radioactivity of the initial [^{32}P]orthophosphoric acid and also by the content of the 'cold' orthophosphate in the reagents employed.

Scheme 3



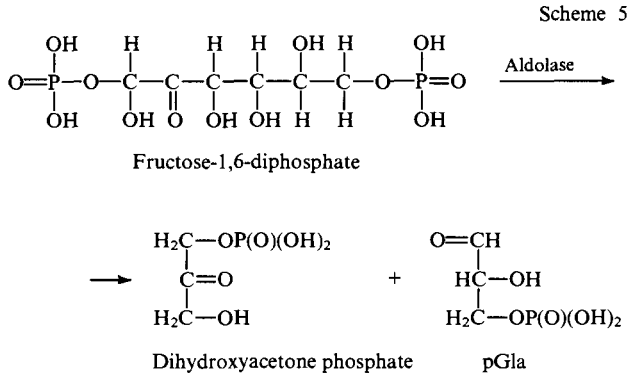
Scheme 4



Instead of ADP, one can use other nucleoside 5′-diphosphates: GPD, IDP, CDP, UDP, dADP, dGDP, which afford the corresponding triphosphates with the phosphorus label in the γ-position. The method is simple and readily reproducible and has found extensive application in various laboratories. Judging from the extremely scanty and fragmentary literature data, all the principal producer companies obtain [γ-^{32}P]ATP precisely by this method (possibly with some modifications).

Banschke and coworkers[15] proposed yet another method of synthesis of glyceraldehyde phosphate. They used the cleavage of fructose-1,6-diphosphate by aldolase (Scheme 5).

Scheme 5



In our view, this path suffers from at least two disadvantages compared with the synthesis in accordance with Scheme 4. Firstly, fructose-1,6-diphosphate is not very stable in solution and there is therefore a real possibility of isotopic dilution by 'cold' phosphorus. Secondly, in order to increase the yield, the accumulated dihydroxyacetone phosphate must be removed, for example with the aid of the same TPI. Thus the method has no special advantages, since the replacement of GPD by aldolase and hence of α-glycerophosphate by fructose-1,6-diphosphate is not justified. Admittedly, the authors indicate the greater resistance of aldolase to the effect of ionising radiation, which may be important for industrial synthesis. There is no doubt that the thoroughly tested synthesis presented in Scheme 4 is preferable for laboratory use in the range 1 – 10 mCi.

Quite recently, ICN Biomedical, Inc. patented[16] yet another method of synthesis of [γ-^{32}P]ATP — a kind of intermediate variant between the Johnson – Walseth and Schendel – Wells methods. Lynn, the author of this scheme, suggested that α-glycerophosphate and glycerophosphate dehydrogenase be abandoned and that dihydroxyacetone phosphate be used immediately as the initial nonradioactive starting material. In fact, he proposed that the Johnson – Walseth scheme 'be shortened' by one (the first) stage (Scheme 4). At the same time, Lynn suggested that the usual NAD-regenerating system (lactate dehydrogenase – pyruvate) be replaced by a more exotic system (malate dehydrogenase – oxaloacetate). According to the authors' communication, these two changes make it possible to scale up the synthesis to a charge up to 500 mCi of [^{32}P]orthophosphate and an unchanged high yield (~95%) over a period of 15 – 20 min. Bearing in mind existing literature data[17] indicating the low stability of glycerophosphate dehydrogenase towards ionising radiation from phosphorus-32 this is extremely likely. Indeed, the direct application of the Johnson – Walseth method makes it possible to obtain satisfactory results for the synthesis involving 1 – 10 mCi of phosphorus-32 (the usual laboratory synthesis). An increase in the amount of phosphorus-32 to 100 mCi or further to 1 Ci reduces sharply the yield of the reaction.

It must be emphasised that in Lynn's method all the ingredients of the reaction mixture, including the enzymes, are taken in logical and justified amounts, which can be in no way said of the original study of Johnson and Walseth. Nevertheless, the 'ICN' patent appears more like an attempt to 'get round' the Johnson – Walseth patent rather than a serious attempt to improve the technology and is hardly likely to be incorporated widely into practice.

We proposed a fairly simple and convenient modification of the Johnson – Walseth method for the large-scale synthesis (100 – 1000 mCi of phosphorus-32). Its laboratory version has been described in Karamyshev's dissertation.[18] The essential feature of the modification consisted in the preliminary formation of glyceraldehyde-3-phosphate directly in the reaction vessel: after centrifugation, the ammonium sulfate residue of the enzyme mixture was dissolved in a buffer containing dithiothreitol and all the necessary ingredients for the synthesis of [γ-^{32}P]ATP, with the exception of [^{32}P]orthophosphoric acid and ADP, were introduced into the solution. After preincubation for 20 min, the above remaining ingredients were added and the synthesis was carried out. Such changes in the order of the introduction of the reagents into the reaction mixture do not entail any fundamental alterations, but, according to our observations, they increase and stabilise the yield of the product of the synthesis by virtue of the effective generation of glyceraldehyde-3-triphosphate (in accordance with Scheme 4) before the start of the synthesis of [γ-^{32}P]ATP proper.

III. Synthesis of nucleoside 5′-[α-$^{32(33)}$P]-triphosphates

The scheme designed for the synthesis of nucleoside 5′-triphosphates (NTP) labelled with phosphorus-32(33) in the α-position is much more complex than those described above and requires the solution of virtually two independent problems. The first involves the synthesis of nucleoside 5′-monophosphate (NMP) with a phosphorus label by introducing [$^{32(33)}$P]orthophosphate rigorously in the 5′-position in the nucleoside. The second problem involves the synthesis of the nucleoside 5′-[α-$^{32(33)}$P]triphosphates themselves from the corresponding 5′-[$^{32(33)}$P]NMP.

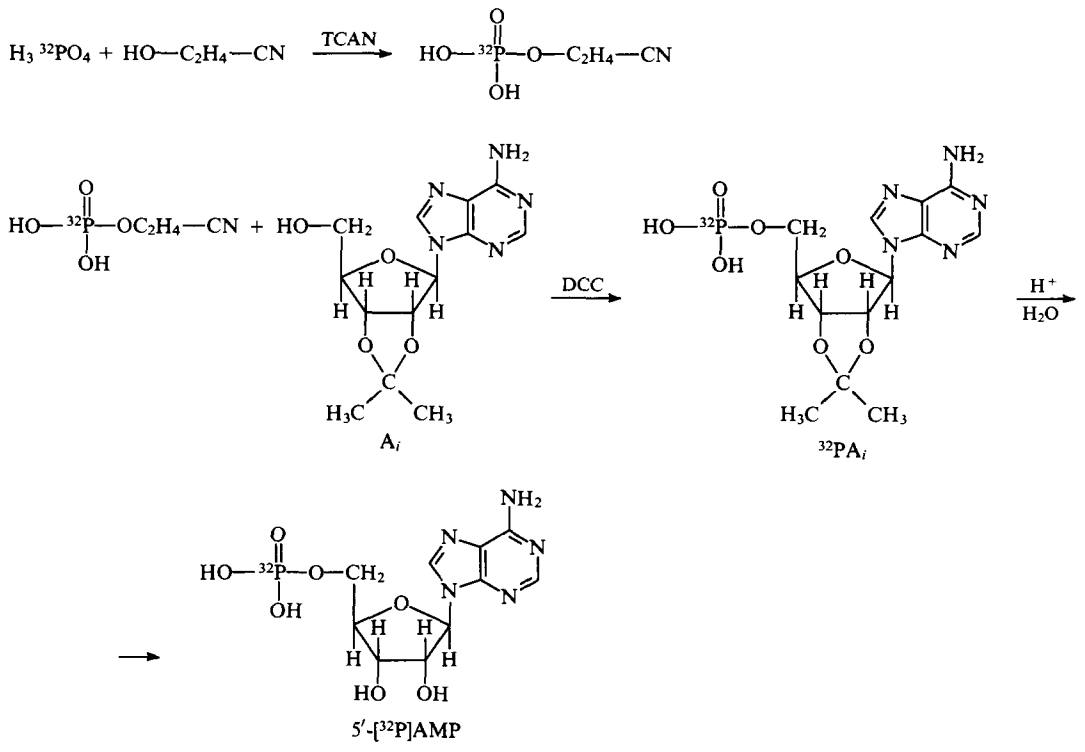
1. Synthesis of nucleoside 5′-[$^{32(33)}$P]monophosphates

a. Chemical methods

Since the majority of the chemical methods for the introduction of labelled orthophosphate into nucleosides are nonspecific, nucleosides with protected 2′- and 3′-hydroxy-groups are employed for the synthesis of 5′-[$^{32(33)}$P]NMP. After the synthesis, the protecting group (the isopropylidene, acetyl, or benzoyl groups) are removed by acid or alkaline hydrolysis.

The first nucleoside 5′-monophosphate labelled by phosphorus-32 was synthesised by Moffat,[7] who employed ^{32}P-labelled β-cyanoethyl phosphate in the presence of DCC in order to phosphorylate 2′,3′-*o*-isopropylideneadenosine (A_i)

Scheme 6



(Scheme 6). The labelled β-cyanoethyl phosphate was obtained by condensing [^{32}P]orthophosphoric acid with β-cyanoethanol in the presence of trichloroacetonitrile (TCAN). $^{32}PA_i$ was hydrolysed in an acid medium to give the ^{32}P-labelled adenosine 5′-monophosphate — 5′-[^{32}P]AMP.

Symons[19] simplified the synthesis of the nucleoside 5′-[^{32}P]monophosphate by employing TCAN in the synthesis of 5′-[^{32}P]AMP directly from the protected adenosine and the triethylammonium salt of [^{32}P]orthophosphoric acid. Such simplification immediately rendered this method extremely popular both in laboratories and in industry. It is noteworthy that, despite its apparent simplicity, the method suffers from a series of disadvantages, the main ones of which — the formation of a considerable amount of side products and the low yield were noted by Maslova et al.[20] The rigorous requirements as regards the quality of the reagents and solvents and also the extremely complex mixture of reaction products forced investigators to continue the search for alternative methods of synthesis.

An improvement of Symons' method was proposed by Ammosov and coworkers.[21] It involved the use of nucleosides with an acetyl protecting group instead of nucleosides with isopropylidene or benzoyl protecting groups. The conditions used in the removal of the acetyl protecting group after the condensation of the protected nucleoside with [^{32}P]orthophosphoric acid are fairly mild (the removal usually involved treatment with an ammonia solution), which makes it possible to obtain the final product in a yield up to 70%–80%. On the other hand, in the case of the isopropylidene protecting group, which is removed under significantly more severe conditions (by treatment with hydrochloric acid), the yield of the pyrimidine nucleosides in the reaction carried out by the Symons procedure does not exceed 40%, while in the case of derivatives of 2′-deoxynucleosides of the purine series the preparation of the nucleoside 5′-[^{32}P]monophosphate becomes altogether problematical.

The attempt by Biebricher[22] to use urea as the condensing agent was interesting. A solution of the corresponding nucleoside, the ammonium salt of [^{32}P]orthophosphoric acid, and urea was evaporated to dryness and the dry residue was heated for several hours at 110–120 °C, cooled, and dissolved in water. Nucleoside 5′-[^{32}P]monophosphates were identified in the solution in yields of 15%–40%, depending on the nature of the heterocyclic base of the nucleoside. Unfortunately, the very complex mixture of unidentified side products of the reaction hinders the use of this method.

The attempt by Hurlbert and Furlong[23] to use a biosynthetic procedure based on *E. coli* to obtain [^{32}P]nucleotides is also of purely historical interest. The main disadvantage of this method is the very low molar radioactivity (10–20 mCi mmol^{-1}). The uncontrolled isotopic dilution and the high requirement by *E. coli* for inorganic phosphate preclude in principle the formation of radioactive phosphorus-labelled nucleotides with a high molar radioactivity.

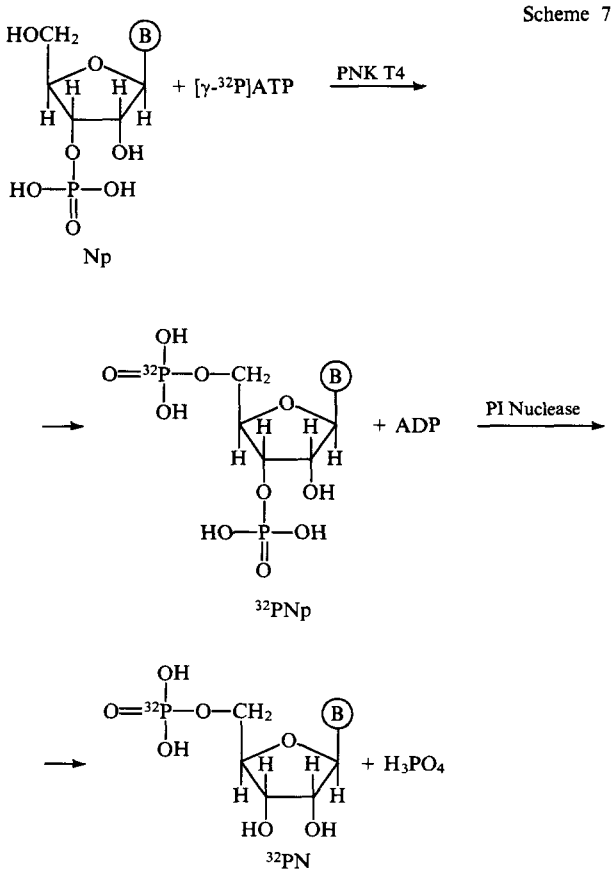
b. Enzymic methods of synthesis of nucleoside 5′-[$^{32(33)}$P]monophosphates

Johnson and Walseth[24] proposed an enzymic method of synthesis of nucleoside 5′-[^{32}P]monophosphates with the aid of a T4 phage polynucleotide kinase (PNK T4) and the PI nuclease (Scheme 7). The nucleoside 3′-monophosphate (Np) is the acceptor and [γ-^{32}P]ATP is the donor of radioactive phosphate.

The use of [γ-^{32}P]ATP for the synthesis of radioactive phosphorus-labelled nucleoside 5′-monophosphates proved to be entirely justified, since the enzymic method of synthesis of [γ-^{32}P]ATP makes it possible not only to synthesise this product rapidly and in a high yield but also to carry out the subsequent synthesis of ^{32}P-labelled nucleoside triphosphates with the aid of PNK T4 in the same reaction mixture without isolating [γ-^{32}P]ATP. This method is universal because PNK T4 phosphorylates all natural nucleoside 3′-monophosphates. The high rate and specificity of the enzymic reactions ensure a minimal amount of side products. All the advantages listed have attracted attention because of their technological applicability. The only significant disadvantage of the method is the need for a number of extremely expensive and very pure enzymes.

The lack of pure and stable enzymes — nucleoside kinases — precluded hitherto a test of yet another possibility of obtaining radioactive phosphorus-labelled nucleotides. This is the procedure based on the direct transphosphorylation of nucleosides

Scheme 7



with the aid of nucleoside kinases and [γ-^{32}P]ATP. The simplicity of this approach is evident, but nucleoside kinases are as a rule rigorously specific to the nature of the heterocyclic base of the nucleoside and it is therefore necessary to have 4–5 highly purified nucleoside kinases in order to synthesise all the natural nucleoside 5'-[$^{32(33)}$P]monophosphates. Attempts to isolate these enzymes from various sources have been frequently undertaken, but so far as we are aware stable preparations suitable for the preparative synthesis of nucleotides have not been obtained hitherto.

2. Methods for the phosphorylation of nucleoside 5'-[$^{32(33)}$P]monophosphates to nucleoside 5'-[α-$^{32(33)}$P]-triphosphates

a. Chemical methods

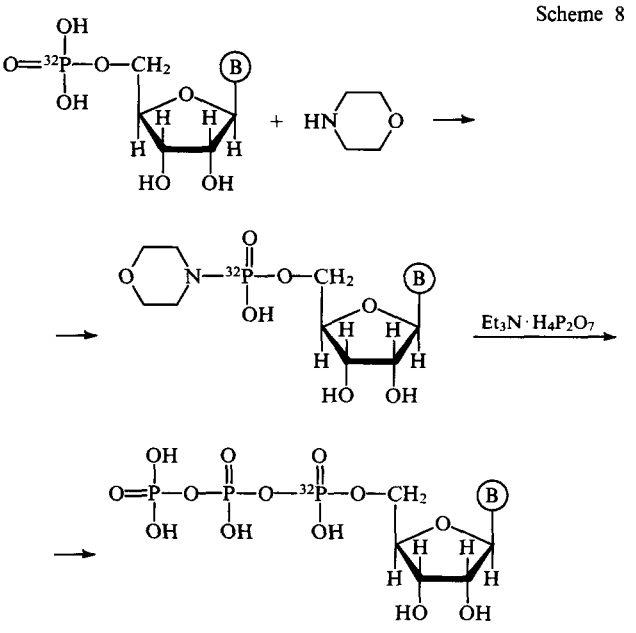
Moffat[7] synthesised nucleoside 5'-[α-^{32}P]triphosphates via the morpholide activation of nucleoside 5'-[^{32}P]monophosphate. The morpholide formed reacts with the triethylammonium salt of pyrophosphoric acid, affording a satisfactory yield (Scheme 8).

The [α-^{32}P]ATP obtained according to Scheme 8 had a very low molar radioactivity — about 10 mCi mmol^{-1}. Despite the satisfactory yield (65%), the method has not received recognition, since attempts to increase the molar radioactivity of the product led to a sharp fall in yield and to the accumulation of side products.

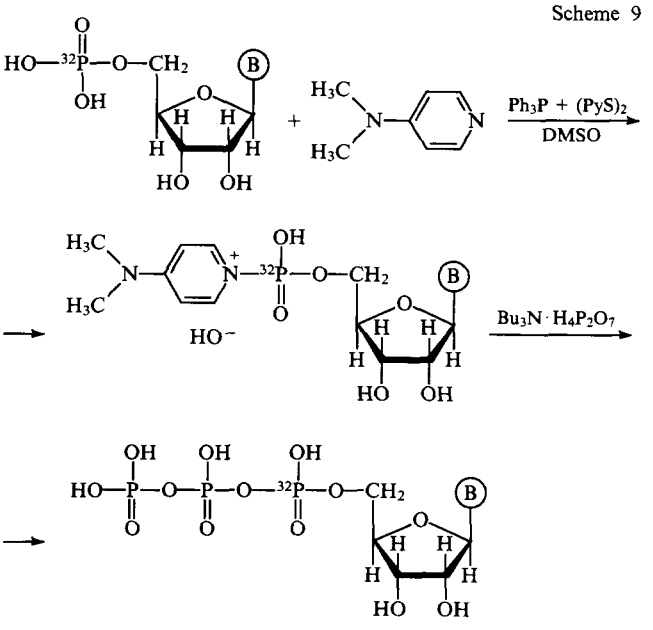
Siberian investigators proposed another more successful method for the activation of the nucleoside 5'-[^{32}P]monophosphate[25] involving the synthesis of an intermediate — a derivative of 4-(*N*,*N*-dimethylamino)pyridine. An oxidation-reduction couple was used as the catalyst: triphenylphosphine and di(4-pyridyl) disulfide. The intermediate formed is extremely unstable — it reacts even with the tributylammonium salt of pyrophosphoric acid directly in the same reaction vessel (Scheme 9).

All the natural nucleoside 5'-[α-^{32}P]triphosphates with a molar radioactivity of 2000–3000 Ci mmol^{-1} and above have

Scheme 8



Scheme 9

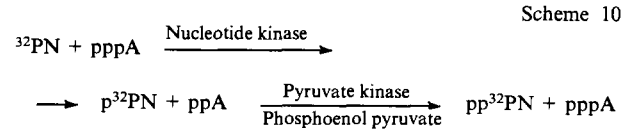


been synthesised in accordance with Scheme 9. The yield was 15%–40% relative to the initial [^{32}P]orthophosphoric acid. The method proved very useful in syntheses involving 1–10 mCi of phosphorus-32. An increase in the activity of the radioactive starting material to 100–200 mCi leads to the formation of a very complex mixture and reduces the yield of the target product, apparently as a consequence of the radiolysis of the reaction components.

b. Enzymic methods

The variants of the enzymic phosphorylation of nucleoside 5'-[$^{32(33)}$P]monophosphates to the triphosphates with the aid of the corresponding nucleotide kinases are more promising for the solution of this problem. The phosphorylation reaction can be represented by Scheme 10.

Scheme 10



The kinase fraction of proteins isolated from the bacterial biomass by means of ammonium sulfate fractionation, and not the individual enzymes, was used initially to phosphorylate nucleoside 5′-[^{32}P]monophosphates.[26] Such an enzyme preparation undoubtedly contained a large amount of ballast protein, including undesirable impurities: phosphatases and nonspecific ATP-ases. In order to suppress the degradation of the labelled nucleotides and nucleoside triphosphates and to maintain a constant level of ATP, the reaction mixture was treated with an ATP-regenerating system: creatine phosphate – creatine kinase or phosphoenol pyruvate – pyruvate kinase.[23,26] Acetyl phosphate was sometimes used, whereupon the addition of an exogenic acetate kinase was not required.[27] Nevertheless, the reproducibility of the results was very poor.

This led Biebricher[22] to develop a simple method for the simultaneous isolation of all the required nucleoside monophosphate kinases from *E. coli*. Although the enzymes were not purified to homogeneity, nevertheless the level of the impurity enzyme activities in the preparations employed by Biebricher was many times lower and the reproducibility of the syntheses was significantly increased.

A method for the isolation from *E. coli* of all the necessary nucleoside monophosphate kinases with a fairly high purity especially for the synthesis of all the nucleoside 5′-[α-^{32}P]triphosphates was developed later.[28]

Johnson and Walseth[24] used in the synthesis commercial preparations of pyruvate kinase and nucleoside monophosphate kinases: adenylate kinase (myokinase), guanylate kinase, and nucleoside monophosphate kinase (all the enzymes were produced by the Boehringer – Mannheim Company). Here attention should be drawn to a number of characteristic features of these preparations.

1. Adenylate kinase (myokinase) and guanylate kinase are individual enzymes and although the preparations of these enzymes produced by the Boehringer – Mannheim Company contain a lot of ballast protein and sometimes also undesirable impurities, nevertheless the synthesis of [α-^{32}P]ATP and [α-^{32}P]-dATP and hence of [α-^{32}P]GTP and [α-^{32}P]dGTP proceeds in an entirely satisfactory manner.

2. The nucleoside monophosphate kinase preparation is not an individual enzyme but a protein fraction containing, apart from the ballast protein, at least two of the required enzymes — thymidine monophosphate kinase and cytidine monophosphate kinase. The names of these enzymes in a pure form are missing from the catalogues of the relevant companies.

3. It has come to be assumed that cytidine monophosphate kinase is capable of phosphorylating also UMP (and conversely), i.e. that cytidine monophosphate kinase and uridine monophosphate kinase are the same enzyme.

4. The ratios of the enzyme activities of the 'nucleoside monophosphate kinase' preparation in relation to TMP, CMP, and UMP differ appreciably from batch to batch. The level of the activity of the TMP kinase and to a somewhat lesser extent the UMP kinase is particularly variable. The effectiveness of the use of the nucleoside monophosphate kinase can therefore be different for different substrates — the synthesis of CTP or dCTP usually proceeds most effectively, that of UTP is less satisfactory, and that of TTP is still less effective.

5. Pyruvate kinase — the enzyme catalysing the phosphorylation of NDP to NTP by phosphoenol pyruvate — leads to more ready phosphorylation of purine nucleotides than pyrimidine nucleotides. The phosphorylation of TDP is especially difficult.

Despite the above features of these Boehringer – Mannheim preparations, the enzymic phosphorylation of 5′-[^{32}P]NMP to give 5′-[α-^{32}P]NTP is greatly superior to all other procedures for the phosphorylation of nucleoside monophosphates as regards the effectiveness and technological applicability of the process.

The overall enzymic synthesis of [α-^{32}P]NTP can be represented by Scheme 11.[29]

Scheme 11

$$ppA + {}^{32}P_i \xrightarrow{GPD,\ TPI,\ GAPD,\ PGK,\ LDH} {}^{32}PppA \quad (1)$$

$$^{32}PppA + Np \xrightarrow{PNK\ T4} {}^{32}PNp \quad (2)$$

$$^{32}PNp \xrightarrow{PI\ nuclease} {}^{32}PN + P_i \quad (3)$$

$$^{32}PpN + pppA \xrightarrow{Nucleotide\ kinase} p^{32}PN + ppA \quad (4)$$

$$p^{32}PN \xrightarrow[Phosphoenol\ pyruvate]{Pyruvate\ kinase} pp^{32}PN \quad (5)$$

$^{32}P_i$ — inorganic orthophosphate ion labelled with the radioactive phosphorus-32 (or phosphorus-33) isotope

All the reactions take place in a single reaction vessel and the intermediates do not have to be isolated. Scheme 11 does not include yet another reaction which the authors recommend should be carried out, but this does not affect the principles of the method. This concerns the decomposition of the residual unreacted [γ-^{32}P]ATP after the reaction with PNK T4. In order to avoid the introduction of a label in the β-position in the nucleoside 5′-diphosphate, the authors suggested that, in the stages following the second stage of the phosphorylation reaction, hexokinase should be used to decompose the residual [γ-^{32}P]ATP after the dephosphorylation of the diphosphate by the PI nuclease. After treatment with hexokinase, the mixture was heated for 2 min on a water bath in order to thermally inactivate the enzymes and the synthesis was continued in the same vessel in accordance with Scheme 11.

The method of synthesis of nucleoside 5′-[α-^{32}P]triphosphates proposed by Johnson and Walseth has incontrovertible advantages over all the methods described above and has found extensive application both in laboratory practice and in the corresponding industrial processes.

Analysis of the trends in the development of the methods of synthesis of nucleoside 5′-[$^{32(33)}$P]triphosphates labelled with radioactive phosphorus in the α- or γ-positions shows that the enzymic methods are preferable and are gradually displacing the chemical and chemicoenzymic methods of synthesis from laboratory practice and from industrial manufacture.

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The nuclear-spin selectivity of chemical reactions

A L Buchachenko

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Abstract. The ability of spin-selective chemical reactions to sort nuclei in terms of two features — their spin and orientation — is discussed. The subdivision into spin (magnetic) and spin-free (nonmagnetic) nuclei constitutes the basis of the magnetic isotope effect; the subdivision of nuclei in terms of orientations and the establishment of the nuclear orientation constitute the content of a second phenomenon — chemically induced [dynamic] nuclear polarisation. The bibliography includes 50 references.

I. Introduction

Chemical reactions are selective as to the electron shells of the reacting species and this factor is the principal feature of a chemical process, namely it determines what is referred to as the reactivity. The second feature of a chemical reaction is its selectivity with respect to nuclei — with respect to their mass and angular momentum (spin). The nuclear mass selectivity of chemical reactions has long been widely known as the classical isotope effect — thermodynamic (in equilibrium processes) or kinetic (in nonequilibrium reactions). The nuclear spin selectivity is manifested by the dependence of the reaction rates on the spin, the magnetic moment, and the orientation of the nuclei of the reacting species. The selectivity of the reaction with respect to the nuclear magnetic moment has been called the magnetic (or nuclear spin) isotope effect. The selectivity with respect to nuclear orientation is the cause of the sorting of nuclei with respect to their orientations, which gives rise to magnetic nuclear polarisation in the products of chemical reactions.

Chemical reactions are selective with respect to the electron spin: they are allowed to give rise only to products the overall electron spin of which is identical with the overall spin of the reactants. Reactions are forbidden if the overall spin of the reactants does not correspond to the spin of the products. Thus, among the four spin states of a radical pair (a singlet and three triplets), only the singlet state is capable of reacting to form the standard (in the singlet spin state) molecule; the reaction involving the triplet states of the pair is forbidden. On the other hand, if the reaction product is a molecule in the triplet spin state [for example in the neutralisation of radical-ions: $M^{+\cdot} + M^{-\cdot} \Rightarrow {}^{1,3}(M^{+\cdot}M^{-\cdot}) \Rightarrow M + {}^{3}M$ with formation of the triplet molecule ^{3}M], then the singlet state of the pair $^1(M^{+\cdot}M^{-\cdot})$ is forbidden for the reaction, but the remaining three triplet states $^3(M^{+\cdot}M^{-\cdot})$ are allowed. The reaction $H + O_2 \Rightarrow HO_2$ takes place only with the doublet states of the pair $(H...O_2)$, preceding the chemical interaction. The reaction involving a quartet state of this pair (with the overall spin $S = \frac{3}{2}$) is forbidden, since the reaction product, the radical HO_2, has a spin of $\frac{1}{2}$ and is in a doublet state. The reactions in which both the reactants and the products have a zero spin (molecular and ionic reactions, electrophilic and nucleophilic substitution reactions, etc.) do not require a change of spin and are therefore allowed.

The spin-forbidden reactions are usually encountered among chemical, physical, and biochemical processes involving paramagnetic species (radicals, carbenes, triplet molecules, electrons, holes), in which the spins of the reactants can combine freely but by no means all of the possible combinations are capable of chemical reaction (for example, for a pair of spins, out of the four combinations only one can lead to the combination of the spin-carrying radicals into a diamagnetic molecule).

The spin-reactive intermediate precursors can be altered and the spin-forbidden unreactive spin states can be transformed into spin-allowed reactive states by means of three types of interactions (Fig. 1):

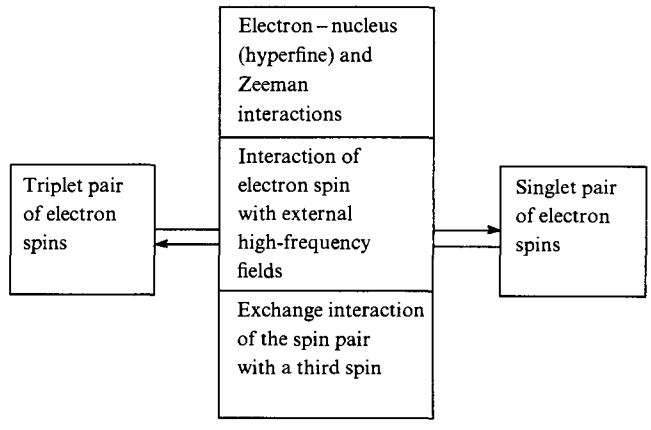


Figure 1. Schematic representation of the interactions inducing the spin conversion of spin pairs.

A L Buchachenko Semenov Institute of Chemical Physics, ul. Kosygina 4, 117334 Moscow, Russian Federation.
Fax (7-095) 938 21 56

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— magnetic interactions of the electron spin with the nucleus and an external magnetic field (hyperfine and Zeeman interactions);
— interaction of the electron spin with the magnetic component of a high-frequency external field;
— exchange interaction of the electron spins with a third spin, which induces the spin triplet–singlet conversion of this pair.

They all have negligible energies, switch the reaction from spin-forbidden paths to open spin-allowed paths, and thus alter the chemical reactivity of the intermediates.

Three types of interactions, controlled by the electron spin, give rise to three generations of magnetic-spin effects. The first includes the magnetic field effect, the magnetic isotope effect, and chemically induced [dynamic] nuclear polarisation. The second generation includes the phenomenon of the chemical detection of magnetic resonance, the radio-induced magnetic isotope effect, and stimulated nuclear polarisation.

The exchange interaction of two spins with a third is not magnetic but it alters the spin of the pair. This phenomenon can be regarded as the catalytic effect of the third spin, inducing spin conversion in the first pair (spin catalysis) and it should be assigned to the third generation of spin effects.

The set of effects generated by the characteristics of the behaviour of the spins of electrons and nuclei in chemical processes is the subject of spin chemistry, to the establishment and development of which Frankevich, Sokolik, Giatsintov, Molin, Sagdeev, Salikhov, Bargon, Fisher, Ward, Kaptein, Lawler, Atkins, Turro, Closs, Step, Tarasov, Berdinskii, Anisimov, etc. have made major contributions. The principal results obtained in this field have been surveyed in a series of reviews and monographs.[1–5]

Being selective with respect to the electron spin, a chemical interaction is inevitably selective also with respect to the nuclear spin, provided that both spin subsystems — electron and nuclear — are linked by the hyperfine or Fermi interaction. The nuclear spin subsystem then acts on the electron subsystem via a hyperfine interaction (HFI), altering the electron spin and removing the spin prohibition. Since the HFI is a property of magnetic nuclei, it selects the isotopic nuclei in terms of the magnetic moment and ensures the sorting of the magnetic and nonmagnetic nuclei (the magnetic isotope effect). Furthermore, the energy of the HFI depends on the orientation of the nuclei, so that the HFI also effects the sorting of the nuclei with respect to their orientations, giving rise to nuclear polarisation in the reaction products. These two effects are the subject of the part of spin chemistry in which the nuclear spin selectivity of chemical reactions is investigated and to which this review is devoted.

II. Sorting of isotopic nuclei

The magnetic isotope effect (MIE) was discovered by two groups of investigators in Russia in 1976,[6,7] although the possibility of its existence had been mentioned by Lawler and Evans in 1971.[8]

The sorting of the magnetic and nonmagnetic nuclei effected by the MIE is clearly illustrated by the photolysis of dibenzyl ketone, in which the molecule undergoes fragmentation in the excited triplet state into a pair of radicals — benzyl and phenylacyl. Being in the triplet state, this radical pair can recombine again, regenerating the initial molecule, or can dissociate and can generate, via the decarbonylation of the phenylacyl radical, the final photolysis products — bibenzyl and carbon monoxide. However, the recombination of the pair is possible only starting with the singlet state, which means that it must be preceded by the triplet–singlet spin conversion of the pair. The hyperfine interaction of the unpaired electron with the ^{13}C nucleus in phenylacyl accelerates the triplet–singlet conversion of the pairs with magnetic ^{13}C nuclei and stimulates their recombination, since radical pairs with nonmagnetic ^{12}C nuclei lag in their spin conversion and undergo preferential dissociation. As a result, the regenerated ketone molecules accumulate the ^{13}C nuclei, while the photolysis products — bibenzyl and CO — are depleted in this isotope. Hence, as a result of the spin selectivity and the hyperfine interaction, the radical pair sorts the nuclei in accordance with their magnetic characteristics, directing the magnetic and nonmagnetic nuclei along different reaction paths, i.e. into different chemical products.

The degree of sorting, i.e. the degree of isotope enrichment of each ketone in the ^{13}C nuclei is defined by the simple equations[9,10]

$$S = (1-F)^{\alpha}\ ; \qquad \alpha = \frac{1-\alpha_G}{\alpha_G}\ ; \qquad \alpha_G = \frac{1-P}{1-P^*}\ . \tag{1}$$

Here S is the isotope enrichment [$S = \delta/\delta_0$, where δ_0 and δ are the contents of the isotope (for example, ^{13}C) in the initial ketone and in its residue] after the attainment of the chemical conversion $1-F$ (F is the fraction of the remaining ketone), α is the coefficient of the single-stage isotope enrichment, and P^* and P are the probabilities of the recombination of the radical pairs with the ^{13}C and ^{12}C isotopes, i.e. the probabilities of the regeneration of the 'magnetic' and 'nonmagnetic' ketones respectively. Evidently, α_G is the ratio of the rates of the chemical decomposition of the nonmagnetic and magnetic ketones. Since $P^* < P$, it follows that $\alpha_G > 1$, i.e. the magnetic ketone decomposes more slowly and is retained during photolysis to a greater extent than the nonmagnetic ketone.

The ideal isotope separation takes place subject to the condition $P^* = 1$ and $P = 0$, which means that the magnetic ketone is fully regenerated, whilst the nonmagnetic ketone is fully decomposed. This regime corresponds to 'chemical isotope purification'; in this case, $\alpha_G \Rightarrow \infty$ and $\alpha = -1$. The attainment of this regime constitutes a major and intriguing problem and we shall return to its discussion below.

The photolysis of dibenzyl ketone was the first chemical process in which the MIE was observed.[6] It is a classical example of the MIE and serves as a test of the physics of this unique phenomenon.

Isotope enrichment obeys rigorously Eqn (1), while the quantity α_G depends on the properties of the medium, varying from 1.05 in hexane at 20 °C to 1.50 in glycerol and 1.37 in hexadecyltrimethylammonium chloride micelles (Fig. 2).

The studies on the MIE developed in two directions: (1) experimental search for the effects involving nuclei heavier

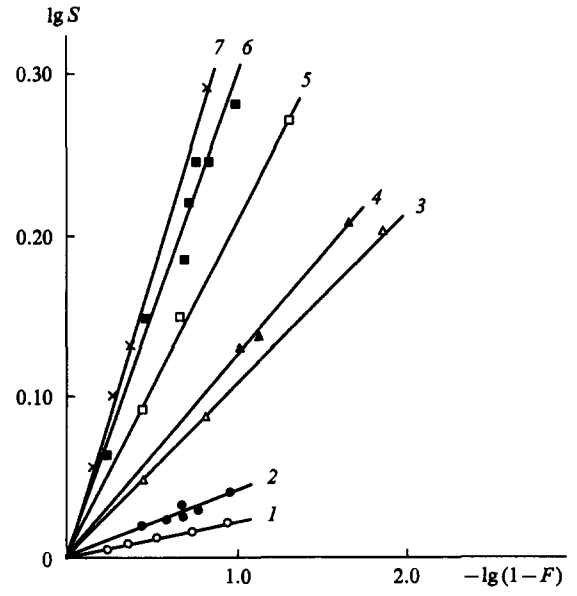


Figure 2. Isotope enrichment (S) as a function of the chemical conversion (F) in terms of the variables of Eqn (1) in the photolysis of dibenzyl ketone: (*1*) benzene; (*2*) hexane; (*3*) cyclohexanol, 20 °C; (*4*) cyclohexanol, 0 °C; (*5*) glycerol, 1700 cP; (*6*) hexadecyltrimethylammonium chloride micelles; (*7*) glycerol, 2400 cP.

than that of carbon and (2) theoretical analysis of the chemical physics of the effect in order to predict the possible ways of increasing it.

Considerable progress has been achieved in both directions: the outcome of the first will be examined briefly in this Section, while that of the second will be discussed below.

The magnetic isotope effect in the $^{13}C/^{12}C$ diad has been known since 1976;[6,7] since then, it has been discovered in the triads $^{16}O/^{17}O/^{18}O$,[11-16] $^{28}Si/^{29}Si/^{30}Si$,[17-18] and $^{32}S/^{33}S/^{34}S$ [19] and also in the diads $^{72}Ge/^{73}Ge$ [20] and $^{238}U/^{235}U$.[21,22]

The magnetic isotope effect of ^{17}O has been discovered in the reactions involving the chain oxidation of carbochain polymers[12] and the liquid-phase oxidation of hydrocarbons[11,13] by molecular oxygen. In the first case, the oxidation reaction and the absorption of oxygen are accompanied by the enrichment of the residual oxygen in the ^{17}O and ^{18}O isotopes (Fig. 3*a*), the enrichment in the magnetic isotope ^{17}O greatly exceeding that in the nonmagnetic isotope ^{18}O, the dependence of the enrichment on the conversion obeying Eqn (1) (Fig. 3*b*). The anomalous behaviour of the magnetic isotope indicates unambiguously that the MIE is the main cause of the isotope selectivity.

The reaction involving the termination of the kinetic oxidation chains, i.e. the interaction of two peroxy radicals in accordance with the scheme

$$RO_2^{\cdot} \Longleftrightarrow (RO_2^{\cdot}\ {}^{\cdot}O_2R) \Longleftrightarrow RO_4R \Rightarrow RO_3^{\cdot} + O^{\cdot}R \Rightarrow 2\,RO^{\cdot} + O_2$$

pin-selective and hence nuclear-selective. Following their encounter, a pair of peroxy radicals either recombines to the unstable tetroxide RO_4R, which subsequently decomposes irreversibly with regeneration of molecular oxygen, or dissociates reversibly, regenerating the initial peroxy radicals. The MIE actually arises

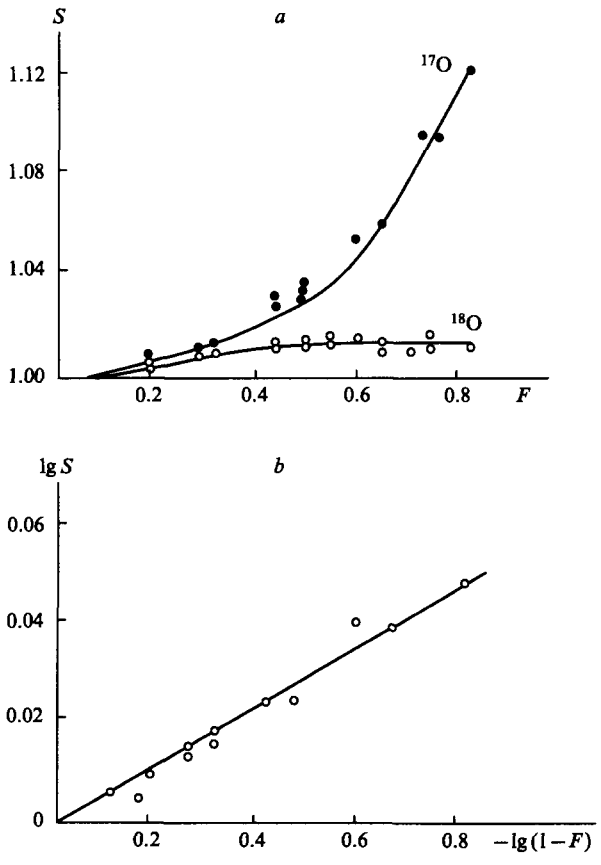


Figure 3. Dependence of the isotope enrichment on the conversion of molecular oxygen in the oxidation of polypropylene at 130 °C (*a*) and its representation in terms of the variables of Eqn 1 (*b*).

in this stage: the pairs containing the $R^{16}O^{17}O^{\cdot}$ radicals recombine faster than the radical pairs with $R^{16}O^{16}O^{\cdot}$ (or $R^{16}O^{18}O^{\cdot}$). As a result, the regenerated oxygen is enriched in the ^{17}O magnetic isotope, while the hydroperoxide $R^{16}O^{16}OH$ is depleted in this isotope. The kinetic theory of this process, developed by Buchachenko et al.,[16] defines the isotope enrichment of the molecular oxygen S as a function of its chemical conversion F in terms of the ratio of the rate constants for the quadratic kinetic chain termination. The ratio of the termination rate constants k_t was found from the $S(F)$ relation (Fig. 3*a*) in terms of the variables of Eqn (1):

$$\frac{k_t(R^{16}O^{17}O + {}^{16}O^{16}OR)}{k_t(R^{16}O^{16}O + {}^{16}O^{16}OR)} = 1.8\ ,$$

i.e. the replacement of the ^{16}O nonmagnetic nucleus by the ^{17}O magnetic nucleus ensures an increase in the rate constant for the annihilation of the peroxy radical almost by a factor of two.

The opposite effect obtains in the liquid-phase oxidation reactions of hydrocarbons[13] — as molecular oxygen is consumed, it is depleted in the ^{17}O isotope, which means that the principal isotope-sorting process in these reactions becomes the addition of the alkyl radicals $R^{\cdot}$ to molecular oxygen. The addition of $R^{\cdot}$ to $^{17}O^{16}O$ is faster than the addition to $^{16}O^{16}O$ and the reason for this is again the acceleration of spin conversion in the pair $(R...O_2)$ as a result of the hyperfine interaction with the ^{17}O magnetic nucleus. However, the quartet–doublet conversion now takes place. The ratio of the rate constants for the $R^{\cdot} + {}^{17}O^{16}O$ and $R^{\cdot} + {}^{16}O^{16}O$ reactions is 1.011, i.e. the $^{17}O^{16}O$ molecules react faster than the $^{16}O^{16}O$ molecules to the extent of 1.1%[16] and this difference between the rates depletes the molecular oxygen in the ^{17}O isotope. The classical mass isotope effect (CIE) in the $R^{\cdot} + {}^{18}O^{16}O$ and $R^{\cdot} + {}^{16}O^{16}O$ reactions is 0.99, i.e. the first reaction is slower than the second by 1%.[16] Clearly the MIE is much greater than the CIE: it fully compensates for the CIE in the $R^{\cdot} + {}^{17}O^{16}O$ reaction and actually reverses the sign of the effect.

The difference in the behaviour of the ^{17}O isotope in two processes — the oxidation of polymers in the viscoelastic state and liquid-phase oxidation — demonstrates the leading role of molecular dynamics in the selection of the spin-selective reaction. Molecular dynamics controls the spin selectivity of the two isotope-sorting reactions (the propagation and termination of kinetic chains). The first of these predominates in solutions with a low viscosity, while the second predominates in viscous systems with greatly retarded molecular motion. The physical cause of the difference between the isotope selectivities of these two reactions is evident: rapid molecular dynamics and a short time of the diffusional 'liquid-phase' trajectories should correspond to rapid spin evolution in the $(R^{\cdot}...O_2)$ pair, while slow dynamics and a long time of the diffusional trajectories in viscous polymers should correspond to slow spin conversion in the $(RO_2^{\cdot}\ {}^{\cdot}O_2R)$ pair. The comparable times of spin conversion and diffusional motions ensure the optimum conditions for the isotope selection in two competing processes — reaction in the pair and diffusional dissociation of the pair.

The high-temperature oxidation of polyaromatic[15] polymers (polypyromellitimide, polyphenylquinoxaline) by molecular oxygen is accompanied by the enrichment of the latter in the ^{18}O isotope and its depletion in the ^{17}O isotope. The kinetics of the oxidation (the absence of autocatalysis and of the inhibiting effect of antioxidants) and the composition of the oxidation products (mainly quinones) indicate a nonchain oxidation mechanism, in which the spin-selective stage is the interaction of molecular oxygen with low-lying excited and thermally accessible triplet states of the polyaromatic fragments of the macromolecules. The product of this reaction is an *endo*-peroxide. Among the nine spin states of the pair of two triplets (oxygen plus the triplet fragment of the macromolecule), only one (singlet) state gives rise to the *endo*-peroxide. The hyperfine interaction in the oxygen with ^{17}O partly removes the spin prohibition and opens an additional reaction path involving other spin states. As a result,

the ^{17}O isotope-containing oxygen reacts faster and its transfer to the products depletes the molecular oxygen in the ^{17}O isotope. The enrichment of the oxygen in the ^{18}O isotope in this reaction takes place due to the CIE.

A magnetic isotope effect of ^{17}O with the opposite sign has been observed by Turro and Chow[14] in the reverse reaction involving the decomposition of *endo*-peroxides. There is no doubt that the decomposition takes place via the singlet state of the biradical $Ar^{\bullet}-OO^{\bullet}$, where Ar is the aryl component of the *endo*-peroxide. The biradical may decompose, generating singlet oxygen, or may be transformed into a triplet state, generating triplet molecular oxygen on decomposition. Clearly in the biradicals with ^{17}O the latter process should predominate and singlet oxygen should therefore be depleted in the ^{17}O isotope, while triplet oxygen should in fact be enriched in this isotope. These predictions have been fully confirmed by experiment.[14]

The discovery of the MIE of ^{29}Si arose from the synthesis of the silicon-containing ketone $PhCH_2COSiMe_2Ph$, which is similar to dibenzyl ketone structurally and to its photolysis in micelles.[18] It was shown with the aid of chemically induced [dynamic] nuclear polarisation that both direct and triplet-sensitised photolysis occur, as in the photolysis of dibenzylketone via radical pairs.

$$PhCH_2\overset{O}{\overset{\|}{C}}SiMe_2Ph \Longleftrightarrow (PhCH_2^{\bullet}\ {}^{\bullet}\overset{O}{\overset{\|}{C}}SiMe_2Ph) \Longrightarrow \text{products}$$

The direct photolysis begins with the excited singlet state, which generates the singlet radical pair (RP). On the other hand, the sensitised photolysis proceeds via the triplet RP.[23] The variation of the silicon isotope composition of the ketone as a function of the chemical conversion of the latter is illustrated in Fig. 4.

The first important result which follows from Fig. 4 is that the enrichment of the ketone in the ^{29}Si magnetic isotope greatly exceeds its enrichment in the ^{30}Si nonmagnetic isotope. Clearly the HFI involving the ^{29}Si nucleus in the triplet RP accelerates its triplet – singlet spin conversion and stimulates the recombination of the pairs with ^{29}Si, whereas the triplet – singlet conversion of the pairs with ^{28}Si lags behind and these pairs dissociate and are converted into other products, the excess ^{28}Si nuclei being removed in these products.

The second striking result which follows from Fig. 4 is that the direct photolysis leads to the depletion of the initial ketone in the ^{29}Si isotope, i.e. the inversion of the spin multiplicity of the RP in the direct and sensitised photolysis is accompanied by the inversion of the sign of the MIE: the enrichment of the ketone in the ^{29}Si isotope in the sensitised photolysis (starting with the triplet) is replaced by depletion in the direct photolysis (starting with the singlet). The cause of the inversion is evident: the initial singlet pairs with ^{29}Si are transformed faster into the triplet pairs and subsequently dissociate, carrying away ^{29}Si and other products and depleting the regenerated ketone in this isotope. We may note that the enrichment of the ketone in the ^{30}Si nonmagnetic isotope is due to the CIE and is therefore insensitive to the spin multiplicity of the RP and to the direction of spin conversion — from the triplet to the singlet or back again.

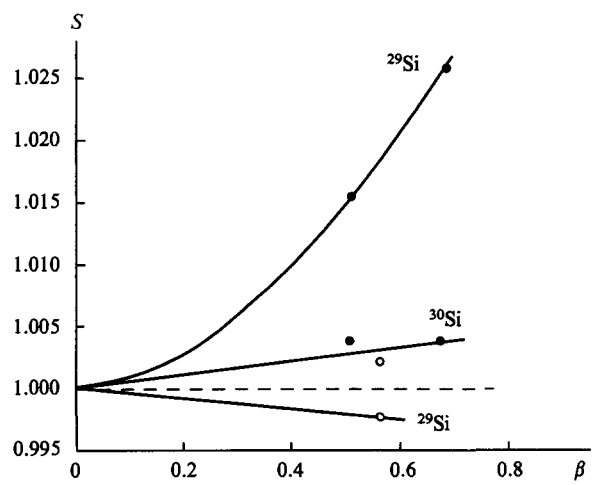


Figure 4. Enrichment in the ^{29}Si and ^{30}Si istopes as a function of the chemical conversion β in the direct (open circles) and sensitised (filled circles) photolysis of silyl ketone.

The ^{33}S magnetic isotope effect was first observed in 1990[19] in the direct micellar photolysis of a sulfur-containing ketone, which was shown with the aid of chemically induced [dynamic] nuclear polarisation to proceed via triplet RP in accordance with the scheme

$$PhC\overset{O}{\overset{\|}{C}}H_2SO_2Ph \rightleftharpoons (PhC\overset{O}{\overset{\|}{C}}H_2^{\bullet}\ {}^{\bullet}SO_2Ph) \Longrightarrow \text{products.}$$

The pairs with the ^{33}S magnetic isotope recombine faster and return this isotope to the regenerated ketone molecules, the enrichment of which in ^{33}S increases with increase in the chemical conversion of the ketone (Fig. 5). The marked predominance of the ^{33}S isotope enrichment over the enrichment in the ^{34}S nonmagnetic isotope demonstrates unambiguously the predominance of the MIE over the CIE.

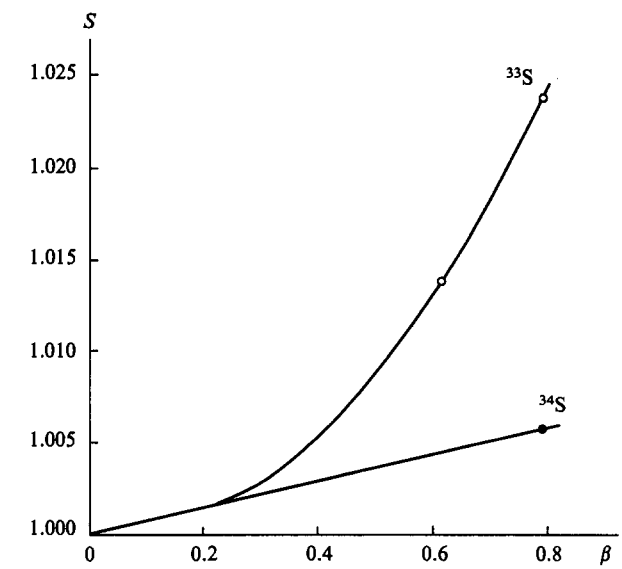


Figure 5. Enrichment in the ^{33}S and ^{34}S isotopes as a function of the chemical conversion in the photolysis of a sulfur-containing ketone.

The ^{73}Ge magnetic isotope effect was discovered quite recently[20] in the photolysis of methyltriphenylgermane in micelles; the initial compound was enriched in the ^{73}Ge magnetic isotope relative to the nonmagnetic ^{72}Ge. The enrichment in ^{73}Ge depends greatly on the magnetic field, whereas the content of the ^{72}Ge isotope does not change, demonstrating the 'classical' origin of the effect involving ^{72}Ge.

The mechanism of the decomposition reaction suggests that the selection of the magnetic and nonmagnetic germanium nuclei takes place in accordance with the same principle as the sorting of the ^{13}C nuclei in the decomposition of dibenzyl ketone.

$$Ph_3GeMe \Longleftrightarrow (Ph_2MeGe^{\bullet}\ Ph^{\bullet})^{T} \Rightarrow \text{products}$$

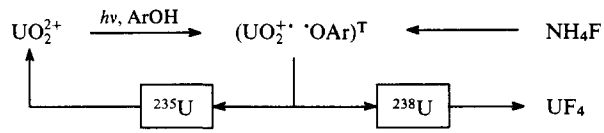
The hyperfine interaction involving the ^{73}Ge nucleus in the radical $Ph_2MeGe^{\bullet}$ is unknown, but one can make the reliable assumption that its magnitude is hardly likely to differ greatly

from that known for the $Ph_3Ge^{\cdot}$ and $Me_3Ge^{\cdot}$ radicals.[24,25] As a result of the HFI, the ^{73}Ge-containing radical pairs rapidly evolve to singlet species and recombine, returning the ^{73}Ge magnetic nuclei to the regenerated methyltriphenylgermane molecule.

Finally, the MIE involving uranium nuclei has been observed independently by two groups of investigators.[21,22] The search for the MIE of uranium nuclei required the solution of three problems: (1) the search for reactions of uranium compounds which could generate paramagnetic intermediates — spin carriers (radicals or radical-ions); (2) the search for spin-selective stages in the reactions of these intermediates; (3) the study of the proportions of the isotopes in the products. The solution of the last of the three problems is the most problematical, because there is no guarantee that the outer unpaired electron in the uranium-containing paramagnetic intermediate is capable of 'breaking through' the thick electron shell consisting of more than 90 electrons and reaching the nucleus in order to give rise to the appreciable HFI necessary to ensure the nuclear spin selectivity.

Among the various reactions of uranium-containing compounds, the photoreduction of uranyl salts was chosen for the search for the MIE. The first stage of this reaction is the reduction of the uranyl ion UO_2^{2+} to the paramagnetic uranoyl ion UO_2^{+}. In three series of elegant experiments {the observation of chemically induced [dynamic] nuclear polarisation in the reactions of the uranyl ion,[26] the observation of the magnetic field effect in a uranyl-photosensitised polymerisation reaction,[27] and the detection of electronic polarisation transferred from the excited UO_2^{2+} ion to the nitroxyl radical[28]}, it was shown unambiguously that the uranyl ion UO_2^{2+} reacts in the excited triplet state, generating the uranoyl ion UO_2^{+}, which subsequently participates in spin-selective reactions, which sort the isotopic nuclei (the magnetic ^{235}U nuclei and the nonmagnetic ^{238}U nuclei).[29]

The most convincing results were obtained in the photolysis of uranyl perchlorate in an aqueous micellar solution of sodium dodecyl sulfate in the presence of NH_4F and 2,6-diphenyl-4-stearoylphenol.[30] The reaction mechanism and the paths followed in the migration of the isotopic nuclei are illustrated below.



The photolysis of uranyl generates a triplet RP made up of the uranoyl ion UO_2^{+} and the phenoxyl radical. The reaction pairs with ^{235}U magnetic nuclei undergo rapid triplet–singlet conversion and disproportionate with regeneration of the initial uranyl enriched in ^{235}U. The 'nonmagnetic' pairs with ^{238}U are converted into tetravalent uranium products (of the type of the insoluble UF_4). The initial uranyl is enriched on photolysis in the light but magnetic ^{235}U isotope, while the product of the photolysis of UF_4 is enriched in the heavy nonmagnetic ^{238}U isotope. This result conflicts with the predictions based on the CIE (it was found that the UO_2^{2+} ions with the heavy isotope are more reactive than those with the light isotope) and indicates unambiguously a contribution by the MIE, which exceeds the CIE in magnitude, compensating for the latter and actually leading to a change in sign. Later the ^{235}U MIE was confirmed in the photolysis of uranyl succinate containing 30% of ^{235}U. On 85%–90% conversion in methanol, the content of ^{235}U in the initial uranyl succinate increases by 6% relative to the initial value.[31]

Fig. 6 summarises the values of α_G for all the MIE discovered hitherto. It provides a clear idea about the quantitative scales of the MIE and the CIE.

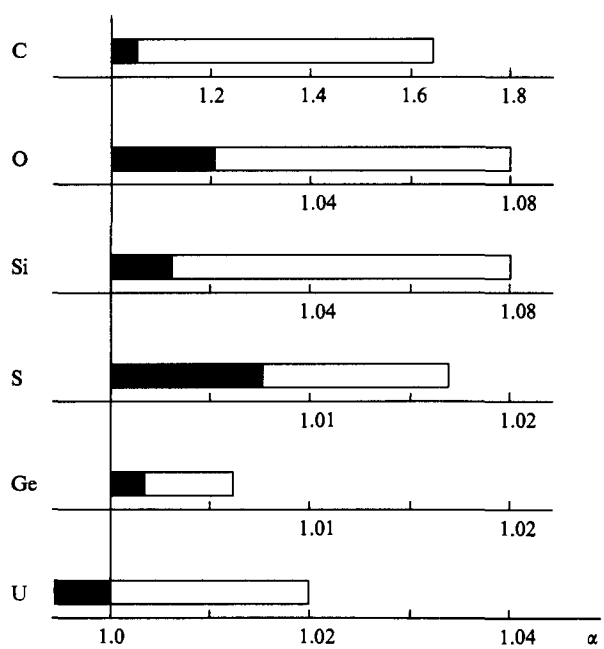


Figure 6. The single-stage isotope enrichment coefficients α_G. The open rectangles indicate the region of α_G for the MIE in the $^{13}C/^{12}C$, $^{17}O/^{16}O$, $^{29}Si/^{28}Si$, $^{33}S/^{32}S$, $^{73}Ge/^{72}Ge$, and $^{235}U/^{238}U$ isotope pairs. The filled rectangles characterise the CIE for the $^{13}C/^{12}C$, $^{18}O/^{16}O$, $^{30}Si/^{28}Si$, $^{34}S/^{32}S$, $^{73}Ge/^{72}Ge$, and $^{235}U/^{238}U$ isotope pairs.

III. Properties of the magnetic isotope effect

Table 1 summarises the characteristic properties and features of the MIE and compares them with those of the CIE. The first fundamental feature of the MIE, which is also its essential feature, is its nuclear spin dependence (in contrast to the nuclear mass dependence of the CIE).

The effectiveness of the nuclear spin selection is controlled by the HFI energy: the higher the HFI energy, the stronger the effect of the nuclear spin system on the electron system with removal of spin prohibition and differentiation of the rates of the triplet–singlet conversions of the 'magnetic' and 'nonmagnetic' radical pairs. The dependence on the HFI energy constitutes the second feature of the MIE, which, in contrast to the CIE, can lead to measurable isotopic enrichments of the atoms at a considerable distance from the reaction centres. The reason for this is that the distribution of the spin density among the chemical bonds in the radicals is not attenuated regularly and may give rise to intense HFI involving remote atoms. At any rate, this attenuation is much gentler than the transfer of perturbations of the molecular vibrations induced by isotope substitution (this is why the CIE is localised at the reaction centre).

The third feature of the MIE is its high sensitivity to molecular dynamics and all the factors influencing the latter: viscosity, temperature, restriction of the reaction in closed volumes — microreactors of the type of micelles or zeolite cavities. The spin conversion develops in a dynamic system — a radical pair, where the partner radicals move apart as a result of diffusion, some of them return and are involved in repeated encounters, move apart again, etc. During the diffusional migrations, spin conversion, induced by the hyperfine and Zeeman interactions, takes place. For the occurrence of nuclear selection, it is important that the diffusional migration times of the partner radicals should be comparable with the spin conversion times of the pair.

The high sensitivity of the isotope enrichment to the molecular-dynamic properties of the medium is demonstrated by Fig. 2. The isotope enrichment coefficient [α_G in Eqns (1)] depends greatly on the visocity: in viscous solutions (cyclohexanol, glycerol), α_G is much greater than in solutions with a low

Table 1. Comparison of the features of the MIE and the CIE.

Feature	MIE	CIE
Selectivity parameter	Nuclear spin and magnetic moment	Nuclear mass
Hyperfine interaction	Strong dependence	No dependence
Magnetic field	Strong dependence	No dependence
Molecular dynamics	Strong dependence	No influence
Chemical dynamics and lifetime of radicals	Dependence	No dependence
Effect of temperature	Strong	Weak
Spin multiplicity	Strong dependence of magnitude and sign	No dependence

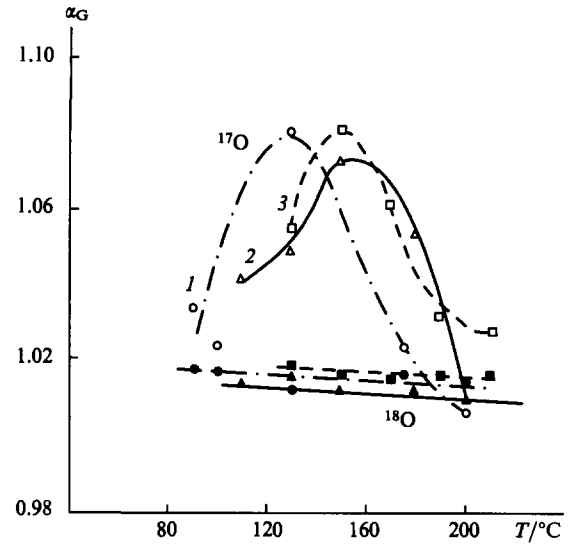


Figure 7. Temperature dependence of the single-stage isotope enrichment coefficient α_G in the oxidation of polyethylene (curve *1*), polypropylene (curve *2*), and poly-4-methylpentene (curve *3*). The open circles, squares, and triangles correspond to ^{17}O, whilst the filled symbols correspond to ^{18}O.

viscosity (benzene, hexane). Thus, for the photolysis of dibenzyl ketone, α_G is 1.054 in hexane[6] and 1.039 in benzene,[32] whereas in vitreous cyclohexanol $\alpha_G = 1.113$[33] and in glycerol (with a viscosity of 2400 cP) $\alpha_G = 1.50$.[34] Turro was the first to show that α_G attains large values when the reaction is carried out in closed microreactors (micelles and the cavities in zeolites or porous glasses). Thus $\alpha_G = 1.37$ in hexadecyltetramethylammonium chloride micelles[35] and $\alpha_G = 1.39$ in the corresponding bromide micelles.[36] The physical causes of such high isotopic selectivity of the reactions in closed microreactors are discussed below.

The magnetic isotope effect depends greatly on the lifetime of the radicals, because the joint molecular and spin dynamics of the pair are limited by its chemical lifetime. For the nuclear spin selection to be successful, it is necessary that the spin conversion time and the lifetime of the pair are comparable. This property of the MIE, namely the dependence on the chemical dynamics of the pair, constitutes its fourth fundamental feature.

Thus the generation of the molecule from the RP is the result of the combined efforts and interactions due to three types of dynamics — spin, molecular, and chemical. Their joint effect prepares the pair for an important event — recombination: the spin dynamics ensures the required (singlet) spin state of the pair, the molecular dynamics guarantees contact between the recombining partners by this instant, and the chemical dynamics ensures the survival of the pair. For this reason, the isotope separation based on the MIE depends on the parameters which influence the molecular and chemical dynamics — temperature[37] and viscosity,[38] the presence of radical acceptors, the wavelength of the photolysis,[39] the size of the micelles,[40] etc.

As an illustration, Fig. 7 shows the enrichment of molecular oxygen in the ^{17}O and ^{18}O isotope as a function of temperature[12] in the chain oxidation of polymers. The enrichment in ^{18}O decreases only slightly with increase in temperature, in conformity with the predictions based on the CIE. However, the MIE-induced enrichment in ^{17}O depends greatly on temperature, passing through a maximum at T_{max}, which reflects the condition for the most effective isotope selection: the time between repeated diffusional encounters of radicals is comparable to the spin conversion time for the pair. On either side of the maximum, the characteristic times of these two dynamic processes (molecular and spin) are not comparable and the MIE decreases sharply. At high temperatures $T > T_{max}$, the lifetime of the RP diminishes sharply (rapid diffusion) and there is insufficient time for the pair to effect spin conversion and isotope sorting. On the other hand, for $T < T_{max}$ the diffusional lifetime of the RP is too long and during it the spin correlation is lost for all the pairs — both 'magnetic' and 'nonmagnetic'. In both extreme cases, the isotope sorting in the pairs is ineffective.

The sign of the CIE is unambiguously dictated by the ratio of the isotope masses; however, the sign of the MIE is determined by the spin multiplicity of the radical pairs (or other electron spin carriers). Strictly speaking, it depends on the direction of the spin conversion — from the triplet to the singlet or conversely. This is an obvious property: in the initial triplet state, the 'magnetic' pairs evolve more rapidly to the singlet state and the recombination product is enriched in the magnetic isotope; in the initial singlet state, the 'magnetic' pairs pass through the triplet state for the same reason and dissociate, depleting the recombination product in the magnetic isotope. An example of the inversion of the sign is provided by the MIE based on the ^{29}Si nuclei (see above). Another example of the inversion of the sign of the MIE is the triplet-sensitised photolysis[7] and thermolysis of benzoyl peroxide.[38] The photochemical reaction involves triplet RP and triplet–singlet conversion, whereas the thermal reaction begins with singlet pairs and involves singlet–triplet spin conversion. These two chemically identical reactions lead to different isotope redistributions: in the first case, the cage product (phenyl benzoate) is enriched in the ^{13}C isotope, while in the second case the excess ^{13}C is found in the reaction product outside the cage — in benzene.[38] Such dependence of the sign of the MIE on the direction of the spin evolution is a reliable test for the identification of the spin multiplicities of the reactants.

Finally, there is yet another important property of the MIE: as a rule, the effect arises in chemical steps which do not limit the overall rate of the process (for example, the formation of chemical bonds on recombination), whereas the CIE occurs in energy consuming chemical decomposition or substitution reactions.

IV. Problems and prospects of the isotopic-spin selectivity

The magnitude of the classical isotope effect is determined by the ratio of the isotope masses, which greatly limits the nuclear mass selectivity of the reactions (provided that tunnelling is excluded). It was shown above that the nuclear spin selectivity is as a rule

much more pronounced, so that the isotope enrichment induced by the MIE can exceed the value expected from the CIE by 1–2 orders of magnitude.

The limiting nuclear spin selectivity and ideal isotope separation are attained for $P = 0$ and $P^* = 1$ [see Eqn (1)]. These are very severe conditions, which fully prohibit the recombination of nonmagnetic RP and at the same time require the complete recombination of pairs with magnetic nuclei. Whether or not these contradictory conditions can be satisfied is a problem which we shall now discuss.

The first step on the way towards a high spin selectivity involves directing the reaction along the path with participation of paramagnetic intermediates (spin carriers), i.e. the adjustment of the chemistry to promote the spin-selective reactions. Naturally, this is not always possible and is not always necessary. For example, it is pointless to seek the nuclear spin selectivity in hydrolytic or nucleophilic substitution reactions. When the reaction proceeds via two parallel competing paths, one of which is radical and spin-selective whilst the other is nonradical, the single-stage isotope enrichment coefficient assumes the following form:

$$\alpha_G = \frac{1 - P\theta}{1 - P^*\theta}, \qquad (2)$$

where θ is the partial contribution of the radical path. For $\theta = 1$, the coefficient α_G is a maximum and Eqn (2) then reduces to Eqn (1). However, if θ diminishes, then α_G also falls and for $\theta = 0$ (the radical path vanishes) there is no nuclear spin selectivity ($\alpha_G = 1$). Eqn (2) may be used also to determine the contribution by the nonradical path. Thus, in the sensitised photolysis of a silicon-containing ketone in micelles, it was found that the radical path (via triplet RP) coexists with the decomposition reaction via a siloxycarbene, which is inserted in the O–H bond of the water molecule; this path amounts to approximately 2/3 of the overall reaction flux and is not spin-selective, which greatly reduces the ^{29}Si MIE.[18]

The second important condition is high reversibility of the spin-selective reaction, which guarantees the possibility that each molecule can undergo repeated reactions of this kind (e.g. dissociation–recombination–regeneration cycles). Each of these repeating cycles is isotope-selective, so that the overall isotope selection is multiplied repeatedly in the multicascade process.

A high reversibility of the reaction can be induced in two ways—by spatial and by physical 'enforcement'. The former implies that the reaction is carried out in closed microreactors (micelles, the cavities in zeolites and porous glasses, microcavities in stressed polymers, etc.), in which the reflecting walls limit diffusion and give rise to the 'capture' of the radical pairs. The theory of microreactors from the standpoint of nuclear spin selectivity has now been fairly thoroughly developed.[33,41]

The physical 'enforcement' is less trivial and merits special consideration. The magnetic isotope effect is a result of the spin conversion induced by the electron-nucleus HFI, so that the greater the extent of the HFI, i.e. the stronger the linkage between the electron and nuclear spin subsystems, the greater the isotope selection. However, the HFI is by no means the only physical interaction giving rise to the triplet–singlet (or any other, for example, quartet–doublet) spin conversion. The spin-rotation, spin-orbit, dipolar, and exchange interactions all induce electron relaxation and hence spin conversion. This additional relaxation path competes with the HFI path and is traditionally regarded as the harmful spin leakage path, because it does not involve the nuclear spin system and thus does not give rise to the MIE. In such cases, the reaction remains selective with respect to the electron spin but loses its selectivity with respect to nuclear spin.

However, even if the contribution of the HFI to the spin conversion is low but the electron relaxation is rapid and stimulates effectively the spin conversion and recombination of the triplet pairs (i.e. forces the radical pairs to recombine), ultimately the isotopic selectivity increases. This paradoxical result has a simple explanation: not only the isotope selection in each reaction step but also the number of such steps undergone by each molecule is important. Here the multicascade nature of the spin-selective process is again manifested.

Thirdly, in order to ensure an appreciable MIE, it is necessary to modify the reaction mechanism in such a way that the spin-selective processes begin with the triplet state of the RP. This is one of the reasons why the triplet-sensitised photolysis is preferable for the observation of the MIE and isotope selection.

The fourth factor controlled by the MIE is the extent of the HFI in radicals participating in spin-selective processes: the greater the extent of the HFI, the greater the difference between the probabilities P and P^*, and the greater the value of α_G. However, the quantities P and P^* themselves are determined by the interaction of three dynamic processes—spin, molecular, and chemical, so that the synchronisation of these dynamic processes in time is an important factor which influences the difference $P^* - P$ (this has already been discussed in the section concerning the properties of the MIE).

Finally, the MIE and isotopic selectivity may be strengthened by the selective microwave pumping of the RP having magnetic nuclei. By acting on the electron spin, the magnetic component of the resonance hyperfine frequency field accelerates the spin conversion and stimulates the selective regeneration of molecules with magnetic nuclei without affecting the RP with nonmagnetic nuclei. This remarkable effect has been called the radio-induced MIE;[42,47] it belongs to the second generation of magnetic effects, namely those which are due to the action of microwave magnetic fields on chemically reacting spin systems.[5] The first generation of magnetic effects are induced by static magnetic fields—external or internal (of the type of HFI). The magnetic field effect, the MIE, and chemically induced [dynamic] nuclear polarisation are effects of this kind.

As an example of the radio-induced MIE, one may quote the enrichment of dibenzyl ketone in the ^{13}C isotope during its photolysis in micelles as a function of the chemical conversion plotted in terms of the variables of Eqn (1). The slope of this plot, which determines the single-stage enrichment coefficient α_G, increases with microwave pumping.[43]

The prospects for the radio-induced MIE are still more promising when one employs a combination of two types of microwave pumping: the low amplitude pumping of the 'magnetic' RP, which stimulates their recombination and the high-amplitude pumping of the 'nonmagnetic' RP, which slows down or altogether suppresses the spin conversion of these pairs, preventing their recombination (the spin locking effect).[44] Under these conditions, the isotope selection is most effective.

Thus there are diverse and almost limitless possibilities for regulating the nuclear spin selectivity of chemical reactions. There is a problem in the choice of the reactions and the methods and conditions for carrying them out; in other words, the problem of controlling the chemistry and physics of the reactions which are a part of spin chemistry—the science of the behaviour of the angular momenta of electrons and nuclei in chemical reactions.

V. Sorting of nuclei in accordance with spin orientations

Thus, by virtue of the MIE, the reaction sorts the magnetic and nonmagnetic nuclei. The next level in nuclear spin selectivity involves the sorting of magnetic nuclei in accordance with their orientations. The hyperfine interaction, which makes it possible to separate nuclei in terms of their magnetic properties, depends on the orientation of the nucleus and in the simplest case is defined as am, where a is the HFI constant proper and m is the projection of the nuclear spin specifiying the orientation of the nucleus. Clearly, the HFI-induced rate of spin conversion depends on m, so that both the conversion and the competition

between the reactions in the RP depend on the orientation of the nuclei. As a result, the reaction directs nuclei oriented in different ways into different products. Thus molecules with oriented (polarised) nuclei are generated. However, the reaction is capable not only of sorting the nuclei in accordance with orientations but also of orienting them. This occurs in very weak magnetic fields, where the external magnetic field $H \ll a$ and is still incapable of rupturing the electron–nucleus linkage. The spin conversion in the electron system is then accompanied by conversion of the nuclear spin. In other words, the change in the electron spin is compensated by the change in the orientation of the nuclear spin (because the overall angular momentum of the electron–nucleus system is conserved).

The phenomena involving the sorting of nuclei and their orientation in chemical reactions are combined under the term chemically induced [dynamic] nuclear polarisation (CIDNP).[1,45,46] The orientation of the nuclei is equivalent to the nonequilibrium (excess) population of the nuclear Zeeman levels in the molecules of the chemical reaction products and is therefore detected by nuclear magnetic resonance methods and is manifested in the NMR spectra as an anomalous absorption or emission (depending on which Zeeman levels are overpopulated and which orientations of the nuclei predominate in the molecules).

Chemically induced [dynamic] nuclear polarisation was discovered independently by two groups of workers (Bargon and Fisher[47] and Ward and Lawler[48]); Sagdeev, Molin, Kaptein, Osterhoff, Closs, Roth, Lippmaa, etc. have made major contributions to the CIDNP. Stimulated CIDNP was a remarkable discovery (Sagdeev, Grishin, Molin, etc.). The idea underlying it was formulated by Sagdeev et al.[49] Stimulated CIDNP is generated by the selective microwave pumping of assemblies of radical pairs with a selected orientation of the nuclei, which leads to the spin conversion of such assemblies and forces them to react. As a result, nuclei with the specified orientation are forcibly directed into the molecules of products and are detected in the latter by NMR methods.

Chemically induced [dynamic] nuclear polarisation is widely used in its diverse variants (in the stationary and time-resolved variants, in the static and flow variants, etc.) in chemistry and biochemistry as a method for the identification of reaction mechanisms, for the detection of radicals and radical stages, and as a method for the study of chemical kinetics and chemical physics (see, for example, Refs 1, 5, and 50).

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Spectroscopic determination and study of the molecular state of water in ultrapure volatile inorganic substances

G G Devyatykh, P G Sennikov

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Abstract. The state of the art in methods for the determination and study of the molecular state of the water admixture in high-purity volatile inorganic substances used in processes for the preparation of materials for new technologies is considered. Primary attention is given to spectroscopic methods in the IR and microwave regions with the highest information content. The bibliography includes 182 references.

I. Introduction

Volatile substances have relatively low melting and boiling points, i.e. they are characterised by typical van der Waals intermolecular interaction, sometimes with a small contribution from other types of interaction, e.g., intermolecular hydrogen bonds. A vapour pressure of 1333 Pa at 500 K can be chosen as a criterion defining an arbitrary threshold of volatility.[1] Permanent gases, chlorides and hydrides of a number of elements and some other substances are usually regarded as volatile inorganic compounds. The interest in high-purity volatile inorganic compounds is caused by their wide application for obtaining many materials for new technologies. For example, high-purity volatile chlorides and hydrides are used as starting compounds in manufacturing optical fibres, semiconductors and optical elements by chemical deposition from the vapour phase (the CVD technology). In this case, a high-purity permanent gas usually serves as the carrier.

Among the impurities most frequently encountered in ultrapure volatile inorganic compounds and most difficult to remove, water is foremost.[2-4] This results from the relatively high concentration of moisture in the starting compounds and in the technological atmosphere, as well as from the tendency of water molecules to be adsorbed on the walls of the equipment and even to diffuse through them at an appreciable rate from the environment (see, e.g., Ref. 5). Thorough elimination of water from volatile compounds is frequently complicated by the ability of water molecules to form rather stable complexes, both with one another and with molecules of the main compound in the liquid phase and sometimes in the gaseous phase. Such complexes can initiate avalanche-like nucleation processes followed by the formation of suspended ice or gas hydrate particles.

G G Devyatykh, P G Sennikov Institute for the Chemistry of High-Purity Substances, Russian Academy of Sciences, ul. Tropinina 49, 603600 Nizhnii Novgorod, Russian Federation. Fax (7-831) 266 86 66. Tel. (7-831) 266 91 62 (P G Sennikov)

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Strict requirements are imposed on the purity of the starting compounds and working gases used in the CVD technology for manufacturing optical fibres and semiconducting epitaxial layers. For example, the water concentration in the starting reagents should not exceed 5×10^{-5} mol% in order to attain the lowest optical loss in quartz optical fibres.[6,7] Perfect crystalline epitaxial GaAs layers on silicon can be obtained by the reaction of arsine with trimethylgallium in a hydrogen atmosphere, provided that the admixture of water in the reactor does not exceed the same value of 5×10^{-5} mol%.[8] On the other hand, the samples presented at the Exhibition-Collection of special purity compounds of the Russian Academy of Sciences, which has been permanently open since 1974 at the Institute of Chemistry of High-Purity Substances of the RAS, contain the following mean water concentrations (mol%): 1×10^{-4} in permanent gases, 1×10^{-2} in chlorides and 5×10^{-3} in hydrides.[9] Therefore, the preparation of high-purity compounds with a water admixture below 5×10^{-5} mol% is an urgent problem. At present, a demand is already felt for compounds with an overall content of admixtures within $10^{-6} - 10^{-8}$ mol%.[6,10] Deep dehydration, storage and transportation of compounds with such a low content of water involve considerable difficulties.

The development of methods for the preparation of volatile compounds with a low water content should be paralleled by the development and improvement of the corresponding analytical methods. In our opinion, two interconnected problems should be taken into account when considering the methods for the determination of water in high-purity volatile compounds: highly sensitive determination of the water admixture and study of the state of admixed water, i.e. study of the nature of the chemical bond in complexes involving water and the thermodynamic characteristics of these complexes.

The present review considers both these problems for volatile inorganic hydrides, chlorides and permanent gases. Attention is concentrated on spectroscopic methods in the IR and microwave ranges, because of their high sensitivity and the possibility of their simultaneous application both for analysis and for studying the molecular state of admixed water.

II. Determination of water

Many publications, including several monographs and reviews,[11-14] have dealt with problems of water determination in various media, including high-purity volatile inorganic compounds. Many chemical, physical and physicochemical methods are known; however, their detection limits are not lower than $10^{-4} - 5 \times 10^{-5}$ mol%. The coulometric method and the dew point method are among the most widespread, rather simple methods.

1. The coulometric method and the dew point method

The coulometric method measures the quantity of electricity required for the electrochemical decomposition of water in an analysed volume of a gas.[15,16] The sensitive element of the corresponding device contains a sorbent, usually phosphorus(V) oxide. For this reason, coulometric hygrometers are used only for analysing compounds that do not react with P_2O_5 or in the cases where the contribution from the corresponding reaction to the overall measurement error is insignificant (see Atamanyuk et al., [17] who report a coulometric analysis of gaseous HCl). The detection limit attainable by this method is $(1-5) \times 10^{-5}$ mol%. The coulometric method usually consumes a large amount ($1-3$ dm^3 s^{-1}) of the analysed gas, which is not always acceptable.

A number of other methods for water determination in volatile compounds have appeared in recent years, such as thermal oscillometry,[18] direct potentiometry,[19] cyclic voltammetry [20] and amperometry.[21] However, these methods also suffer to some extent from the above drawbacks.

The measurement of water concentration by the dew point method is based on the visual or optical monitoring of the fogging of a cooled mirror in a stream of the analysed gas.[15,16] The temperature, at which dew appears on the mirror, is measured and the pressure of saturated water vapour corresponding to this temperature is determined. The detection limit can be as low as 10^{-6} mol%. This method is unsuitable for analysing readily condensing gases, such as ammonia, certain other hydrides and hydrocarbons. Various modifications of this method have been described in Refs 22 and 23.

A novel method for the determination of micro admixtures of water based on measuring the temperature of the start of sublimation of a condensate, which is first placed in a definite volume, has been proposed.[24] The authors determined the solubility of water in liquid nitrogen, which was found to be 4×10^{-7} mol%. In their opinion, there is no limit to the detection of water by this method. However, the authors do not report any comparative analyses or methods for preparing the equipment for assaying such a low water content.

Other fairly sensitive methods for water determination include gas chromatography and mass spectrometry.

2. Gas chromatography

Various problems in the application of gas chromatography for the determination of water in volatile compounds have been discussed in a number of communications.[11,25-28] Both direct determination of the water admixture without changing its chemical form and reaction chromatography are used. In order to determine water in gases by reaction chromatography, reactions transforming water into other compounds (most frequently, ethyne) more convenient for gas chromatographic detection were used.[28,29] Ref. 28 reports an estimation of water content in ammonia at a level of $10^{-3}-10^{-4}$ mol% by passing ammonia through a reactor with calcium carbide. The poor reproducibility of the results obtained by a one-step technique, i.e. when the reactor with calcium carbide was directly connected to the chromatograph, was noted. The error probably appeared because not all the water could undergo reaction due to the insufficient reaction rate. In later work the sample was first passed several times through the reactor and only then analysed.

The determination of water in gases based on its reaction with calcium carbide is applicable to a wide range of compounds inert towards calcium carbide, oxide, and hydroxide.

Ref. 30 describes a technique for water determination in volatile hydrides and permanent gases (detection limit: 1×10^{-5} mol%). The technique is based on the oxidation of methane by water and the products of its dissociation in a spark discharge occurring in the reaction vessel. The change of the amount of methane due to its oxidation is detected by a flame ionisation detector. The relative standard deviation was $0.01-0.2$ in the range of water contents of $1 \times 10^{-2}-5 \times 10^{-5}$ mol%.

The improvement of materials for packing chromatographic columns made it possible to determine the water admixture directly in gases without changing its chemical form and to decrease the detection limit. For example, Snopatin et al.[31] determined the water content in hydrogen sulfide, hydrogen selenide, arsine, and germane using the selective adsorption of the hydrides on a Saran charcoal (detection limit: 5×10^{-5} mol%).

Preconcentration is also used in gas-chromatographic determinations of the water admixture. Ref. 32 reports the gas-chromatographic determination of water in high-purity nitrogen (detection limit: 2×10^{-6} mol%). Water was concentrated by adsorption in columns packed with cooled (3 °C) Porapack T, then blown out of the column and detected with a catharometer. A technique for water determination in ammonia (detection limit: 1×10^{-4} mol.%) was reported in Ref. 33. The lowest detection limit of water in nitrogen (2×10^{-6} mol%) was attained when water was concentrated on a sorbent, while gas chromatographic techniques offered limits of water detection within 10^{-3} to 10^{-5} mol%.

3. Mass spectrometry

Similar or even lower limits for water determination can be attained using mass spectrometry. For example, Ref. 34 reports a technique for the mass-spectrometric determination of water and other admixtures in SiH_4, HCl and other compounds (the detection limit was 1×10^{-4} mol%). The authors draw attention to the correctness of the analysis and consider adsorption-desorption processes in the connecting tubes to the quadrupole mass spectrometer, the 'memory' effect of the ion source, and various background ion-molecule reactions. All of these questions are of primary importance for the determination of microamounts of water in gases. Water can be to a considerable extent adsorbed on the walls of the injection system and the ion source of the mass spectrometer, which adversely affects the detection limit. Refs 35 and 36 report results of mass-spectrometric determinations of the water content in the residual atmospheres of evacuated sealed vessels. It was noted that the results obtained in different laboratories are not reproducible. This probably results from the fact that the vapour pressure in the vessels varied within 0.01–0.1 atm, so that from three to ten water monolayers were present on the vessel walls. The gas was injected into an ion source, whose volume and surface area were greater than those of the vessel by a factor of several tens. As a result, adsorption and desorption of water in the ion source affected considerably the accuracy of the measurement.

Recent publications deal with the mass spectrometric determination of water in gases.[37,38] Hydrogen and nitrogen were added to a sample, which was then ionised at atmospheric pressure. Water reacted with the N_2H^+ ion in the ion source, which resulted in a decrease in the fraction of these ions

$$N_2H^+ + H_2O \rightarrow H_3O^+ + N_2.$$

The concentration of water was determined from the intensity of the N_2H^+ ion peak using a quadrupole mass spectrometer. The authors succeeded in plotting the dependence of water content on the change in the intensity of the N_2H^+ ion band in the low concentration region down to 5×10^{-7} mol%. However, no data were reported to confirm the validity of the above analytical technique.

Although there are several examples of successful application of gas chromatography and mass spectrometry for water determination in volatile high-purity compounds, these methods have not become widespread. This results from the difficulties in specimen preparation, the considerable probability of uncontrolled substance loss and irreversible transformations of the analysed compounds in chromatographic columns [39-41] and/or in the ionisation chamber.[34]

Spectroscopic methods do not suffer from many of the above drawbacks. These methods have high sensitivity, selectivity and accuracy and provide the possibility of the unambiguous

identification of components in the sample. A water molecule is characterised by intense absorption in many regions of the electromagnetic spectrum. The 'strong' lines in the medium IR and sub-millimeter ranges are the most suitable for performing highly sensitive analyses.

The quantitative absorption spectroscopic analysis is based on the relation between the concentration of absorbing atoms and the change in the intensity of radiation passed through the analysed medium, i.e., the Bouguer – Lambert – Beer law:

$$I(\nu) = I_0(\nu)\exp[-k(\nu)x]. \quad (1)$$

Here $I(\nu)$ and $I_0(\nu)$ are the intensity of the radiation passed through the sample and that of the incident radiation, respectively. The x parameter is related to the concentration of absorbing molecules n, and the length of the optical path l:

$$x = nl; \quad (2)$$

$k(\nu)$ is the absorption coefficient,

$$k(\nu) = A f(\nu - \nu_0), \quad (3)$$

where the $f(\nu - \nu_0)$ function characterises the shape of the spectral line contour (the Lorentz, Doppler or Voigt profile or their combination), and ν_0 is the frequency corresponding to the centre of the absorption line. The A parameter is usually called line intensity, line strength, or integral absorption coefficient.

$$A = \int_{-\infty}^{+\infty} k(\nu)\mathrm{d}\nu, \quad (4)$$

Analysis of Eqns (1) and (4) shows that the dimensionality of A is $\nu[x^{-1}]$, where ν is usually expressed as the wave number (cm^{-1}), and the diversity of measurement units for the concentration and optical path length predetermines the existence of various units for A. The relations between these units have been reported, for example, by Pugh and Rao.[42] Some researchers assume that $x = 1$ in equation (1) (unit concentrations and lengths), and in some cases the absorption coefficient γ is used, which is measured in reciprocal centimetres. The minimum γ determined usually characterises the sensitivity of the spectroscopic method.

Given the known values of A or γ for a spectral line (band) and having measured its integral (peak) intensity, one can determine the desired concentration of the analysed compound. If A or γ are unknown, a calibration plot should be used.

Let us consider the main results in determining micro-amounts of water in volatile high-purity compounds by IR absorption and microwave absorption spectroscopy.

4. Infrared spectroscopy

Table 1 presents the average and relative integral absorption coefficients for the main vibrational bands of water molecules in the gas phase. One can see that the band due to deformation vibrations, ν_2, which is the least affected by intermolecular interactions, has the maximum intensity. Refs 43 and 44 report the calculated and experimental integral absorption coefficients of separate lines in the regions corresponding to the stretching and deformation vibrations. Although the IR region contains the most intense vibrational-rotational transitions of water molecules, standard diffraction instruments, even those equipped with multiple-pass cells, probably do not provide detection limits below 10^{-4} mol%.[11,45]

In recent years, IR spectroscopy with Fourier transformation of the spectrum has found wide use. This method has a much higher sensitivity and selectivity, and its application for determining water in gases shows much promise. Ref. 47 presents a procedure for the Fourier-IR spectroscopic determination of traces of water in gaseous nitrogen and hydrogen chloride (detection limit: 10^{-5} mol%). Andreev et al.[46] proposed a procedure for determination of water in oxygen with a detection limit of 6×10^{-6} mol%. According to this procedure, a stream of the gas to be analysed passes through a multiple-pass cell, whose optical path is 20.75 m. The water concentration was found to be 7×10^{-5} mol%, this limit being imposed by the capacity of the device for the drying of oxygen by cryofiltration.[7]

Table 1. Integral absorption coefficients (A/cm^2 atm^{-1}) of the vibrational–rotational bands in the IR spectrum of water in the gas phase.[42]

Frequency (spectral region)/cm^{-1}	A_{mean} (at 300 K)[a]	A_{rel}[b]
1595 (ν_2)	277.8	100
3152 ($2\nu_2$)	1.73	0.6
3657 (ν_1)	10.2	3.7
3756 (ν_3)	202.3	72.8
2.7 μm	182.8[c]	65.8
1.9 μm	20.3[c]	7.3
1.4 μm	16.7[c]	6.0
1.1 μm	1.78	0.6

[a] The mean value of A given is based on data from different authors. [b] The relative value of A is given (the value of 100 corresponds to A for the most intense band, ν_2). [c] The overall value of A for all the lines in the specified range is given.

It was noted above that the limit of water detection in gases below 10^{-4} mol% cannot be attained by diffraction IR spectrometers, primarily because of the low resolution of these instruments. The resolution of the classical molecular spectroscopic methods in the gas phase is generally restricted by the instrumental resolution of the spectrometers. This value is as low as 0.003 cm^{-1} for interferometric spectrometers.[48] The resolution of dispersion spectrometers is normally 0.1 cm^{-1}. For comparison, the interferometric order of magnitude of the Doppler width of the stretching–rotational absorption lines of molecular gases is 10^{-3} cm^{-1} (in the middle IR region).

It can be shown [42] that the following relation is valid for the intensity of the radiation absorbed by a substance (ΔI) and the incident radiation (I_0)

$$\frac{\Delta I}{I_0} = k(\nu)\frac{\delta\nu}{\Delta\nu}, \quad (5)$$

where $\delta\nu$ is the width of the absorption line and $\Delta\nu$ is the spectral resolution.

It follows from the above that the use of instruments with a higher spectral resolution (low $\Delta\nu$) makes it possible to decrease the instrumental detection limit for molecular admixtures.

The creation of more sensitive analytical IR spectrometers became possible owing to the use of lasers with tuneable wavelength as radiation sources. Lasers have a higher spectral power, and the lines generated by them are narrower than the resolution achieved in dispersion and interference instruments. For example, Kreuzer et al.[49] showed, on an experimental basis, the possibility of determining water vapour in nitrogen and air when its content was ca. 1.4×10^{-6} mol%, using a CO laser and an optical-acoustic detector. The measurements were carried out at a wavelength of 5.94 μm ($\nu = 1683.02\,cm^{-1}$).

The use of a Nd laser makes it possible to record ca. 116 absorption lines of water vapour. The most intense line has an absorption coefficient of 10^{-9} cm^{-2} atm^{-1} (1.7×10^{-8} cm^{-1}),[50] which allowed the authors [51] to attain a ca. 10^{-4} mol% detection limit for the concentration of water in air.

It was proposed [52] to determine the content of water by the optical-thermal method. A CO laser served as the radiation source. From an estimate based on the signal/noise ratio, the practical detection limit for the method is 7.5×10^{-6} mol%.

Record-breaking low limits for the detection of water in various gases were attained using spectrometers based on tuneable diode lasers. The use of such instruments in molecular analysis has been reported in Refs 53 – 56.

The authors [57] managed to determine the minimum width of lines generated by semiconductor $PbS_{1-x}Se_x$-based lasers, which

was as low as 7×10^{-7} cm^{-1} at a wavelength of 5.3 μm. The line width of the radiation of diode lasers is usually $\sim 10^{-5}$ cm^{-1}, but this is much less than the width of the Doppler contour of the absorption line, which is, for example, $\sim 10^{-3}$ cm^{-1} near $\lambda = 10$ μm. On the other hand, the spectral density of the power of diode lasers is $\sim 10^9$ times higher than that of thermal radiation sources, which makes it possible to determine the concentration of molecular admixtures below 10^{-5} mol%.

As noted above, the theoretical maximum sensitivity of high-resolution spectrometers can be characterised by the minimum detectable absorption coefficient, γ_{min}. The following expression for this value was found using the data in Refs 58 – 60:

$$\gamma_{min} = \left[\frac{4}{l\sqrt{2}}\right]\left[\frac{N}{P_0}\right]^{1/2}, \quad (6)$$

where $N = 2h\nu\Delta f$ is the power of the quantum noise ($\Delta f = 0.5\pi\tau$ is the transmission band width of the detection system (Hz); τ is the constant of accumulation time, s; ν is the wavenumber, cm^{-1}; and h is the Planck constant); P_0 is the power of the incident radiation; and l is the optical path length, m.

Assuming that $P_0 = 0.71$ mW, $l = 1$ m, and $\tau = 1$ s, and that a signal/noise ratio of $3\sqrt{2}$ is required for a minimum determination,[58] we obtain $\gamma_{min} = 2 \times 10^{-9}$ cm^{-1}. A relation is known between the absorption coefficient and the concentration x (ppm) of molecules absorbing the radiation, the half-width of the analytical line ($\Delta\nu$), and the pressure in the cell (p).[61]

$$\gamma = \frac{kxp}{\Delta\nu} \quad (7)$$

The proportionality coefficient k is determined from the parameters of the analytical line of the additive in the pure state at the same pressure p. When the concentration of the additive is x, we have:

$$x = \frac{\gamma_{min}}{\gamma_0}\frac{\Delta\nu}{\Delta\nu_0}, \quad (8)$$

where γ_0 and $\Delta\nu_0$ are the above parameters for the pure additive.

Taking into account the data in Refs 44, 46 and 62, the $\gamma_0\Delta\nu_0/\Delta\nu$ value for lines in the region of 1600 cm^{-1} (which is usually chosen as the analytical region for water) can be assumed to be 20 cm^{-1}. Then, the theoretical minimum water concentration that can be determined by this method is as low as 9×10^{-9} mol%.

Relatively few studies dealing with the use of diode laser spectroscopy for water determination in permanent gases are known. In Ref. 63, the study was carried out in a multiple-pass cell with an effective length of 500 m using an analytical line at 1135 cm^{-1}. The detection limit was 5×10^{-6} mol%. In Ref. 64, a differential method was proposed for water determination in helium, nitrogen, oxygen, and argon based on the line at 1653 cm^{-1}. Two laser beams were passed through a reference cell ($l = 7$ cm) containing water vapour at a pressure of 6.7 Pa and then through a working cell ($l = 28$ cm) with a stream of the analysed gas at a pressure of 1.3 kPa. The instrument was calibrated by the standard addition method in the concentration range of $2 \times 10^{-7} - 1 \times 10^{-4}$ mol% for a 2 m absorbing path. Mucha[65] used a simplified version of the instrument described in Ref. 64 for determining ca. 5×10^{-4} mol% water in small volumes (of the order of magnitude of the volume of an integrated microcircuit, 0.01 – 0.1 cm^3). The undesirable effect of gas liberation due to adsorption — desorption was eliminated as a result of the short measurement time ($\leqslant 10$ μs). In Ref. 66, an admixture of water was determined in helium serving as the heat carrier for several types of nuclear reactors. The detection limit was $(1 - 6) \times 10^{-5}$ mol% for the analytical line at 1435 cm^{-1} with an absorption path of 100 m.

The authors of a work cited above [46] report the determination of the water admixture in high-purity oxygen, dehydrated by cryofiltration,[67] using the diode laser spectrometer described in Ref. 68. The analytical line at 1675.17 cm^{-1} was used; the gas pressure in a flow cell ($l = 1.5$ m) was 40 Torr. The minimum measurable absorption coefficient was 2×10^{-7} cm^{-1}, and the water detection limit was 8×10^{-7} mol% (the standard deviation was $s_r = 0.4$ for $c_{H_2O} < 8 \times 10^{-7}$ mol%). These values differ from the above theoretical limiting values of γ_{min} and x_{min}. However, one should take into account that the diode laser used in Ref. 46 operated in a pulse mode with an averaging time $\tau \simeq 10^{-3}$ s. Under these conditions, the corresponding limiting values of the γ and x parameters increase by a factor of ~ 30, according to Eqns (6) and (8). The difference between the values of γ and x predicted and obtained experimentally [46] is not high if one bears in mind that the γ_{min} was estimated assuming an ideal receiving system.

Table 2. Detection limits c_{min} (mol%) and relative standard deviations s_r of the water admixture in high-purity permanent gases and hydrides obtained by absorption diode laser IR spectroscopy together with the half-widths of the analytical line $\Delta\nu$ (cm^{-1}) and its broadening coefficients ξ (cm^{-1} Torr^{-1}).[68,69]

Compound	$c_{min} \times 10^5$	s_r (c_{H_2O})[a]	$\Delta\nu \times 10^2$	$\xi \times 10^3$
O_2	0.08	0.4 ($< 8 \times 10^{-7}$)	0.86	0.24
Ar	0.04	0.17 (1.6×10^{-6})	0.66	0.158
He	0.04	0.11 (1.3×10^{-4})	0.66	0.158
GeH_4	4	0.15 (2.0×10^{-6})	0.66	0.158
H_2Se	1	0.08 (2.0×10^{-3})	3.2	1.06
NH_3	6	0.06 (3.0×10^{-2})	7.2	2.40

[a] The s_r values refer to the water concentrations specified in parentheses.

Ref. 69 reports a technique for determining a micro admixture of water in argon, neon, germane, hydrogen selenide, and ammonia. The analytical part of the instrument was first dried by passing through it dry oxygen with a water content below the detection limit of the method (4×10^{-7} mol%). The above gases were analysed by the pumping in – pumping out technique, rather than in a gas stream. Table 2 presents the water detection limits and some spectral parameters of the analytical line.

One can see that diode laser spectroscopy makes it possible to obtain record-breaking low water detection limits in nonpolar high-purity gases, including those whose molecules are characterised by considerable inherent absorption in the regions of the analytical lines of water (germane, ammonia).

An urgent problem is the determination of water in the condensed phases of low-boiling compounds (permanent gases, halides, hydrides, etc.) and in volatile compounds that are liquid under the usual conditions. IR spectroscopy seems to be the most convenient method for this purpose; however, high- and ultrahigh-resolution spectroscopic methods cannot be used because of the strong broadening of spectral lines due to intermolecular interactions. Increasing the thickness of the absorbing layer used in the traditional IR spectroscopic method is often also impossible because of the overlap of absorption bands (in many cases, even the second- and third-overtones) of the main compound. The above restrictions should be of little importance when analysing liquefied monotonic and diatomic permanent gases that are transparent in the IR region. Low temperatures favour the disappearance of the rotational fine structure of the analytical bands of admixed molecules and their narrowing in comparison with the bands of gases and solutions under the usual conditions. In addition, liquefaction leads to concentration of a number of admixtures, so that relatively thin optical layers can be used. In fact, IR cryospectroscopy has been used successfully for analysing liquid oxygen and certain permanent gases.[70,71] However, the use of this method for water determination in the above objects by measuring the intensities of absorption bands in the regions of stretching or deformation vibrations is hindered by the very small solubility of water at low temperatures. In particular, this follows from the experimental data in Refs 70 and 71. For example, only a broad band of varying intensity (depending on the degree of

Table 3. The positions of the maxima of the analytical bands, detection limits, and standard deviations of the determination of the water admixture and hydroxyl-containing hydrolysis products in liquid volatile inorganic chlorides obtained by IR spectroscopy.[74-76]

Chloride	Substance to be determined	ν/cm^{-1}	$c_{min} \times 10^4$ (mol %)	s_r
$SeCl_4$	H_2O	1600	10	4.32
	$Ge(OH)Cl_3$	3603	80	3.60
$SnCl_4$	H_2O	1586	5	3.23
	H_2O	3553	6	2.69
	H_2O	3636	7	3.05
$AsCl_3$	H_2O	1600	5	3.74
	H_2O	3659	8	4.22
	$As(OH)Cl_2$	3525	3	2.61
$SiCl_4$	$Si(OH)Cl_3$ (see [a])	3670	1-9	–
$POCl_3$	$PO(OH)Cl_2$ (see [a])	3200	5	–

[a]The anticipated hydrolysis products.

drying) in the region of 3000 – 3600 cm^1, which corresponds to an ice solid phase, is observed in liquid oxygen.

Rebiai et al.[72] reported that they recorded intense narrow lines at 3604 and 3707 cm^{-1} in the IR spectrum of liquid nitrogen exposed to air. These lines were attributed to the stretching vibrations of water, indicating an unusually high ($\sim 10^{-3}$ mol%) solubility of the latter. It has been noted that such interpretation of the observed bands is erroneous;[73] more likely, they correspond to the Fermi-resonance doublet of CO_2 molecules. As noted above, the solubility of water in liquid nitrogen is 4×10^{-7} mol%.[24]

Refs 74 – 76 describe an IR spectroscopic technique for the determination of the concentrations of water and/or hydrolysis products in liquid high-purity germanium, tin, arsenic, silicon and phosphorus chlorides. Table 3 presents the detection limits found.

Within the scope of an IR spectroscopic study of the molecular state of the water impurity in liquefied high-purity volatile inorganic hydrides of Group V and VI elements (see below), the following estimates of the detection limit of water at 290 K were obtained (mol%):[77] $\sim 3 \times 10^{-4}$ (PH_3), $\sim 7 \times 10^{-5}$ (AsH_3), $\sim 3 \times 10^{-4}$ (H_2S) and $\sim 2 \times 10^{-4}$ (H_2Se).

5. Microwave spectroscopy

Microwave spectroscopy provides high-resolution spectra of the purely rotational transitions of molecules (the relative width of lines in the spectra can be as low as 10^{-6}). The practical application of microwave spectroscopy for the analysis of mixtures is mostly restricted by technical factors: only the millimetre range (4 – 0.7 cm, 8 – 40 GHz), in which the line intensities for the majority of light molecules are low, has been developed sufficiently. For water, the most intense rotational transitions (whose intensities are, however, by one or two orders of magnitude lower than those in the IR range) are observed in the submillimetre range (10^{-1} to 10^{-2} cm, 100 – 1200 GHz).[78,79]

The 'adoption' of the sub-millimetre range started about 30 years ago after sufficiently powerful coherent tuneable radiation sources, the backward wave oscillators (BWO), had been created. However, the construction of 'classical' spectrometers (in which the useful signal is found from changes in the parameters of the radiation passed through a sample) on the basis of these sources did not give the desired result. In fact, expression (6) allows one to estimate the minimum determinable absorption coefficient for any 'classical' spectrometer (CS). For a typical power of a BWO equal to 1 mW (which is an order of magnitude higher than for diode lasers), $\tau = 1$ s, and $l = 1$ m, we obtain $\gamma_{min} \simeq 10^{-10}$ cm^{-1} (for a $3\sqrt{2}$ signal/noise ratio). It should be noted that the actual sensitivity with respect to the absorption coefficient does not exceed 10^{-6} cm^{-1} of separate points of the range [80] due to the considerable interference in the ultrahigh frequency region. The possibilities of the submillimetre spectroscopy were implemented in a radio-frequency spectrometer with acoustic detection (RAD), whose principle of operation is analogous to the above optical-acoustic spectrometer based on a CO-laser.[81] In this case, the expression for the minimum determinable absorption coefficient has the form [81]

$$\gamma_{min} = \frac{3 \times 10^{-9}}{P_0}. \quad (9)$$

For a power of a BWO equal to 1 mW and for a $3\sqrt{2}$ signal/noise ratio, we obtain $\gamma_{min} = 10^{-8}$ cm^{-1}. The actual sensitivity coincides with the predicted value ($\gamma_{min} = 3 \times 10^{-8}$ cm^{-1}, see Ref. 81) and can be as high as 10^{-10} cm^{-1} when a resonator cell is used (see Ref. 82). Using formula (8), one can also estimate the theoretical detection limit for a water admixture on a RAD. For the analytical line at 556.436 GHz, $\gamma_0 = 0.9$ cm^{-1},[79] $\Delta\nu/\Delta\nu_0 = 10^{-1}$ (water in argon [83]), and $x_{min} \approx 1 \times 10^{-7}$ mol%.

The above method was used for assaying water in certain volatile inorganic hydrides.[84] When the analysed gas was passed through a cell, the detection limit was found to be 1×10^{-5} mol%. The considerable difference between the theoretical and actual detection limits results primarily from the design features of the analytical cell of the spectrometer (the presence of a polymer membrane which hindered heating of the cell) and the imperfection of the receiving device, an amplifying microphone. The following results were obtained:

Hydride	NH_3	GeH_4	H_2S	H_2Se	H_2Te
$x_{H_2O} \times 10^3$ (mol %)	0.3	0.8	0.6	1	70

Water determination by submillimetre radio-frequency spectroscopy in volatile inorganic nonpolar silicon and germanium chlorides was studied in Ref. 85. In order to increase the sensitivity, a cylindrical multi-mode nontuneable resonator 20 mm in diameter and 300 mm long with two fixed reflectors was used as the analytical cell. The detection limit in this technique was 9×10^{-7} mol% at a sample pressure of 2.5 – 13 kPa. It was also reported that, at the optimum pressure in the cell (270 – 800 Pa), determination of water at a concentration of 3×10^{-7} mol% is possible. However, this requires that the water background be diminished by more thorough degassing or by creating a stream of the analysed compound through the measuring cell. The water contents (in the molecular form) in high-purity samples of $GeCl_4$ and $SiCl_4$ were $(5 \pm 0.3) \times 10^{-5}$ and $(2 \pm 0.2) \times 10^{-5}$ mol%, respectively. According to the data in Ref. 85, hydrolysis of the chlorides in the cell during analysis did not lead to a systematic error in the determination.

The use of resonator cells in the RAD increases the amount of radiation absorbed by the sample. It is also a realistic way of increasing the sensitivity of submillimetre spectroscopy. A gain in signal intensity by a factor of 3 – 4 can be attained by using the water line at 1097 GHz with $\gamma = 2.8$ cm^{-1} (see Ref. 79). Note that the power of radiation sources in the submillimetre range is 1 – 2 orders of magnitude higher than that in diode laser spectroscopy, and the averaging times are much longer (by 2 – 3 orders).

Thus, although the sensitivity with respect to the absorption coefficient of submillimetre radiofrequency spectroscopy is somewhat less than that of diode laser spectroscopy, the sub-millimetre radiofrequency spectroscopy with acoustic detection can be used successfully for high-sensitivity assays of water in volatile compounds, such as inorganic hydrides and chlorides of subgroup IVA elements that are transparent in the microwave region. It would be undoubtedly useful to combine microwave spectroscopy with a 'pure' analytic cell (without foreign internal elements) similar to those used in the 'classical' IR spectrometers (preferably, with retention of the sensitivity of the latter). The first step in this direction is the creation of a microwave spectrometer based on coherent spontaneous radiation (CSR), which currently operates in the 70 GHz region. The expression for the minimum absorption coefficient determinable by this spectrometer is similar

to expression (6)[60]

$$\gamma_{min} = \left(\frac{4}{l}\right)\left(\frac{P_t}{P_0}\right)^{1/2}, \quad (10)$$

where $P_t = 4kT\Delta f$ is the power of the thermal noise (Δf is the pass band of the recording system); l is the length of the measuring cell, whose design is analogous to that of the cell used in diode laser IR spectrometers.

For a BWO power equal to 1 mW, $T = 300$ K, $\tau = 1$ s and a $3\sqrt{2}$ signal/noise ratio, we obtain $\gamma_{min} = 8 \times 10^{-10}$ cm^{-1}, which is somewhat better than for a diode laser IR spectrometer. A sensitivity of 1×10^{-10} cm^{-1} has been obtained experimentally in the region of 37–178 GHz.[86] The analytical possibilities of the a CSR spectrometer were also studied in this work for the determination of an admixture of methanol in ethanol. The detection limit was found to be 8×10^{-5} mol%.

Thus, the combination of absorption IR spectroscopic methods with thermal and diode-laser radiation sources as well as microwave spectroscopy in the millimetre and sub-millimetre regions makes possible highly-sensitive determinations of water admixtures in gaseous and liquid inorganic compounds. The preparation of the samples needs particular attention in such cases.

III. Molecular state of water

In order to determine the structural and energetic (thermodynamic) characteristics of complexes formed by water molecules with molecules of the environment, it is necessary to study the properties of such complexes both in the gas and liquid phases. Under real conditions in dilute solutions, the concentration of the complexes is generally low, but they can affect considerably the physicochemical properties of high-purity compounds.[87] Therefore, preliminary investigation of water-based complexes at comparable concentrations of the components or at a small excess of one of them is of great importance. This task is accomplished by theoretical quantum-chemical methods and experimentally, primarily by spectroscopic methods.

1. Water complexes in the gas phase

For most of the gases, the depth of the potential well D_e is of the order of magnitude of the translational energy of molecules at the critical temperature $D_e = kT_k$, where T_k is the critical temperature. At $T < T_k$, the energy of molecular interaction exceeds the thermal energy, and stable complexes are formed. However, the number of complexes is strongly dependent on temperature and pressure. For the equilibrium complex-formation process

$$B..HA \leftrightarrows B + HA \quad (11)$$

the equilibrium constant is expressed as [88]

$$\frac{n_{B...HA}}{n_B n_{HA}} = \left(\frac{h^2}{2\pi kT\mu}\right)^{3/2} \exp\frac{D_0}{RT}, \quad (12)$$

where $n_{B...HA}$, n_B and n_{HA} are the numbers of the corresponding species in a unit volume in the equilibrium vibrational–rotational state; D_0 is the dissociation energy corresponding to this state;

$$\mu = \frac{M_B M_{HA}}{M_B + M_{HA}},$$

where M_i are molecular masses.

The equilibrium constant is determined experimentally by microwave spectroscopy by measuring the absolute intensities of the rotational transitions for two or three participants of reaction (11) in an equilibrium gaseous mixture. This can give the dissociation energy of the complex in the zero-point vibrational–rotational state D_0, which is related to the dissociation energy D_e by the expression [88,89]

$$D_e = D_0 + N_A\sum_i \tfrac{1}{2}h\nu_i(B...HA) - N_A\sum_i \tfrac{1}{2}h\nu_i(B) - N_A\sum_i \tfrac{1}{2}h\nu_i(HA), \quad (13)$$

where the second, third, and fourth terms contain sums of the contributions of zero-point vibrations from all vibrational modes except those of intermolecular deformation vibrations in the complex; N_A is the Avogadro number.

It should be noted that the equilibrium constant of reaction (11) can also be determined purely thermodynamically from the second virial coefficient. In particular, microwave spectroscopy was used to study in detail the dimerisation of water. [88]

In order to calculate theoretically the equilibrium constant of reaction (11), one should know the molecular constants of the complex and its dissociation energy D_e. The latter coincides with the electronic intermolecular interaction energy ΔE, which is found by nonempirical quantum-chemical calculations.

Many studies have been devoted to calculations for complexes of water with light molecules. It is noteworthy that the resulting values of intermolecular interaction energies ΔE depend on the chosen basis set and on the number of corrections introduced additionally, which are related both to physical effects (allowance for the correlation energy ΔE_{cor} in the second- and fourth-order Moeller–Plesset perturbation theory) and the errors in the computational methods (the superposition error due to incompleteness of the basis set ΔE_{BSSE}). These problems are discussed in more detail in Refs 90 and 91 for example.

Table 4 presents the results of a series of studies dealing with the calculation of the energies of the intermolecular interaction of water with certain monotonic and diatomic molecules.

According to the data in Refs 93 and 95, water molecules form linear complexes with molecules of the inert gases, nitrogen, and carbon monoxide. These complexes can be regarded as hydrogen-bonded. Detailed calculations of the potential surface of the HOH...Ar complex showed [94] that other orientations of an argon atom relative to a water molecule are possible, up to a mutually perpendicular orientation of the symmetry axis of the water molecule and the Ar–O axis. In the oxygen complex, the O–O...OH_2 orientation is preferable. On the whole, calculations predict that complexes of water with permanent gases are very weak.

Ref. 100 reports the results of calculations for complexes of water with hydrides. The calculations were performed in terms of the widest possible basis set and took the correlation energy into

Table 4. Results of quantum-chemical calculations of energies of complexes of water and certain permanent gases.

Complex	$-\Delta E$/ kcal mol^{-1}	Method	Ref.
HOH...N_2	0.9	Self-consistent field (SCF), 4-31G and MINI-4 basis sets	92, 93
HOH...Ne	0.1	SCF, 6-31G** basis set with allowance for electron correlation energy in the second-order perturbation theory of Moeller–Plesset	93
HOH...Ar	0.4	ditto	93, 94
HOH...CO	1.3	SCF, 4-31G and MINI-4 basis sets	95, 98
HOH...O_2	0.9	SCF, 6-31G** basis set	96, 97
HOH...H_2	0.6	Moeller–Plesset perturbation theory	99

Table 5. Results of quantum-chemical calculations of the energies and structures of water–hydride complexes [100]

Complex	R/Å	r/Å	θ/deg.	$-\Delta E$/kcal mol^{-1}		$-\Delta H^{298}$/kcal mol^{-1}
				CF	MP4	
HOH...NH_3	3.039	0.955	2.3	4.9	6.6	4.7
HOH...PH_3	3.928	0.949	3.0	1.6	2.2	0.8
HOH...OH_2	2.971	0.952	5.3	4.1	5.3	3.6
HOH...SH_2[a]	3.774	0.949	3.4	1.8	2.7	1.3
HSH...OH_2	3.619	1.327	3.0	1.9	2.9	1.5
FH...OH_2	2.720	0.922	4.6	7.6	9.1	7.4
ClH...OH_2	3.243	1.277	2.2	4.1	576	4.4

Note. The following designations are used: R is the distance between the X and Y atoms linked by a hydrogen bond; r is the length of a X–H bond participating in hydrogen bond formation; θ is the angle between the X–H bond and the X–Y line; the structural parameters were calculated by the SCF method in terms of the 6-31G(d) basis set; CF is the electron energy calculated by the SCF method in terms of the 6-31+G(2d,2p) basis set with the geometry optimised in terms of the 6-31G(d) basis set; MP4 is the energy with allowance for electronic correlation calculated by the fourth-order Moeller–Plesset perturbation theory; ΔH is the enthalpy of the complex calculated by the method from Ref 101 using the electronic energy in terms of the MP4/6-31+G(2d,2p) basis and vibrational frequencies in terms of the 6-31G(d) basis set.

account. These results are given in Table 5, together with the complex-formation enthalpies and structural parameters of isolated complexes. The formation of linear H-bonds X–H...Y was found to occur in all the complexes. The HOH...NH_3 complex (C_s symmetry) is the most stable, while the water dimer (C_s symmetry) is markedly less stable. It should be noted that the calculated enthalpy of the latter is in good agreement with the value determined experimentally, [88] which is 3.7± 0.5 kcal mol^{-1}. The structure of the HOH...PH_3 complex is similar to that of the ammonia complex,[100] but the low enthalpy of formation makes it doubtful if the phosphine–water complex exists at room temperature. The same conclusion applies to hydrogen sulfide–water complexes, in which water acts both as a proton donor and a proton acceptor.

An analysis performed for complexes of hydrides with water taking into account ΔE and ΔH_{298} values suggests that their stability changes in the following order:

$$FH...OH_2 > HOH...NH_3 > ClH...OH_2 > HOH...OH_2 >$$
$$> HSH...OH_2 > H_2S...HOH > HOH...PH_3.$$

A comparative calculation of the structures and energies of the complexes of CH_4 and SiH_4 with water [103] in terms of the 6-31G* basis set taking into account the correlation energy showed that the structures of the complexes of CH_4 and SiH_4 with water differ considerably, which is explained by differences in the polarity of the $C^{\delta-}-H^{\delta+}$ and $Si^{\delta+}-H^{\delta-}$ bonds. The water–silane complex ($\Delta E = -2.4$ kcal mol^{-1}) is more stable than the complex with methane ($\Delta E = -1.3$ kcal mol^{-1}).

Despite the considerable progress in the quantum-chemical computational methods achieved in the recent years, experiment remains the main source of information about the structure and energy of weak complexes. High-resolution IR and microwave spectroscopic methods are used primarily for this purpose in the gas phase.

Data on the structure of complexes and their potential surfaces can be obtained by analysing the following spectral features: appearance of new lines corresponding to the complex itself; disappearance or displacement of lines of the starting monomeric components; changes in the intensities of lines corresponding to the monomers and complexes as a function of temperature and pressure.

It is convenient to study the above spectroscopic behaviour in high-resolution spectra, i.e. in the spectra of gases at low pressures and temperatures. This, in turn, means highly sensitive equipment is needed. The known methods for studying weak complexes in the gas phase are usually divided into equilibrium and non-equilibrium ones, depending on the thermodynamic state of the complexes under the experimental conditions.

When equilibrium methods are used, one tries to attain the highest possible concentrations of complexes by performing the measurements near the liquid–vapour phase equilibrium line. This approach makes it possible to measure the equilibrium constant and the enthalpy of formation of the complex. However, it is used only for sufficiently stable complexes, due to the low sensitivity of the equipment available at present.

Thomas [104] used IR spectroscopy to study the spectral characteristics of the $H_2O...HF$ gas-phase complex. Three bands characterising intermolecular hydrogen bonds were found, one band in the region of HF stretching vibrations, another in the region of water deformation vibrations, and the third, around 780 cm^{-1}, which corresponds to vibrations of the complex itself. Estimation of the enthalpy of complex formation gave the value of -6.2 kcal mol^{-1}, which corresponds to $D_0 = -5.5$ and $D_e = -7.1$ kcal mol^{-1}.

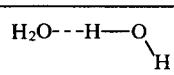
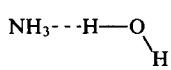
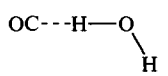
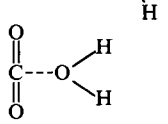
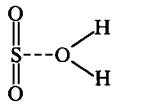
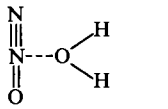
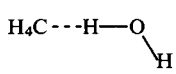
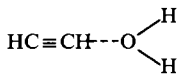
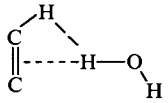
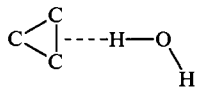
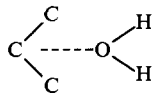
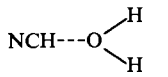
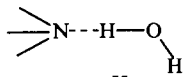
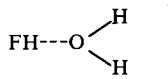
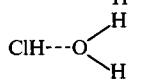
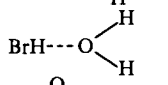
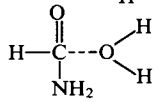
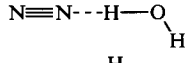
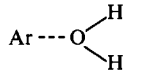
This is the only example, known to us, of a detailed study of a water complex in an equilibrium gas phase by IR spectroscopy in the traditional version using a diffraction spectrometer.

It was noted in a study cited above [47] that, for a resolution of 0.5 cm^{-1}, a broadening of water lines at 3803.8 and 3151.9 cm^{-1} in the region of the stretching vibrations of water was detectable in a gaseous mixture containing 2.6×10^{-3} mol% H_2O. This suggests that a hydrogen-bonded complex is formed in the gas phase between the molecules under consideration even at such a low concentration of water. When the resolution was altered to 2 cm^{-1}, the broadening of lines did not exceed the instrumental function. An indirect confirmation that hydrogen-bonded complexes are formed between water molecules and ammonia and hydrogen selenide in the gas phase at a water concentration of 10^{-2} mol% comes from data on the broadening of the analytical line of water in the region of its deformation vibrations presented in Table 2. Indeed, under the experimental conditions chosen,[47] the width of the absorption bands is mainly determined by the Doppler and collision broadening mechanisms. Taking into account the constancy of the Doppler-type contribution and the gas pressure in the cell, the broadening coefficients, differing by an order of magnitude, may indicate that the type of interaction in mixtures containing water in nonpolar gases (the van der Waals interaction) differs from that in mixtures containing water in polar gases (specific interaction with hydrogen bonds). As predicted by calculation (see Table 5), interaction of water with ammonia is considerably stronger than that with hydrogen selenide.

Thus, new high resolution IR spectroscopic methods, such as diode laser spectroscopy and Fourier-transform spectroscopy, show promise in the studies of weak complexes of water in the gas phase.

Microwave spectroscopy with Stark modulation in the millimetre range up to 75 GHz was used [105,106] to study the above

Table 6. Molecular constants of water complexes in the gas phase according to microwave spectroscopic data.

Molecule	Intermolecular distance[a]/Å	Force constant k_s/N m^{-1}	Dipole moment μ/D	Structure of the complex	Ref.
H_2O	2.05 (O...H)	11.7	2.64307		112
NH_3	2.02 (N...H)	14.5	2.972		113
CO	2.407 (C...H)	2.74	—		114, 115
CO_2	2.836 (C...O)	6.4	1.8522		116
SO_2	2.824 (S...O)	5.3	1.984		117
N_2O	2.97 (N...O)	—	1.480		118
CH_4	3.702 (C...H)	1.53	0.728		119
C_2H_2	2.229 (H...O)	6.5	2.0124		120
C_2H_4	2.481 ( ...H)	—	1.0943		121, 122
C_3H_6	2.34 	—	1.209		123
C_3H_8	4.35 (C...O)	—	0.73		124
HCN	3.139 (C...O)	11.1	—		125, 126
$(CH_3)_3N$	1.82 (N...H)	—	2.37		127
HF	2.662 (F...O)	24.9	4.073		128–131
HCl	3.215 (Cl...O)	12.5	—		132
HBr	3.411 (Br...O)	10.5	—		133
H_2NCHO	—	—	1.05		134
N_2	2.42 (N...H)	—	0.833		135
Ar	3.398 (Ar...O)	0.90	0.73		136–138

[a]The symbols in parentheses indicate which pairs of atoms correspond to the distances specified.

H_2O...HF complex in an equilibrium gas phase. The composition of the following equilibrium mixture has been determined[105] at a pressure of 188 mTorr and a temperature of 238 K: $n_{H_2O} = 1.85 \times 10^{19}$, $n_{HF} = 6.66 \times 10^{20}$, $n_{H_2O...HF} = 10.03 \times 10^{15}$ m^{-3}; using Eqn (12), the dissociation energy of the complex was calculated to be $D_0 = -8.1$ kcal mol^{-1}. The total dissociation energy, $D_e = -10.2$ kcal mol^{-1} is in good agreement with the values in Table 5 obtained by quantum-chemical calculations, but is markedly higher than the spectroscopic value, which is -7.1 kcal mol^{-1}.[104]

The rotational spectrum of the H_2O...HF complex in the equilibrium gas phase at low temperatures was first observed in the submillimetre range of 180–350 GHz on a RAD-type spectrometer.[107] In this study [107] the experimental data (including those on the excited states of complexes) were considerably expanded in comparison with the data of previous studies,[105,106] the assignment of the previously observed spectral lines was corrected, and the spectroscopic constants were revised. The usefulness of studies on the submillimetre spectra of molecular complexes in equilibrium gas phases was demonstrated.

At present, the methods of microwave spectroscopy are used quite widely in studies of weakly bound complexes under non-equilibrium conditions. These methods include primarily molecular-beam electroresonance spectroscopy and the microwave Fourier spectroscopy of a pulsed beam.[108,109] In the former method, the complexes are formed in a gas, which flows into a vacuum from a premix chamber containing a mixture of an inert carrier gas and the gases under study at a pressure of 1 – 3 atm and $T = 300$ K. In the second method, the complexes are generated by a pulsed flow of a gas injected into a Fabry – Perot resonator at a frequency of $\sim$ 10 pulses per second.

Table 6 presents some molecular parameters of complexes of water with various proton donors and acceptors found by the specified methods. One can see that water exhibits proton-donating properties with respect to the NH_3, CO, CO_2, C_2H_4 and N_2 molecules. Conversely, water acts as a proton acceptor in other cases. One of the important molecular constants determined experimentally is the centrifugal distortion constant D_j. The latter is linked to the force constant of the vibration of the intermolecular hydrogen bond by the relation [110,111]

$$k_s = \frac{16\pi^2 B^3 \mu}{D_j} \eta , \qquad (14)$$

where B is the rotational constant, μ is the reduced molecular mass of the complex, and η is a correction introduced for complexes of a given type.

In turn, k_s is related to the depth of the potential well of the complex D_e by the expression [109]

$$D_e = \tfrac{1}{72} k_s r_e^2 ,$$

where r_e is the equilibrium intermolecular distance.

It is evident from the data in Table 6 that the complex of water with HF has the highest stability. As noted above, the thermodynamic characteristics of this complex were determined by microwave spectroscopy.[128] At $T = 298$ K and partial pressures of the starting components equal to 1 Torr, ca. 10% of the H_2O and HF molecules are bound in the complex. For comparison, in the case of HCN and HF ($k_s = 11.1$ N m^{-1}), only 5×10^{-4}% of the molecules are involved in complexes.[125] It is impossible to detect such complexes under the usual conditions.

Another method for studying experimentally isolated water-based weak molecular complexes in a nonequilibrium state is IR spectroscopy with low-temperature matrix isolation, in which a mixture of a gas or vapour under study and a diluent gas is rapidly condensed on a support at 4 – 20 K.[139,140] It is possible to observe simultaneously bands of monomers and 1:1 complexes under such nonequilibrium conditions only at high dilution (when the ratio of the concentrations of the gas under study and the diluting gas exceeds 10^3). Otherwise, bands corresponding to more complex associated species manifest themselves as the above ratio decreases. In addition, the important role of the non-uniform broadening in matrices makes it difficult to measure the shapes and intensities of the spectral bands of the complexes and, hence, to obtain quantitative information about their compositions and energies. The relative stability of the complex can be determined qualitatively from the low-frequency shifts of the bands of the stretching vibrations of water. Table 7 shows the results of studies on certain complexes of water with various inorganic proton acceptors, including two hydrides, viz. ammonia and hydrogen sulfide. It is seen that the band due to the symmetric stretching vibrations of water (ν_1) has the highest sensitivity to the electronic structure of acceptor molecules. Among the compounds studied, the maximum shift of this band is observed for the complex with NH_3, in agreement with the maximum value of the force constant of the NH_3...H_2O complex in the gas phase (see Table 6). The complex with H_2S is less stable than that with ammonia, but is more stable than the water dimer under the matrix conditions. It is noteworthy that, according to the results of studies [148,150] on the H_2S...H_2O complex, hydrogen sulfide displays proton-accepting properties with respect to water (Table 8).

The resulting HOH...SH_2 and HSH...OH_2 complexes have a linear structure. A number of bands were attributed to the $H_2S(H_2O)_2$ complex.

In complexes with hydrogen halides,[141,151–156] water also displays proton-accepting properties. Complexes of water with the halogens [149,157–159] and SO_2 in low-temperature matrices[144] are likely to be of the donor-acceptor type. Analysis of IR spectroscopic data for H_2O in Ar, Kr and N_2 matrices shows that the complexes of water with krypton are the most stable.

Thus, there are few hydrogen-bonded complexes of water with light molecules studied by IR spectroscopy in low-temperature matrices and directly in the gas phase, and complexes of only two hydrides, NH_3 and H_2S, have been studied. It should be noted that this is the only experimental evidence that a weak hydrogen-bonded complex is formed in the case of hydrogen sulfide.

2. Molecular complexes of water in the liquid phase

The interaction of water with the main compound in the liquid phase is more complex, since it can be paralleled by the association of molecules of the main compound as a background. To consider this aspect theoretically, one has to calculate the potential surfaces not only of the simple 1:1 water – main compound complex but also of more complex ones, $H_2O...n$ B, where $n \leqslant 4$ (in accordance with the coordination number of the water molecule). An experimental investigation of association processes in the condensed phase is very difficult because it is impossible to use high-resolution spectroscopy. However, much experience has been accumulated in spectroscopic studies of intermolecular interactions in solutions based on shifts and intensity changes of bands in the spectra of complexes with various compositions (see, for example, Refs 160–162). In particular, the IR spectra of complexes containing a hydrogen bond display bathochromic shifts $\Delta\nu$ of the stretching vibration bands of the proton donor in parallel with an increase in the integral absorption coefficient A relative to the spectral parameters of the isolated proton donor. Many empirical and semiempirical equations relating the $\Delta\nu$ and ΔA values to the stability of complexes characterised by the enthalpy of formation of the hydrogen bond have been proposed. The following relation can be taken as an example:[163]

$$\Delta H = (80 \pm 20) \frac{\nu'_{AH} - \nu''_{AH}}{\nu_{AH}} , \qquad (15)$$

where ν'_{AH} and ν''_{AH} are the frequencies of the stretching vibrations of an AH molecule in the free state and in a complex, respectively.

It seems more correct to use the increment of the integral absorption coefficient, for example in the form of the equation proposed by Iogansen,[164]

$$\Delta H = 2.9 \Delta A^{1/2}, \qquad (16)$$

Table 7. Frequencies of the main vibrations of the H_2O molecule (cm^{-1}) in the free state and in complexes with some inorganic molecules according to the data obtained by IR spectroscopy with matrix isolation.

Inorganic molecule	ν_1	$\Delta\nu_1$	ν_3	$\Delta\nu_3$	ν_2	$\Delta\nu_2$	Ref.
Free state of water, H_2O (gas)							
	3657		3756		1595		
Complexes with inorganic molecules							
Ar	3638	19	3734	22	1589	6	141
N_2	3634	23	3728	28	1597	−2	143
Kr	3628	29	3724	32	1586	9	142
H_2O [a]	3575 [c]	63	3710 [c]	24	1611 [c]	−22	141
H_2O [b]	3634 [c]	4	3723 [c]	5	1594 [c]	3	141
SO_2	3631	7	3723	11	1591	−2	144
NH_3	3434	204	3702	32	1625	−36	145–147
H_2S [c]	3536	102	—	—	1614	−25	148
Cl_2	3637	0.5	3724	10	1587	2	149

[a] The water molecule acts as a proton donor.
[b] The water molecule acts as a proton acceptor.
[c] The ν values for complexes in an argon matrix are given.

where $\Delta A^{1/2} = (A'_c/m)^{1/2} - (A')^{1/2}$ is the difference between the integral absorption coefficients (in 10^4 cm mmol^{-1}) of the molecules bound in hydrogen-bond complexes (liquid phase) and of free molecules (gas or an inert solvent), and m is the number of hydrogen bonds.

It is reasonable to estimate the stability of the complexes using relations such as Eqns (15) and (16) for series of isotypical compounds under similar conditions.

The solubility of water is an important factor in experimental studies of the molecular state of water in liquid volatile compounds by IR spectroscopy. It is lower than the method sensitivity in liquefied permanent gases and in some polar compounds. Therefore, it is impossible to detect the changes in the intensity or positions of the stretching vibration bands of water due to its interaction with molecules of environment. However, the molecular state of water in liquid volatile inorganic chlorides of Subgroup IVA and VA elements has been studied by IR spectroscopy in sufficient detail.[165–167]

The IR spectrum of an aqueous solution of germanium tetrachloride ($c_{H_2O} < 10^{-2}$ M) in the region of 4000–1100 cm^{-1} displays bands at 3691, 3603, 2845 and 1600 cm^{-1}.[165] The relation between the intensities of the first two bands was found to be the opposite to that known from the literature for the ν_1 and ν_3 bands of water in CCl_4, an inert solvent structurally related to germanium tetrachloride. It was concluded that the vibrations of free water molecules correspond to the bands at 3691 (ν_3) and 1600 (ν_2) cm^{-1}.

The small low-frequency shift of the ν_3 band relative to the gas phase results from van der Waals interaction HOH...$GeCl_4$, whose energy, estimated from the relation between ΔH and $\Delta\nu$ proposed in Ref. 168, was found to be −1.4 kcal mol^{-1}. The band at 3603 cm^{-1} was attributed to the ν(OH) vibrations of the hydroxyl groups in the hydrolysis products, while the band at 2845 cm^{-1} was attributed to the stretching vibration of the HCl molecule. The hydrolysis of $GeCl_4$ in accordance with the simplest scheme

$$GeCl_4 + HOH \leftrightarrows Ge(OH)Cl_3 + HCl, \quad (17)$$

probably occurs only at low concentrations of water in $GeCl_4$ (<10^{-2} M). When the concentration is increased, the intensities of the bands at 3691, 3603 and 1600 cm^{-1} increase, while that of the band at 2845 cm^{-1} decreases. Simultaneously, a series of new bands appear. Together these facts led the authors[165] to the conclusion that complex germanium hydroxochlorides $Ge(OH)_n.Cl_{4-n}$ and oxochlorides $Ge_nO_{n-1}Cl_{2n+2}$ are formed in solution.

The equilibrium of reaction (17) was studied directly in liquid $GeCl_4$ and in a CCl_4 solution. The hydrolysis constant $K_c = 1.74 \times 10^{-3}$ at 20 °C and concentrations of water in the range 10^{-3}–10^{-2} M, together with its temperature dependence in the range of 10–60 °C, were determined. It has been shown[169] that an admixture of water in $GeCl_4$ influences decisively the chemical forms of microadmixtures of sulfur, selenium, boron, silicon, aluminium, titanium, phosphorus and carbon.

The IR spectra of water solutions in $AsCl_3$ display bands at 3659, 3574 and 1600 cm^{-1} assigned to the ν_3, ν_1 and ν_2 vibrations of a water molecule respectively. The ν(OH) vibrations of hydroxyl groups correspond to a band at 3525 cm^{-1}, while the stretching vibrations of the HCl molecule are observed as a band at 2800 cm^{-1}.[167] The energy of the HOH...$AsCl_3$ interaction is somewhat higher than that for $GeCl_4$ and equals −2 kcal mol^{-1}. When the concentration of water is below 4×10^{-2} M, the hydrolysis follows the scheme

$$AsCl_3 + HOH \leftrightarrows As(OH)Cl_2 + HCl, \quad (18)$$

while at higher concentrations, arsenic hydroxochlorides $As(OH)_nCl_{3-n}$ and the oxochloride AsOCl are formed. The hydrolysis constant remains unchanged up to a water concentration of $\sim 10^{-2}$ M and equals 4.2×10^{-3} at 20 °C.

The IR spectrum of a solution of water in $SnCl_4$ displays bands at 3636, 3563 and 1586 cm^{-1} assigned to the ν_3, ν_1 and ν_2 vibrations of the water molecule.[166] In contrast to the IR spectra of solutions of water in $GeCl_4$ and $AsCl_3$ and the spectrum of the $SnCl_4 \cdot n H_2O$ crystal hydrate, the ν_2 deformation vibration band undergoes a bathochromic shift relative to its position in the gas phase. Taking into account the much higher intensity of the ν_2 band compared with those of the ν_3 and ν_1 bands (as in the gas phase), the authors[166] concluded that the intermolecular bond in the H_2O...$SnCl_4$ complex, involving an unshared electron pair of the oxygen atom in the water molecule and the unoccupied orbitals of the tin atom is of the donor–acceptor type, unlike the hydrogen bonds between the molecules of H_2O and $GeCl_4$ or $AsCl_3$. The energy of this interaction was estimated as −2.4 kcal mol^{-1}. Unlike germanium, arsenic, and tin chlorides, the concentration of free water in liquid silicon tetrachloride is lower than 10^{-4} mol%, which is in agreement with the above radio-frequency spectroscopic determinations of water in $SiCl_4$ in the gas phase.[85]

Table 8. Frequencies of the main vibrations (ν/cm^{-1}) of H_2O and H_2S in the free state and in complexes in a nitrogen matrix.[148,150]

Type of vibration	H_2O...HSH		H_2O			H_2S		
	H_2O	H_2S	monomer	dimer		monomer	dimer	
				D	A		D	A
ν_1	3628.1	2574.2 2570.2	3634.5	3627.2	3550.0	2619.3	2617.7	2579.0
ν_3	3719.0	2625.0 2623.6	3726.9	3715.0	3698.8	2632.4	2630.4	2624.7
ν_2	1597.9		1597.6	1601.0	1618.6	1179.6	1178.0	1181.5

Note. D = proton donor, A = proton acceptor.

Table 9. Spectral parameters of the stretching and deformation vibration bands of water in the gas phase, in CCl_4 solutions, and in liquid hydrides at 298 K.[170-173,180]

Solvent	ν/cm^{-1}								$A \times 10^8$/cm^2 molecule^{-1} s^{-1}	
	ν_1	$\Delta\nu_{1/2}$ [a]	ν_3	$\Delta\nu_{1/2}$	$\Delta\nu_{1/2}^{str}$	$\nu_1-\nu_3$	ν_2	$\Delta\nu_{1/2}^{str}$	$A(\nu^{str})$ [b]	$A(\nu^{def}) \times 10^8$ [b]
Gas	3657	—	3756	—	—	99	1596	—	22.8	25.2
CCl_4	3616	35	3707	45	—	92	—	—	30	—
PH_3	3606	60	3696	160	160	90	1598	~55	84	28
AsH_3	3610	~75	3698	120	170	88	1600	~50	71	35.5
H_2S	3560	~80	3645	110	~150	85	1606	42	203	32
H_2Se	3555	~80	3643	105	~150	88	1600	45	168	33

[a] The half-width of the ν^{str} overall band at half-height. [b] The integral absorption coefficient.

Hence, the equilibrium on the hydrolysis of $SiCl_4$ is almost completely shifted to the right.

$$SiCl_4 + n\,HOH \leftrightarrows SiCl_{4-n}(OH)_n + n\,HCl\,. \quad (19)$$

A similar behaviour of water is observed in phosphoryl chloride, in which the equilibrium of the reaction

$$POCl_3 + HOH \leftrightarrows PO(OH)Cl_2 + HCl\,, \quad (20)$$

is also shifted to the right,[76] and free water is not detected.

Information about the molecular state of water in liquid volatile inorganic hydrides of Group IV–VI elements at concentrations ca. $10^{-2}-10^{-3}$ mol% was obtained by a number of workers.[73,77,170-172] The considerable experimental difficulties encountered in studying the IR spectra of dilute solutions of water in hydrides come from the relatively 'narrow range of existence' of the liquid phase of hydrides and their low boiling points (<273 K). However, IR spectra can be recorded at higher temperatures (~ 300 K for all hydrides except silane, whose b.p. is 269.4 K) at increased pressures, but the cells must then withstand pressures of several tens of atmospheres. The appropriate experimental techniques are reported in Ref. 174. As noted above, the very low solubility of water in liquefied permanent gases at their boiling points precludes the recording of the bands of dissolved water even for considerable thicknesses of the absorbing layer (up to 100 mm). It has been shown [73] that the same problems in recording the bands of dissolved water arise in studies of systems based on nonpolar silane and germane. In addition, the region of stretching and deformation vibrations of water includes the rather intense overtone and combination bands of these hydrides.[77]

A different situation is observed in the case of dilute solutions of water in liquid hydrides of Group V and VI elements:[175,176] the 3400–3700 cm^{-1} region displays bands of the antisymmetric (ν_3) and symmetric (ν_1) vibrations of water molecules (similarly to solutions of water in organic solvents [177] and in liquid volatile chlorides) and a band due to deformation vibrations (ν_2); the integral absorption coefficient of these bands increases approximately by an order of magnitude compared with that in the gas phase (Table 9). This suggests that hydrogen bonds are formed between the molecules of dissolved water and the hydrides. The estimated energies of intermolecular interactions are presented in Table 10. For ΔH, the ranges of values estimated by Eqn (16) are given,[170-172] since the exact number m of hydrogen bonds formed by a water molecule with the hydrides in the liquid phase is unknown. For this reason, the limiting values were adopted — one and two H-bonds per molecule of water, representing the upper and lower limits of the strength of the hydrogen bond.

It follows from these data that, first, the stability of complexes of hydrides of Group VI elements with a proton donor — water — is higher than that of the complexes of Group V elements. Second, the stability of complexes of hydrides of the Fourth Period elements is lower than that of complexes of hydrides of the Third Period elements. It should be emphasised once more that these conclusions refer to two-component liquid solutions with a great excess of the proton acceptor. Nevertheless, the trends noted above are also observed in the calculated enthalpies of the hydrogen bond (see Table 5). The ΔH_{298} values for the complexes of PH_3 and H_2S fall within the range of experimental values. On the whole, the above series of the hydrogen bond strengths follow from the analysis of $\Delta\nu_s$, the low-frequency shift of the band due to the stretching vibrations of the proton donor (the HF molecule) in complexes with hydrides in an argon matrix,[178] although, according to these data, the complex of phosphine is more stable than that of hydrogen sulfide. Also, the data obtained do not contradict the results obtained in studies of the microwave spectra of complexes of certain hydrides in the gas phase [179] and by quantum-chemical calculations for such complexes.[180]

IR spectroscopy has been used[77,170-172] to determine the solubility of water in hydrides of Group V and VI elements, which are correlated with the energy of intermolecular interaction. A similar relationship was also established for the liquid–vapour separation factors α in the systems water–hydrides of Group V and VI elements:[77] although the ideal separation factors are much less than unity, the α value determined experimentally from solubility data is only a little less than unity for the H_2S-H_2O system and is markedly higher than unity for the AsH_3-H_2O system. As follows from Table 10, the intermolecular interaction energies in the systems differ markedly.

According to experimental results,[77] gaseous hydrates stable up to ~ 305 K are formed in saturated solutions of water (water concentrations of $10^{-1}-10^{-2}$ mol%) in hydrides of Group V and VI elements. A thermodynamic analysis of the structures of the hydrates and of the conditions governing their formation in processes involving the extensive purification of hydrides has been carried out.[181]

Table 10. Energy characteristics of hydride–water complexes.

Complex	$\Delta\nu_3$/cm^{-1}	$-\Delta H_{298}$/ kcal mol^{-1}, according to data in Refs		$-\Delta H^{theor}$/ kcal mol^{-1}	$\Delta\nu_s$/cm^{-1}
		77	170–172		
HOH...NH_3	–	–	–	4.7	913
HOH...PH_3	60	1.3	0.4–1.6	0.8	327
HOH...AsH_3	58	1.2	0.2–1.2	–	260
HOH...SH_2	111	1.9	1.2–2.5	1.3	302
HOH...SeH_2	113	2.2	1.0–2.4	–	299

Notes. $\Delta\nu_3$ is the difference between the frequencies of the stretching vibrations (ν_3) in the gas phase and in the complex in the liquid phase; ΔH_{298} is the enthalpy of formation of a hydrogen bond calculated from spectroscopic data for a solution of H_2O in a liquid hydride [from the shift of the ν_3 band according to Eqn (15)][77] or determined by the Iogansen Eqn (16) for $m = 1$ and $m = 2$;[170-172] ΔH^{theor} are the calculated enthalpies of the hydrogen bond (see Table 5); $\Delta\nu_s$ is the difference between the frequencies of the stretching vibrations of an HF molecule in the free state and in a complex with a hydride in an argon matrix.[178]

Table 11. Positions of the bands (cm^{-1}) due to the fundamental vibrations of water dissolved in organic and inorganic bases with different donor numbers (DN) according to Gutmann.[77, 165–167, 182]

Solvent	ν_1	ν_3	ν_2	$\Delta\nu$	DN
Gas	3657	3756	1595	99	–
Trichloro-trifluoroethane	3628	3721	–	93	–
Carbon tetrachloride	3613	3705	–	92	–
Tetrachloro-ethene	3613	3705	–	92	0
Carbon disulfide	3610	3701	–	91	2
Phosphine	3606	3696	1598	90	–
Arsine	3610	3698	1600	88	–
Chloroform	3607	3690	–	83	4
Germanium tetrachloride	–	3691	–	–	–
Toluene	3595	3681		86	4
p-Xylene	3592	3680		88	5
Mesitylene	3590	3677		87	10
Nitromethane	3579	3663	1623	84	6
Anisole	3548	3662		114	9
Arsenic trichloride	–	3659		–	–
Epichloro-hydrin	3542	3653	1621	111	13.9
Benzonitrile	3545	3650		105	11
Hydrogen selenide	3555	3693	1600	88	–
Hydrogen sulfide	3560	3645	1606	85	–
Benzaldehyde	3544	3639		95	16
Tin tetrachloride	–	3636		–	–
Acetonitrile	3543	3636	1632	93	14
Cyclohexanone	3530	3610		80	18
Acetophenone	3535	3612		77	15
Diethyl ether	3518	3590	1628	72	19.2
Dioxane	3517	3584	1639	67	14.8
Dimethyl sulfoxide	3444	3494	1663	50	29
Pyridine	3405	3450		45	33

A review[177] summarises the main spectroscopic parameters of water dissolved in various organic solvents. Some of these data are presented in Table 11. It is seen that an increase in the proton-accepting capacity of solvent molecules (basicity), characterised by the donor number (DN) leads to an increase in the low-frequency shift of the ν_1 and ν_3 bands and a decrease in the difference between them (the bands of symmetric and anti-symmetric vibrations approach each other). Liquid chlorides and hydrides can also be regarded as nonaqueous inorganic solvents. For example, germanium tetrachloride, phosphine and arsine are located in Table 11 between carbon disulfide and toluene, arsenic tetrachloride is located between anisole and epichlorohydrin (DN = 9 – 14), while hydrogen sulfide, hydrogen selenide, and tin tetrachloride occupy a position between benzonitrile and acetonitrile (DN = 13 – 18).

IV. Conclusion

Modern spectroscopic methods make it possible to solve fairly complex problems in the determination and study of the molecular state of water present as an admixture in high-purity volatile inorganic compounds. The theoretical instrumental limit in the detection of water by diode laser spectroscopy and sub-millimetre spectroscopy (10^{-8} mol%) is quite sufficient for analyses in studies on the extensive purification of these compounds. The detection limits actually achieved are generally one or two orders of magnitude higher due to methodologology difficulties resulting from the impossibility of taking full account of all the ways in which background moisture can enter the substance analysed. The use of unique apparatus, the long preparation of spectrometers for analyses, and the use of expensive cooling agents (liquid helium) make the cost of one analysis rather high.

The optimisation of methods for the removal of water from volatile compounds and of the processes for the gas-phase synthesis of materials involving these compounds, as well as investigation of processes associated with the storage of high-purity compounds, especially those tending to react chemically, require data concerning not only the concentration of the water admixture but also the form of its existence in the gas and liquid phases. It was shown above that such information has been obtained for solutions of water in certain liquid high-purity chlorides and hydrides. However, the data on the stability of the resulting complexes, their concentration and the mean number of intermolecular bonds are clearly insufficient. The methods of diode laser spectroscopy and microwave high resolution spectroscopy are promising for investigating the mechanism and thermodynamics of complex formation reactions involving water in the gas phase under equilibrium conditions. However, systematic studies in this field are so far lacking.

It seems very important from the practical viewpoint to study in greater detail the effect of the formation of molecular complexes between the main compound and an admixture in the equilibrium phases on the quantitative characteristics of the processes in the interphase separation of admixtures. It is likely that the weak molecular complexes formed by admixture molecules with those of the main compound due to specific and non-specific interactions can be considered as a new class of admixtures in high-purity substances.

It should be noted that the investigation of the nature of intermolecular interaction in such systems and of the dependences of the characteristics of molecular complexes on the structure of their fairly simple constituent molecules is outside the scope of the chemistry of high-purity compounds but is of definite interest for other branches of chemistry and physics which deal with problems of the theory of intermolecular interactions, as well as for biochemistry.

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The photochemistry of transuranic elements in solution

A B Yusov, V P Shilov

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Abstract. The literature data on the photochemical reactions of neptunium, plutonium, and americium in HNO_3, $HClO_4$, HCl, H_2SO_4, and Na_2CO_3 solutions as well as certain extraction systems are surveyed. The mechanisms of the photochemical reactions are discussed and it is concluded that those proposed in the literature do not account for those reactions in solutions occurring without added oxidants or reductants. The possibilities of the practical application of photochemistry in the processing of spent nuclear fuel are examined. The bibliography includes 53 references.

I. Introduction

Numerous photochemical studies have been devoted to the ions of metals with unfilled electron shells. The photochemical properties of uranyl have already been investigated quite fully. The UO_2^{2+} ion can exist in the excited state for hundreds of microseconds, exhibiting strong oxidising properties. Uranyl photochemistry constitutes a large independent field. The principal data accumulated in this field have been presented in a monograph[1] written more than thirty years ago and also in a review.[2] Uranyl photochemistry continues to develop vigorously at the present time.

In recent years, appreciable attention began to be devoted to the ions of other *f* elements: lanthanides (cerium, europium, and samarium) and actinides [the first transuranic elements (TUE) — neptunium, plutonium, and americium]. The photochemistry of the last three elements will be the subject of the present review.

It may be assumed that the photochemistry of TUE began to develop since 1958 when the photochemical reduction of Np(VI) to Np(V) in perchloric acid solutions was observed.[3] Later, in 1965, Indian investigators[4] showed that Pu(VI) is reduced to Pu(IV) in the extraction of plutonium(VI) from acid solutions with a benzene solution of thenoyltrifluoroacetone under illumination and that this process does not occur in the dark. Systematic studies on the influence of light on the chemical behaviour of plutonium and neptunium in solutions began in the 1970s. Reports concerning the photochemical reactions of americium also appeared subsequently.

A B Yusov, V P Shilov Institute of Physical Chemistry, Russian Academy of Sciences, Leninskii prosp. 31, 117915 Moscow, Russian Federation. Fax (7-095) 335 17 78. Tel. (7-095) 330 41 70

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Despite the more than twenty year history of the photochemistry of TUE, the accumulated data, particularly those obtained in recent years, have not been analysed. There have been only brief reviews on the photochemistry of plutonium and on the application of photochemical processes in the processing of irradiated nuclear fuel. The aim of the present review is to give a systematic account of the available data on the photochemistry of all the transuranic elements and to assess the prospects for its further development.

II. The photochemistry of plutonium and neptunium

1. The photochemistry of aqueous acid solutions

a. Nitric acid solutions

Visible light does not affect the chemical behaviour of plutonium in nitric acid solutions in the absence of additives, but on exposure to UV light (mercury lamps were usually employed) plutonium passes to the Pu(VI) state regardless of the initial valence form — Pu(III) or Pu(IV).[5] The reaction takes place both in air and under a CO_2 atmosphere. Pu(III) is oxidised particularly rapidly. With increase in the concentration of acid (up to 3.5 M), the rate of oxidation also increases. According to the data of Duan Yunfu et al.,[6] the rate of the photochemical oxidation of Pu(III) to Pu(IV) is proportional to the concentrations of Pu(III), H^+, and NO_3^-. The authors[6] believe that the comversion of plutonium to the hexavalent state takes place by disproportionation of Pu(IV) to Pu(III) and Pu(VI). In the presence of H_2O_2, plutonium is quantitatively converted into Pu(III) on UV irradiation and at a higher rate than in the dark.

It is believed[7,8] that, on UV irradiation of any valence form of neptunium — Np(IV), Np(V), and Np(VI) — over a wide range of HNO_3 concentrations (0.1 – 6.0 M), the final form is Np(V). However, it has been noted that other photochemical reactions also occur in solution, for example the oxidation of Np(V) to Np(VI) and the reduction of Np(V) to Np(IV).[8] The quantum yields η of various photochemical reactions of neptunium in nitric acid solutions on irradiation with light at λ = 254 nm have been measured.[8] In the absence of additives in 1.0 M (solution I) and 4.0 M (solution II) of HNO_3, the following values of η were obtained:

Process	η for solutions	
	I	II
Reduction of Np(VI) to Np(V)	0.03	0.003
Oxidation of Np(IV) to Np(V)	0.053	0.017
Oxidation of Np(V) to Np(VI)	0.015	0.022

These reactions proceed also under the influence of light at λ = 300 nm but with much lower yields.

Somewhat different results have been obtained by Galkin et al.,[9] although they employed the same light source as Nemodruk et al.[7] Galkin et al.[9] note that Np(V) accumulates only at $[HNO_3] < 1$ M, whereas at $[HNO_3] = 2$ and 4 M, the concentration of Np(V) increases only during the first 5–10 min of irradiation and then falls as a result of the formation of Np(VI). The authors explained this by the reversibility of the reaction

$$2NpO_2^{2+} + HNO_2 + H_2O \rightleftharpoons 2NpO_2^{+} + NO_3^{-} + 3H^{+}. \quad (1)$$

The passage of air through the irradiated solution leads to the quantitative formation of Np(VI). The difference between the results obtained in the above two studies[7,9] at identical acid concentrations may be associated with the influence of factors which have not been taken into account, for example, micro-impurities inhibiting or catalysing the photochemical reactions.

The introduction of various additives into nitric acid solutions with $[HNO_3] = 0.1-4$ M changes the results of the photochemical experiments. In the presence of urea—a substance which removes NO_2^- ions from the system—it is possible to obtain Np(VI) solutions virtually without an admixture of Np(V).[7,9] However, our data have shown that in weakly acid solutions, even those containing many NO_3^- ions, neptunium(VI) is not formed. Thus, when $NpO_2(ClO_4)_2$ is irradiated in 1×10^{-3} M $HClO_4$ + 1 M $LiNO_3$ in the presence of 0.1 M urea, Np(V) is formed quantitatively. The presence of hydrogen peroxide accelerates the photo-chemical oxidation of Np(IV) to Np(V), but the HNO_3 concentration should not then exceed 1 M,[7] while the introduction of hydrazine leads to the photochemical reduction of Np(V) to Np(IV), but the reaction does not go to completion. Its quantum yield in 4 M HNO_3 was found to be 0.006.[8] In ethanol, neptunium(VI) is reduced photochemically to Np(V) in 0.094 yield $\{[HNO_3] = 4$ M$\}$.[8]

The photochemical reactions of neptunium in nitric acid solutions in the presence of uranyl have been investigated in a number of studies (see, for example, Refs 9–11). The aim of these studies was to investigate the possibility of using the photochemical reactions for the separation of neptunium from uranium and plutonium in technological processes. It was observed that at low concentrations ($\sim$5 g litre^{-1}) uranyl does not influence the photochemical reactions and the dark equilibria involving neptunium. However, at high uranyl concentrations ($\geqslant$100 g litre^{-1}), uranyl is photolysed, which increases the yield of pentavalent neptunium. This effect has been attributed to the sensitising effect of uranyl and the photochemical formation of NO_2^- from NO_3^- [9] and to the stabilisation of Np(V) towards oxidation as a result of the formation of the cation–cation complexes between Np(V) and UO_2^{2+}.[11]

In one of the studies, a photocatalyst, namely Pt/TiO_2, was introduced into a nitric acid solution of neptunium $\{[HNO_3] = 3$ M$\}$ before irradiation.[12] In solutions without added urea, the photocatalyst does not affect the results, i.e. the neptunium is entirely converted, and at the same rate, into Np(V). On the other hand, in the presence of urea the photocatalyst accelerates the transition of neptunium to the hexavalent state to the extent of $\sim$30%, ensuring an almost 100% yield of Np(VI). The authors believe that this acceleration is associated with the occurrence of the reactions on the surface of the photocatalyst (PC).

$$PC \xrightarrow{h\nu} h^{+} + e^{-} \text{ (where } h^{+} = \text{hole)}, \quad (2)$$

Hydrated electrons react with the nitrate ion while the hole participates in the oxidation of the neptunium:

$$NpO_2^{+} + h^{+} \longrightarrow NpO_2^{2+}. \quad (3)$$

b. Perchloric acid solutions

Not only oxidation-reduction reactions of plutonium but also its ability to form polymers have been investigated in perchloric acid solutions exposed to light. In contrast to the behaviour in nitric acid solutions, in $HClO_4$ the final result depends on the initial form of the plutonium. When aerated solutions are irradiated, the Pu(III) is partly converted into Pu(IV). Plutonium(VI) remains unchanged on irradiation.[5] These data were obtained at acid concentrations >0.5 M. Our experiments with dilute $HClO_4$ solutions (10^{-3} M) showed that, on exposure to the UV light from the SVD-120a mercury lamps, Pu(VI) is fully converted into Pu(V).

In the presence of reductants, the photochemical behaviour of plutonium in $HClO_4$ changes. The introduction of H_2O_2 stabilises Pu(III), suppressing fully its oxidation to Pu(IV).[5] Oxalic acid reduces Pu(VI) to Pu(IV), which results in the precipitation of Pu(IV) oxalate.[4] Ethanol reduces photochemically both Pu(VI) to Pu(V) and Pu(IV) to Pu(III).[13] The authors[13] were the first to determine the quantum yields of the photochemical reaction involving plutonium. For the reaction

$$PuO_2^{2+} + C_2H_5OH \xrightarrow{h\nu} PuO_2^{+} + C_2H_5O^{\cdot} + H^{+}, \quad (4)$$

[taking into account the disproportionation of the Pu(V) obtained], η was found to be 0.02, while for the reaction

$$Pu^{4+} + C_2H_5OH \xrightarrow{h\nu} Pu^{3+} + C_2H_5O^{\cdot} + H^{+}, \quad (5)$$

the quantum yield was 0.03.

Irradiation with UV light accelerates sharply the disproportionation of Pu(IV) and a pseudoequilibrium is established, differing appreciably from the dark equilibrium: whereas in the dark or with room illumination, the disproportionation of the 9.9×10^{-3} M Pu(IV) solution in 0.47 M $HClO_4$ continues for tens of hours, on irradiation with UV light only a few hours are required and the degree of conversion of Pu(IV) increases appreciably: the pseudoequilibrium constant for the reaction

$$3\,Pu^{4+} + 2\,H_2O \overset{h\nu}{\rightleftharpoons} 2\,Pu^{3+} + PuO_2^{2+} + 4H^{+}, \quad (6)$$

is 0.025, whereas the constant for the dark reaction is 0.0086.[13–15] The process is reversible, i.e. when irradiation stops the system returns to the dark equilibrium.

Under the influence of UV light, the degradation of the polymeric forms of Pu(IV) accelerates severalfold in 0.47 M $HClO_4$.[13–15] Such solutions were prepared by precipitating plutonium hydroxide with its subsequent dissolution in $HClO_4$ at the required concentration. Under these conditions, both freshly prepared solutions and solutions kept for some time undergo photochemical decomposition. Furthermore, in solutions at a lower $HClO_4$ concentration (0.13–0.16 M) the dark decomposition of the polymers does not occur at all and only the photochemical decomposition is observed.

In the first study on the photochemistry of neptunium,[3] it was established that the UV irradiation of perchloric acid solutions of Np(VI) results in the reduction of the latter to Np(V). The concentrations of ^{237}Np was 0.045 M, while the concentration of the acid was 0.22–1.00 M. The quantum yield of this reaction was measured ($\eta = 0.032 \pm 0.011$). It has been suggested that the reductant is the photolysis product of water. Our data also indicate that, on irradiation with UV light in dilute $HClO_4$ (10^{-3} M), Np(VI) is fully reduced to Np(V). According to other data,[16] in sufficiently concentrated solutions of perchloric acid Np(IV) is oxidised to Np(V), while the latter is oxidised to Np(VI). Friedman et al.[17] believe that mainly photochemical reactions involving the oxidation of neptunium take place in perchloric acid solution without additives. They found that, following an increase in the $HClO_4$ concentration from 0.1 to 4.0 M, the quantum yield in the oxidation of Np(IV) to Np(V) falls from 0.02 to 0.0049, while the quantum yield in the oxidation

of Np(V) to Np(VI) increases from 0.004 to 0.010 and further (for light at $\lambda = 254$ nm).

In the presence of ethanol (acetaldehyde or other moderately strong reductants), the Np(VI), Np(V), and Np(IV) ions are capable of being photochemically reduced.[16,17] Prolonged irradiation results in the conversion of all the neptunium to the tetravalent state, a process which may be used for analytical purposes.[16] The quantum yields of the reactions of different neptunium ions with ethanol are within the limits from several thousandths to several hundredths.[17]

The photochemical oxidation of Np(V) in perchloric acid solutions with xenon trioxide has been investigated.[18] The ionic strength of the solution was kept constant at 2 with the aid of sodium perchlorate. The reaction is first order relative to XeO_3 and zero order relative to Np(V). It obeys the equation

$$\frac{d[Np(V)]}{dt} = k_1[XeO_3].$$

Thus the photochemically active substance in this reaction is XeO_3 and the rate of reaction is limited by the rate of its photochemical decomposition. It does not change when the $HClO_4$ concentration is raised from 0.5 to 2.0 M. The constant k_1 depends on the intensity of the irradiation and the spectral composition of the light. Under the experimental conditions, the average value of k_1 obtained was 6.28×10^{-6} s^{-1}. In the absence of light, the reaction is very slow and proceeds via a different mechanism.

c. Hydrochloric acid solutions

When hydrochloric acid solutions of Pu(III) with [HCl] = 0.5–5.5 M are irradiated with UV light in air, Pu(IV) gradually accumulates. Under a CO_2 atmosphere, the process is somewhat slower. The oxidation of Pu(IV) to Pu(VI) is not observed under these conditions[5] (plutonium concentration $\sim 10^{-3}$ g ml^{-1}). A mixture of Pu(IV) and Pu(VI) hardly changes on UV irradiation. In the presence of hydrogen peroxide, Pu(VI) is reduced to Pu(IV) and partly to Pu(III).

Under the influence of UV irradiation, Np(V) in hydrochloric acid solutions is oxidised to Np(VI), while Np(IV) is initially oxidised to Np(V) and then to Np(VI).[19] At [HCl] > 3 M, the oxidation to Np(VI) is quantitative. Deaeration of the solution does not affect the course of the reaction. Our results show that, in both perchloric and nitric acid solutions, the final form of neptunium depends not so much on the concentration of the anion as on the concentration of H^+. Thus in a solution containing 1×10^{-3} M HCl, 1 M KCl, and 1×10^{-3} M Np(VI), Np(VI) is converted quantitatively into Np(V) on UV irradiation.

In the presence of hydrogen peroxide, Np(IV) and Np(VI) are converted into Np(V), while in the presence of ethanol Np(V) and Np(VI) are quantitatively converted into Np(IV), a reaction which can be used for analytical determinations.[19]

d. Sulfuric acid solutions

The behaviour of plutonium in sulfuric acid solutions is similar to its behaviour in hydrochloric acid solutions. Plutonium(III) is converted photochemically into Pu(IV) but not into Pu(VI). Even daylight is sufficient for this purpose. Plutonium(VI) is inert in sulfuric acid solution, but in the presence of ethanol it is converted into Pu(IV).[5]

On the whole, UV irradiation intensifies the reduction of Pu(VI) to Pu(IV) in acid media by reagents such as ethanol, hydrogen peroxide, oxalic acid, ethylenediaminetetraacetic acid (EDTA), and probably others.[5] The possibility of using the above reactions, occurring on UV irradiation, for the monitoring of oxidation–reduction reactions in the processing of irradiated nuclear fuel has been briefly discussed in a review.[20]

Neptunium(IV) in H_2SO_4 solutions at concentrations from 1 to 2 M is oxidised photochemically to Np(V) and further to Np(VI), the oxidation being quantitative after prolonged irradiation. At $[H_2SO_4] > 2$ M, Np(IV) is also detected in the reaction mixture after prolonged irradiation and its amount is greater the higher the acid concentration.[21]

Neptunium(V) is oxidised photochemically to Np(VI); the rate of oxidation increased with increase in the H_2SO_4 concentration. At $[H_2SO_4] = 1-3$ M, the oxidation is quantitative. Nemodruk et al.,[21] who used at PRK-7 lamp, required 20 min to complete the reaction.

The introduction of ethanol, suppresses the oxidation of Np(IV) and Np(V) and at ethanol concentrations of several per cent Np(V) is reduced quantitatively to Np(IV).[21]

Novikov[22] considered the photochemical reactions of neptunium in acid solutions from the standpoint of its isolation and determination.

e. The mechanisms of the photochemical reactions in acid solutions

The mechanisms of the photochemical reactions of plutonium and neptunium in acid solutions were not investigated in the studies examined above. Only certain hypotheses were put forward. For example, perchloric acid does not absorb light from the mercury lamp, so that in this medium the reaction should begin with the excitation of plutonium or neptunium ions. It has been suggested[17] that, after the excitation of the Np(III), Np(IV), or Np(V) ions, they are oxidised by the perchlorate ions. It has also been suggested that plutonium ions are also excited in sulfuric acid, since the oxidation of Pu(III) takes place even under the influence of the usual room illumination, where the photolysis of sulfate ions is impossible. On the other hand, in nitric acid, UV light leads to the photolysis of the NO_3^- ion.[7]

$$NO_3^- \xrightarrow{h\nu} NO_2^- + O^\cdot. \quad (7)$$

This accounts for the accumulation of the Np(V) ions: oxygen oxidises the lower valence forms of neptunium, while the permanent presence of nitrite in solution leads to the reduction of Np(VI).[7]

According to Nemodruk et al.,[19] the oxidation of Np(IV) and Np(V) in hydrochloric acid is associated with the reactions

$$Cl^- \xrightarrow{h\nu} Cl^\cdot + e_{aq}^-, \quad (8)$$

$$Np^{4+} + Cl^\cdot + 2H_2O \longrightarrow NpO_2^+ + 4H^+ + Cl^-, \quad (9)$$

$$NpO_2^+ + Cl^\cdot \xrightarrow{h\nu} NpO_2^{2+} + Cl^-. \quad (10)$$

These reactions result in the formation of hydrated electrons e_{aq}^-, which react with H^+, affording hydrogen atoms, while the latter recombines at a sufficiently high HCl concentration to form H_2. However, one cannot agree with these hypotheses. According to literature data,[23] the rate constant for the interaction of the H atom with Np(VI) is $(4.0 \pm 0.5) \times 10^8$ litre mol^{-1} s^{-1}, which is ~ 500 times smaller than the rate constant for the recombination of H atoms. However, the stationary concentration of H atoms during the irradiation process is lower by many orders of magnitude than the Np(VI) concentration (especially at the end of the reaction), so that Np(VI) is reduced before the recombination of H atoms. Thus the oxidation state of neptunium does not change. A similar situation is characteristic also of other acids.

An alternative explanation of the photochemical reactions of transuranic elements (TUE) may be, in our view, the formation of excimers (dimers) from the excited and unexcited ions. Two TUE ions then participate simultaneously in the reaction, so that the less reactive molecular products are formed instead of radicals. From this standpoint, the oxidation of Pu(III), for example, in perchloric acid solutions can be represented by the reactions

$$Pu(III) \xrightarrow{h\nu} Pu(III)^*, \quad (11)$$

$$Pu(III)^* + Pu(III) \longrightarrow [Pu(III)^*...Pu(III)], \quad (12)$$

$$[Pu(III)^*...Pu(III)] \longrightarrow 2(Pu^{3+}_{aq} \cdot OH) + H_2, \quad (13)$$

$$Pu^{3+}_{aq} \cdot OH + H^+ \longrightarrow Pu^{4+}_{aq}. \quad (14)$$

A similar mechanism is possible also for the oxidation of Pu(III) and Np(III) in hydrochloric and sulfuric acid solutions and also for the reactions of other oxidation states of plutonium or neptunium in these acids, for example, the reduction of Pu(VI) in dilute perchloric acid:

$$Pu(VI) \xrightarrow{h\nu} Pu(VI)^*, \quad (15)$$

$$Pu(VI)^* + Pu(VI) \longrightarrow [Pu(VI)^*...Pu(VI)], \quad (16)$$

$$[Pu(VI)^*...Pu(VI)] \longrightarrow 2Pu(V) + H_2O_2, \quad (17)$$

$$Pu(VI) + H_2O_2 \longrightarrow Pu(V) + HO_2 + H^+, \quad (18)$$

$$Pu(VI) + HO_2 \longrightarrow Pu(V) + O_2. \quad (19)$$

Bearing in mind that in most cases the preferential formation of higher oxidation states of neptunium is observed with increase in the acid concentration, one may postulate that, at low and high H^+ concentrations, the Np(VI) and Np(V) excimers respectively are formed more effectively, which leads to the respective reduction of Np(VI) or oxidation of Np(V).

In nitric acid, the photolysis of the NO_3^- ion with formation of HNO_2 makes an additional contribution. This is the only medium in which Pu(VI) accumulates photochemically, which is evidently associated with the formation of nitrogen compounds capable of oxidising plutonium to the hexavalent state. In dilute HNO_3 solution, the Pu(VI) reduction reaction predominates, which agrees with the hypothesis of the formation of Pu(VI) [as well as Np(VI) excimers] in dilute solutions. The reaction

$$Pu(VI) + HNO_2 \longrightarrow Pu(V), \quad (20)$$

probably also makes its own contribution.

The acceleration of the disproportionation of Pu(IV) in $HClO_4$ solutions is also associated with the excitation of the plutonium ions themselves. In the presence of reductants, mixed mechanisms are possible where plutonium ions are excited and the additive is photolysed simultaneously.

Thus the studies on the photochemistry of plutonium and neptunium have shown that the reactions in acid media involve the excitation of plutonium and neptunium themselves (similarly to the photochemical reactions of uranyl). However, the mechanisms proposed in the literature do not withstand criticism in our view.

2. The photochemistry of alkaline carbonate solutions

a. The flash photolysis of Pu(VI)

There has been only one communication on the flash photolysis of the ions of transuranic elements.[24] This is the photolysis of the PuO_2^{2+} ions in sodium carbonate solution with $[Na_2CO_3] = (5-30) \times 10^{-3}$ M at pH 12.5. The authors[24] designed and constructed a special apparatus for the flash photolysis of the actinides, which included a glove box and a system for the evacuation of the specimens.[25] During flash photolysis,[24] the reaction is similar to the pulse radiolysis of actinide ions, including their radiolysis in carbonate media (see, for example, Gogolev et al.[26]). The authors were able to demonstrate the possibility of the oxidation of Pu(VI) to Pu(VII) by the CO_3^- radical-ion formed on photolysis of the carbonate ion. However, in the medium investigated, Pu(VII) is very unstable and disappears with a rate constant of $(7.61 \pm 0.09) \times 10^2$ s^{-1}. The constant is independent of the pH in the range from 10 to 12.6, of the initial Pu(VI) concentration, and also of the CO_3^{2-} concentration in the range 5–30 mM. In a CO_3^{2-} free medium Pu(VII) is not formed. These results appear somewhat surprising, since in the pulsed radiolysis of N_2O-saturated neptunium(VI) carbonate solutions Gogolev et al.[26] observed the formation of Np(VII) only in the presence of NaOH at a concentration of the latter not less than 0.01 M.

b. The photochemical oxidation of Np(VI)

In the only study on the photochemistry of neptunium in alkaline carbonate solutions,[27] it was reported that Np(VI) had been oxidised to Np(VII) on irradiation with the light from a mercury lamp in a nitrous oxide-saturated solution containing 0.09 M LiOH and 0.28 M K_2CO_3. It is known[28] that neptunium(VII) can be most readily obtained in an alkaline solution, but the photochemical oxidation of Np(VI) to Np(VII) does not occur in an alkaline solution without additives. Under the influence of UV light, the CO_3^{2-} ion is converted into the radical oxidant CO_3^-, while N_2O captures the hydrated electrons, whereupon yet another oxidant is obtained — the radical-ion O^-:

Thus the reaction does not proceed due to the excitation

$$CO_3^{2-} \xrightarrow{h\nu} CO_3^- + e^-_{aq}, \quad (21)$$

$$N_2O + e^-_{aq} \longrightarrow N_2 + O^-, \quad (22)$$

$$O^- + H_2O \rightleftharpoons OH^\cdot + OH^-, \quad (23)$$

$$OH + CO_3^{2-} \longrightarrow OH^- + CO_3^-. \quad (24)$$

of neptunium itself but is a result of the photochemical decomposition of CO_3^{2-}. The CO_3^- radical-ion or OH is apparently the direct oxidant of Np(VI).

3. The photochemistry of extraction systems containing plutonium and neptunium

In the extraction systems containing plutonium and neptunium organic substances are present, so that the reduction of higher oxidation states of plutonium and neptunium becomes probable and exposure to light can also lead to the photolysis of the organic compounds. As early as 1952, it was noted that, during the extraction of Pu(VI) in the water–hexane system, the partition coefficient decreases as a function of time. The authors[29] postulated that this is associated with the photochemical reduction of Pu(VI) to Pu(IV). The photochemical reduction of microconcentrations of Pu(VI) to Pu(IV) was achieved in nitrate–perchlorate–benzene–thenoyltrifluoroacetone (TTA) and chloride–perchlorate–benzene–TTA extraction systems,[14] Pu(VI) not being reduced in the dark. Somewhat different results were obtained for Pu(VI) in a TTA solution in toluene with [TTA] = 0.5 M:[30] it is reduced slowly over several days even in the dark; on illumination under room conditions or on irradiation with visible light, the rate of reduction increased sharply and became proportional to the light intensity. In benzene, Pu(VI) is reduced photochemically more slowly, while in heptane it is reduced faster than in toluene. The Pu(V) form is reduced further to Pu(IV). No relation was observed between the relative permittivity of the solvents and the rate of the photochemical reduction of plutonium. The influence of added tributyl phosphate on the rate of reduction of Pu(VI) in TTA-containing extraction systems was also investigated.[30] Tributyl phosphate intensifies the extraction and slows down the reduction of Pu(VI) and Pu(V). Choppin and Saito[30] showed that the products of the photochemical decomposition of TTA have a reducing capacity and that plutonium is reduced not only during irradiation but also in its absence — in TTA solutions subjected to preliminary irradiation. The authors were unable to isolate the reductant itself. There have been reports also about the photochemical reduction of Pu(IV) to Pu(III).[31,32] The reduction of Pu(IV) takes place in the aqueous phase and its rate increases with increase in the concentration of H^+ ions. The reduction mechanism is apparently similar to the mechanism of the reduction of Pu(VI) and Pu(V).[31]

Methods for the photochemical reduction of Pu(IV) have been patented in the USA for use in industry.[33,34] The photochemically active substance is in both cases not plutonium itself but uranyl. According to a patent,[33] the organic phase obtained in the extraction purification of irradiated nuclear fuel and containing tributyl phosphate, U(VI), and Pu(IV) is treated with tributyl phosphite and H_3PO_4 and is irradiated with UV light. Uranyl is then reduced by tributyl phosphite to U(IV), which reduces Pu(IV) to Pu(III). Tributyl phosphite is oxidised in this process by uranium(VI) to tributyl phosphate, as a result of which the re-extraction of plutonium is achieved without introducing additional substances. Another patent[34] describes the use of hydrazine for the photochemical reduction of uranyl to U(IV), the latter reducing in its turn Pu(IV) to Pu(III). These reactions are also employed to separate plutonium from uranium with the aid of the tributyl phosphate extraction system.

Thus, in the extraction systems considered, the photochemical reactions involve the photolysis of the additive — TTA or uranyl, and not the excitation of the plutonium ion itself.

Like plutonium(VI), neptunium(VI) can also be reduced by the TTA photolysis product in extraction systems.[30] Thus in the dark Np(VI) is stable in 0.5 M TTA solution in toluene, but on illumination under room conditions it is reduced in several hours.

4. The use of photochemistry for the extraction of neptunium from irradiated nuclear fuel

The photochemical formation of neptunium(V) in nitric acid solutions, including those having a composition similar to those employed in the purex process, may serve as the basis for the extraction of neptunium from irradiated nuclear fuel.[35-37] (This process has been patented in the USA.[38]) Thus it becomes possible to separate Np(V) from plutonium(IV) and uranium(VI). The krypton-fluoride excimer laser may be used to increase the irradiation intensity. The authors[35-37] prepared the neptunium solutions for irradiation in nitric acid with $[HNO_3] = 0.75-3$ M in the following way: Np(IV) was obtained by reducing Np(V) with iron sulfamate, whilst Np(VI) was prepared by oxidising Np(V) with potassium permanganate. On irradiating these solutions with light from a krypton-fluoride laser, neptunium(V) is formed even in the presence of an excess of oxidant or reductant.[35,37] This makes it possible to introduce the photochemical method into the usual extraction process, for example into the purex process, without its significant modification. Fukasawa et al.[39] investigated the stability and extraction of the Np(VI) obtained photochemically in nitric acid solution with $[HNO_3] = 3$ M in the presence of urea. They showed that a 30% solution of tributyl phosphate in dodecane may be used to extract the Np(VI) obtained photochemically and that irradiation in the course of prolonged extraction improves the results, compensating for the partial reduction of Np(VI) in the organic phase.

The possibility of separating neptunium and plutonium in nitric acid solutions with the aid of photochemical methods has also been considered by Wada et al.[40] When a hydrazine-containing nitric acid solution with $[HNO_3] = 3$ M is irradiated with the light from a 150 W mercury lamp, Pu(III) is oxidised to Pu(IV) to an extent greater than 95%, while neptunium remains as Np(V). This combination is optimal for the separation of neptunium and plutonium by extraction with tributyl phosphate in dodecane.

5. The photochemical dissolution of plutonium dioxide

A familiar radiochemical problem, the difficulty of dissolving plutonium dioxide, led Panigrahi et al.[41] to try to use UV light for this purpose. The dissolution was carried out in hydrochloric acid in the presence of uranyl and hydrazine with exposure to the light from a mercury lamp. The authors were able to achieve the dissolution of PuO_2 even at room temperature. For example, at $[HCl] = 5$ M, $[UO_2^{2+}] = 0.015$ M, and $[N_2H_4] = 0.2$ M, 95.6% of PuO_2 dissolved in 5 h. At a higher hydrochloric acid concentration, the dissolution is impaired. This effect is attributed to the excitation of the PuO_2 surface and also to the photochemical generation of U(IV). The following reactions were postulated:

$$PuO_2^*(\text{solid}) + U(IV) \longrightarrow Pu(III)_{aq} + U(VI), \quad (25)$$

$$PuO_2^*(\text{solid}) + N_2H_4 \longrightarrow Pu(III)_{aq} + N_2. \quad (26)$$

III. The photochemistry of americium

1. The photochemical reactions of americium in bicarbonate–carbonate solutions

The possibility of photochemical reactions with participation of americium was pointed out as early as 1981.[42] It was noted that americium is probably more difficult to photolyse than neptunium and plutonium. The first communication concerning the use of photochemistry for the changing of the oxidation states of americium appeared in 1992.[43] In this[43] and subsequent studies,[44-47] the photochemical behaviour of americium in bicarbonate–carbonate solutions was investigated. It was observed that, on irradiation with the UV light from a mercury lamp, Am(III) may be oxidised in such solutions to Am(IV). The most complete conversion of Am(III) into Am(IV) (up to ~60%) occurs at pH 9–10 and $[CO_3^{2-}] = 1-2$ M, the quantum yield of the reaction reaching 0.3 under these conditions. The further oxidation of Am(IV) to Am(V) and Am(VI) was not observed. At pH 11 and above, Am(III) is not oxidised at all.[45] The characteristic features of the photochemical oxidation of americium(III) in bicarbonate–carbonate solutions in the presence of specially introduced oxidants have been discussed in a number of studies.[44,46,47]

By employing XeO_3 and $S_2O_8^{2-}$, BrO^-, and BrO_3^- ions, it is possible to oxidise americium photochemically in bicarbonate–carbonate media to both the IV and the VI states. The quantum yields in the photochemical oxidation of Am(III) to Am(IV) in bicarbonate–carbonate solutions at pH ~ 9.9 are 1.07 for $S_2O_8^{2-}$, 0.56 for BrO^-, and 0.20 for BrO_3^-.[45] The possibility of the further oxidation of americium depends mainly on the pH of the solution and the carbonate concentration: at pH 9–10 and $[CO_3^{2-}] > 1$ M, Am(IV) is obtained quantitatively, while at pH 11 and above or at low concentrations of the bicarbonate–carbonate solution the product is Am(VI). The results for the sodium and potassium solutions are similar; the only difference is the possibility of obtaining Am(IV) in concentrated K_2CO_3 solutions (4 M and above), whereas only Am(VI) is formed in Na_2CO_3 soutions. Americium(III) is oxidised photochemically to Am(IV) also in bicarbonate–carbonate solutions saturated with N_2O.[47] Thus it is possible to obtain an Am(IV) solution without the addition of extraneous substances. It is noteworthy that, before the employment of photochemistry, the only method for the preparation of Am(IV) in bicarbonate–carbonate solutions remained the electrochemical procedure.[48]

Am(V) is also photochemically reactive in bicarbonate–carbonate solutions. On irradiation with UV light, it disproportionates partly to Am(IV) and Am(VI), traces of Am(III) appearing under these conditions.[49] Ultimately the solution contains a mixture of different oxidation states of americium, which enter into both photochemical and dark reactions with one another. The quantitative formation of any oxidation states is not therefore observed. The quantum yield of the photochemical disproportionation of Am(V) has been estimated as ~0.003.

2. The mechanisms of the photochemical reactions of americium

As mentioned above, the carbonate ion is a photochemically reactive species affording the CO_3^- radical oxidant and e_{aq}^- on photolysis [see Eqn (21)]. This feature has been used for the oxidation of plutonium(VI)[24] and neptunium(VI).[27] The oxidation potential of the CO_3^- radical-ion enables it to oxidise also americium (III) in bicarbonate–carbonate media:

$$Am(III) + CO_3^{\cdot-} \longrightarrow Am(IV) + CO_3^{2-}. \quad (27)$$

This reaction does indeed take place, but it is effective only in the presence of N_2O, which reacts with e_{aq}^- [see Eqn (22)]. On the other hand, in solutions without N_2O or oxidant ions, the same difficulties arise as in acid solutions of neptunium and plutonium, namely e_{aq}^- should ultimately reduce the Am(IV) formed. For this reason, according to Shilov and Yusov,[50] Am(III) is oxidised in this case too via the formation of excimers. Within the excimer, Am(III) is oxidised by water, from which a H_2 molecule, which is a relatively weakly reactive reductant, is split off and the dimer decomposes into two Am(IV) complex species.

$$Am(III)^* + Am(III) \longrightarrow [Am(III)^*...Am(III)], \quad (28)$$

$$[Am(III)^*...Am(III)] \longrightarrow 2\,Am(IV) + H_2. \quad (29)$$

The incomplete oxidation of Am(III) to Am(IV) indicates the occurrence also of the reverse photochemical reaction — the reduction of Am(IV) to Am(III).[50] One cannot rule out the possibility that it too proceeds via a stage involving the formation of excimers.

If the photochemical oxidation of americium takes place in a solution containing XeO_3 or the oxidant ions $S_2O_8^{2-}$, BrO^-, or BrO_3^-, the reaction proceeds as a result of the photolysis of the latter, for example:

$$S_2O_8^{2-} \xrightarrow{h\nu} 2\,SO_4^{\cdot-}, \quad (30)$$

$$BrO^- \xrightarrow{h\nu} Br^{\cdot} + O^-, \quad (31)$$

$$Br^{\cdot} + Br^- \longrightarrow Br_2^{\cdot-}, \quad (32)$$

$$Br_2^{\cdot-} + CO_3^{2-} \longrightarrow Br_2 + CO_3^{\cdot-}, \quad (33)$$

$$SO_4^{\cdot-} + CO_3^{2-} \longrightarrow SO_4^{2-} + CO_3^{\cdot-}. \quad (34)$$

This is followed by reaction (27).

3. The photocatalytic properties of Am(III) in bicarbonate–carbonate solutions

Our latest data indicate that Am(III) can serve as a photocatalyst of the oxidation of Np(IV) and Pu(IV) in bicarbonate–carbonate solutions free from other additives. Americium(III) is not itself oxidised quantitatively to Am(IV) under these conditions, but it does catalyse the oxidation of Np(IV) to Np(VI) and of Pu(IV) to Pu(VI).[51,52] The oxidation of neptunium and plutonium is quantitative. The reaction mechanism involves the intermediate formation of Am(IV) (see above) and the subsequent oxidation of Np(IV) and Np(V) or Pu(IV) and Pu(V). Without americium, the photochemical oxidation of Np(IV) or Pu(IV) is not observed.

IV. Reversible charge transfer in americium(III) and curium(III) luminescence quenching processes

It is known that the luminescence of many variable-valence ions may be quenched by an electron transfer mechanism. For example, the luminescence of uranyl is effectvely quenched by many reductants precisely by such a mechanism. This initiates the actual photochemical reduction of uranyl. Reversible electron transfer leading to quenching of the excited states of the Am(III) and Cm(III) ions is a similar reaction. Among the first four transuranic elements, only the ions of these two elements, especially Cm(III), exhibit luminescence in solutions. As a result of the ability of curium and americium to pass to the +4 oxidation state, the luminescence of Cm(III) and Am(III) may be quenched via charge transfer in those cases where the atom of an element capable of being reduced is present in the vicinity of the excited TUE ion. The Am(III) and Cm(III) complexes of unsaturated polytungstate anions of the type $PW_{11}O_{39}^{7-}$ and $SiW_{11}O_{39}^{8-}$, in which the luminescence of curium is significantly weakened while that of americium is altogether absent, may serve as examples. This is associated with the quenching of the luminescence with formation of the Cm(IV)–W(V) or Am(IV)–W(V) charge-transfer state.

An even more pronounced quenching effect with charge transfer is observed in the complexes of the same elements with polymolybdate anions: here there is no luminescence even in the case of curium. As a consequence of the constant close proximity of the TUE and W or Mo ions, the reverse charge transfer takes place after the removal of excitation and ultimately there is no photochemical oxidation of americium or curium. Nevertheless, one cannot rule out the possibility that it may be possible to select conditions under which such a photochemical reaction could be achieved. We emphasise that a reaction of this kind should in fact follow the excitation of the TUE ion and should not be a result of the oxidation of TUE by the products of the photochemical decomposition of the added oxidant. We shall not consider reversible charge transfer here in detail. The reader is referred to a review[53] on the luminescence of TUE, in which there are a series of references to the original studies where the quenching of the luminescence of Am(III) and Cm(III) as a result of charge transfer was investigated.

V. Conclusion

The above survey of the literature permits a series of conclusions.

Firstly, the photochemical method is fairly promising from the standpoint of its application in radiochemical industries. For this reason, its improvement is being continued, including the application of lasers.

Secondly, despite the outward similarity, a significant difference between photochemistry and radiation chemistry should be noted. Oxidation–reduction processes take place in both cases but in radiolysis (be it by γ-quanta, fast electrons, or heavy particles) energy is adsorbed by the medium and the molecules and ions of the latter are excited. On the other hand, in photolysis, the energy entering the system is absorbed preferentially by the solute. The final molecular products in the radiolysis and photolysis of aqueous solutions may be the same: H_2O, H_2O_2, and H_2. However, in radiolysis they are formed as a result of the processes involving the recombination of e_{aq}^-, H, OH, H^+, and OH^- in tracks, whilst in photolysis they are produced by the interaction of the excited molecules with the medium. Certain excited substances decompose, affording radicals. This resembles the situation which obtains on thermal excitation (for example, the decomposition of the $S^2O_8^{2-}$ ions, H_2O_2 molecules, etc.)

Thirdly, the question of the mechanisms of the photochemical reactions in solutions without added oxidants or reductants remains open. We tend to the view that the mechanisms put forward in the literature cannot lead to the occurrence of the observed reactions and believe that the results can be explained by the formation of excimers. However, this hypothesis requires an experimental test.

Fourthly and finally, the photochemistry of transuranic elements has so far been investigated only in acid and carbonate solutions of neptunium and plutonium, in carbonate solutions of americium, and a little in plutonium-containing extraction systems. Thus the possibilities of the photochemistry of TUE have still not been fully discovered and studies involving other media, including neutral, alkaline, complex-forming, etc., may yield very interesting results.

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Macromolecular and macrocyclic polyunsaturated silicohydrocarbons

O G Yarosh, M G Voronkov, E I Brodskaya

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Abstract. The results of studies on polyunsaturated macromolecular and macrocyclic silicohydrocarbons, the skeleton of which is made up of silicon atoms and the $-C\equiv C-$ or $-CH=CH-$ groups or of a combination of these and certain other fragments, are surveyed and treated systematically for the first time. Attention is concentrated on studies in the field of polyunsaturated macrocyclic silicohydrocarbons. The methods of synthesis of macromolecular and macrocyclic silicohydrocarbons, their structures, and physical and chemical properties, are examined. The bibliography includes 110 references.

I. Introduction

Macromolecular polyunsaturated hydrocarbons containing isolated or conjugated multiple bonds have been very widely investigated. They include, in particular, synthetic or natural rubbers, polyethynes, etc.[1] On the other hand, the polymers made up of the $-CR_2CH=CH-$ and $-CMe_2C\equiv C-$ units are little known and difficult to obtain. The question of the existence of organic macrocycles of similar structure was not even formulated for many years and the possibility of the incorporation of $C\equiv C$ bonds in a hydrocarbon ring was regarded at one time as extemely problematical.[2] Macrocycles synthesised by a multistage procedure and having the general formulae $(Me_2CC\equiv C)_n$, where $n = 5-8$, and $(Me_2CC\equiv CC\equiv C)_n$, where $n = 5$ or 6, have been only recently described in a series of publications by Scott and coworkers.[3–10]

The possibility of the existence of macromolecular polyunsaturated silicohydrocarbons, made up of the $-SiR_2CH=CH-$ and $-SiR_2C\equiv C-$ units, was predicted in 1952.[11] It was proposed that they be called polydialkylsilethenes and polydialkylsilethynes respectively. Polymers of this type were obtained in 1960.[12] At the present time, a large number of such polymers with a wide variety of structures have been synthesised and, apart from their theoretical importance, they have acquired a practical importance for the preparation of ceramic materials and fibres and photo- and radiation-sensitive materials. The first macrocyclic silicohydrocarbon — octamethylcyclotetrasilethyne $(Me_2SiC\equiv C)_4$ — was synthesised in 1973. Its preparation initiated fundamental studies on these lines by the authors of the present review and their foreign colleagues. The present review is in fact devoted to the synthesis and study of the macromolecular and macrocyclic silicohydrocarbons and covers the publications in the periodical and patent literature from 1960 up to 1994.

The nomenclature of the compounds considered is fairly simple for polymers and macrocycles with a regular structure. The units from which they are made up are named in accordance with the corresponding hydrocarbon fragment with the prefix sil — for example, polysilbuta-1,3-diene $H(H_2SiCH=CHCH=CH)_nSiH_3$ or permethylcyclooctasil-1,4-but-2-yne $(Me_2SiCH_2C\equiv CCH_2)_8$. The oxa-aza nomenclature is needed to name the polymers and macrocycles under consideration when these have an irregular structure.

II. Macromolecular polyunsaturated silicohydrocarbons

1. Polysilethynes

The first communication on the macromolecular polyunsaturated silicohydrocarbons of the ethyne series — perorganylpolysilethynes $(R_2SiC\equiv C)_n$ — appeared in 1960 when Jenker patented a polymer obtained by the reaction of disodioethyne with diethyldifluorosilane.[12]

Two years later, Korshak and Sladkov[13,14] synthesised analogous polymers from bis(bromomagnesio)ethyne (the lotsich reagent) and dichlorodiorganylsilanes or dichlorodiorganylgermanes.

$$BrMgC\equiv CMgBr + R_2ECl_2 \longrightarrow [-R_2EC\equiv C-]_n$$

R = Me, Ph; E = Si, Ge.

The interaction of disodioethyne with dichlorodimethylsilane in hexadecane at 250 °C led to the same polymer $[(Me_2SiC\equiv C)_n]$ in 52% yield.[15,16]

The reaction of dialkylbis(lithioethynyl)silanes with dialkyldichlorosilanes was used for the same purpose.[17,18]

$$R_2Si(C\equiv CLi)_2 + R'_2SiCl_2 \longrightarrow [-R_2SiC\equiv CSiR'_2C\equiv C-]_n$$

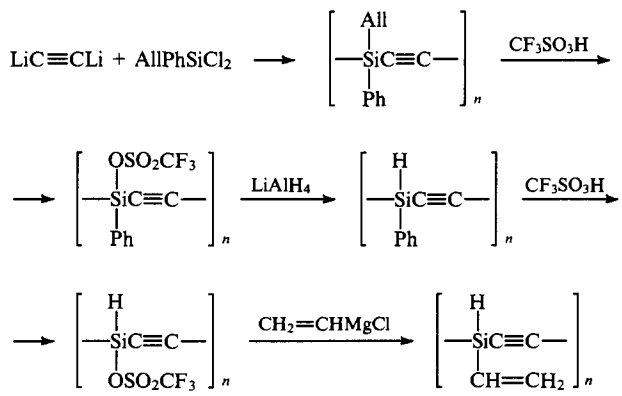
R = Me, Ph, $CH=CH_2$; R′ = H, Me, Ph.

The sequence of the monomer units in the copolymer obtained was established by ^{13}C and ^{29}Si NMR spectroscopy.[19]

O G Yarosh, M G Voronkov, E I Brodskaya Irkutsk Institute of Organic Chemistry, Siberian Division of the Russian Academy of Sciences, ul. Favorskogo 1, 664033 Irkutsk, Russian Federation. Tel. (7-395) 246 06 85 (O G Yarosh); (7-395) 246 24 00 (M G Voronkov); (7-395) 246 27 (E I Brodskaya). Fax (7-395) 246 03 31

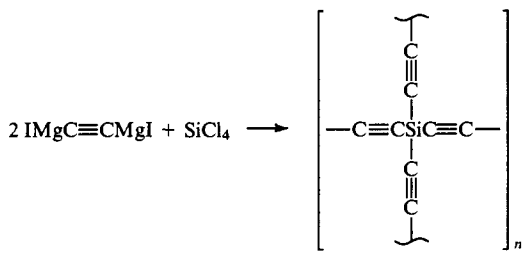
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Polyallylphenylsilethyne, synthesised by the reaction of dilithioethyne with allyldichlorophenylsilane, readily splits off the allyl group with formation of the corresponding triflate on reaction with trifluoromethanesulfonic acid. Its reduction with lithium tetrahydroaluminate leads to polyphenylhydrosilethyne. On treatment with trifluoromethanesulfonic acid, the latter splits off also the phenyl group. The resulting triflate reacts with vinylmagnesium chloride to form a polyvinylhydrosilethyne.[20]



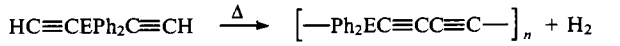
All = allyl

Bis(iodomagnesio)ethyne and tetrachlorosilane have been used to obtain materials with a ceramic coating.[21]



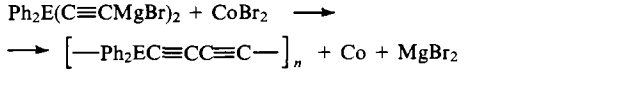
2. Polysilalkadiynes

Perorganylpolysilbutadiynes $[-R_2SiC{\equiv}CC{\equiv}C-]_n$ and their germa-analogues $[-R_2GeC{\equiv}CC{\equiv}C-]_n$ were first obtained in 1968 by the thermal polydehydrocondensation of the diethynyldiphenyl derivatives of silane or germane at 150–180 °C under a nitrogen atmosphere.[22]



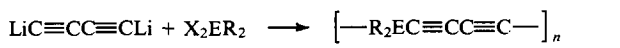
E = Si, Ge.

It proved possible to synthesise the same polymers by treating bis(bromomagnesioethynyl)dimethyl derivatives with $CoBr_2$.[22]



E = Si, Ge.

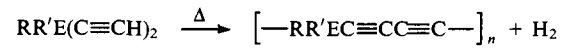
Almost a quarter of a century later, similar polymers were synthesised from dilithiodiethyne and dialkyldihalosilanes or dialkyldihalogermanes.[23–25]



E = Si, Ge; R = Me, Et, Ph, 4-MeC_6H_4; X = Cl, Br.

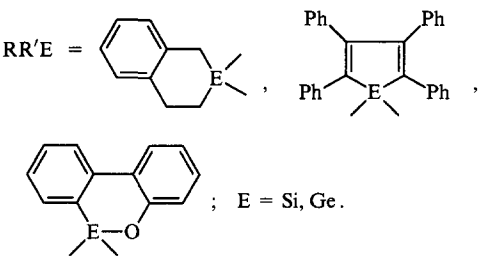
Their pyrolysis at 1400 °C leads to a mixture of silicon carbide and carbon with the ratio SiC : C = 1 : 4.[26,27]

A large series of new preorganylpolysilbutadiynes and their germanium analogues containing fairly complex substituents at the silicon or germanium atoms have been synthesised by thermal polydehydrocondensation of diethynyldiorganylsilanes and the corresponding germanes.[28,29]



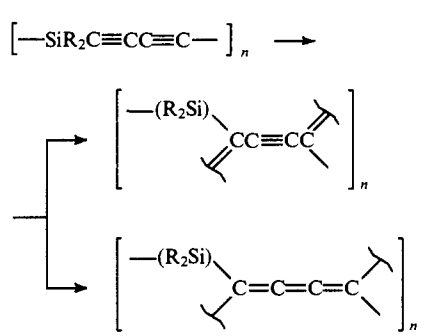
R = Ph, R′ = C_5H_5, $CH{=}CH_2$;

R = R′ = C_6H_5, 4-$MeOC_6H_4$, 4-$Me_2NC_6H_4$;

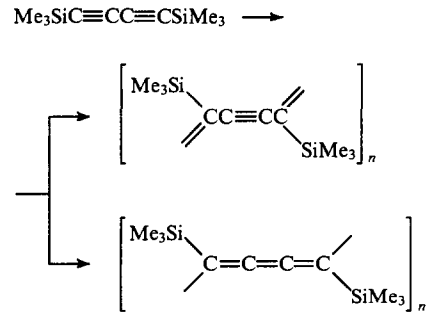


Polymers of the type $[-RR'SiC{\equiv}CC{\equiv}C-]_n$ proved to be high-resistance semiconductors at room temperature.[30]

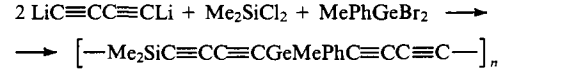
The pyrolysis of organosilicon diethyne polymers in a stream of argon at 1400 °C leads to the formation of a ceramic material containing the SiC group in a yield up to 85%. Before the mineralisation stage (~300 °C), the macrochains are cross-linked with participation of the diethyne fragments.[31]



On heating to 200 °C (for 30 days), bis(trimethylsilyl)-butadiyne gives rise to a polymer with butadienyne and butatriene fragments.[27]

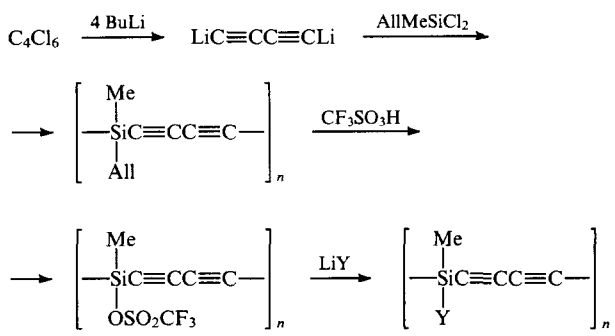


Polymers of the butadiyne series, containing simultaneously silicon and germanium atoms in the main chain, have also been synthesised.[25]



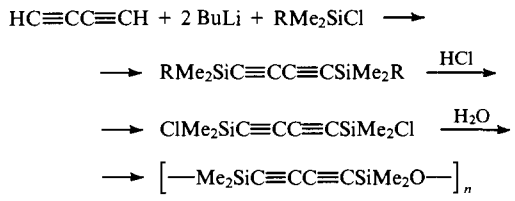
Polyallylmethylsilbutadiyne has been obtained by the reaction of dilithiodiethyne with allyldichloromethylsilane.[20]

Its interaction with trifluoromethanesulfonic acid proceeds with the elimination of the allyl group and the formation of the corresponding triflate. The latter reacts with lithioethynyltrimethylsilane to form polymethyl(trimethylsilylethynyl)silbutadiyne. The reactions with vinyllithium and triphenylsilyllithium proceed similarly.



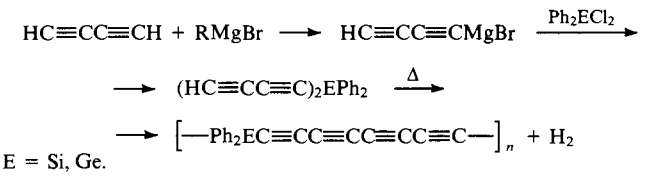
Y = CH_2=CH, $Me_3SiC{\equiv}C$, Ph_3Si.

Polymers with alternating SiC≡CC≡C and SiOSi fragments, which are stable up to 700 °C, have been synthesised by the reaction of dilithiodiethyne with chloromethoxydimethylchloro(dimethylamino)dimethyl-, and chlorohydrodimethylsilanes, the monomers obtained being subsequently treated with hydrogen chloride and water.[32]



R = H, MeO, Me_2N.

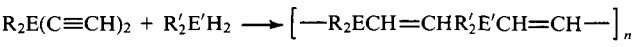
Polymers containing octatetraynyl fragments — perphenylpolysiloctatetraynes [and the corresponding germanium-containing polymers (Ed. of Translation)] — have been synthesised by the thermal polydehydrocondensation of dibutadiynyldiphenylsilane or the corresponding germane.[33]



E = Si, Ge.

3. Polysilethenes

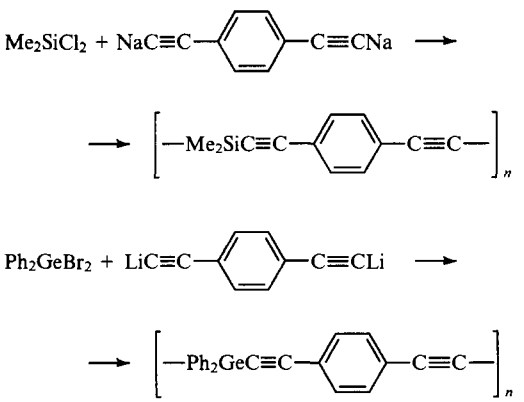
Polydiorganylsilethenes have been obtained by the hydrosilylation of diethynyldiorganylsilanes with the corresponding diorganylsilanes.[34] Their germanium and tin analogues were synthesised by a similar procedure.



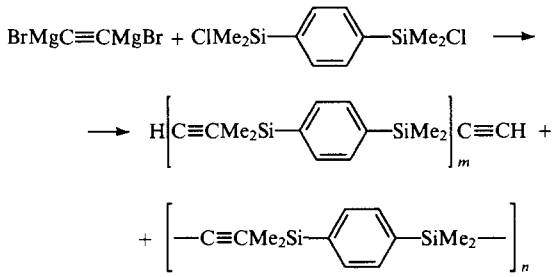
R, R′ = Me, Et, Ph; E, E′ = Si, Ge, Sn.

4. Polymers containing the C≡C and C=C multiple bonds and arylene or heteroarylene fragments

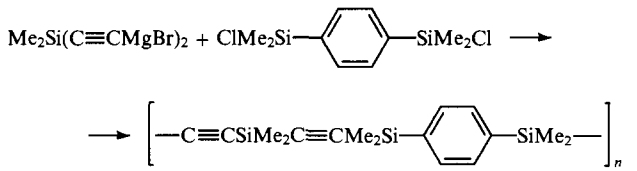
High-molecular-mass polyunsaturated silicohydrocarbons, containing simultaneously triple bonds and phenylene fragments in the macrochain, have been synthesised by the reaction of the sodium or lithium derivatives of 1,4-diethynylbenzene with dichlorodimethylsilane [35,36] or dibromodiphenylgermane.[37]



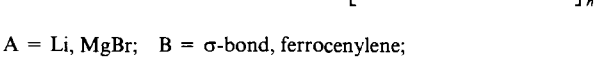
Analogous oligomers and polymers have been obtained from 1,4-bis(chlorodimethylsilyl)benzene and Iotsich reagent or bis(bromomagnesioethynyl)dimethylsilane.[38]



m = 2–6.



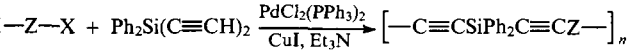
Silicoethyne polymers containing ferrocenylene nuclei in the macrochain have been synthesised from dilithio- or bis(bromomagnesioethynyl)ferrocene by reaction with dialkyldichlorosilanes.[39]



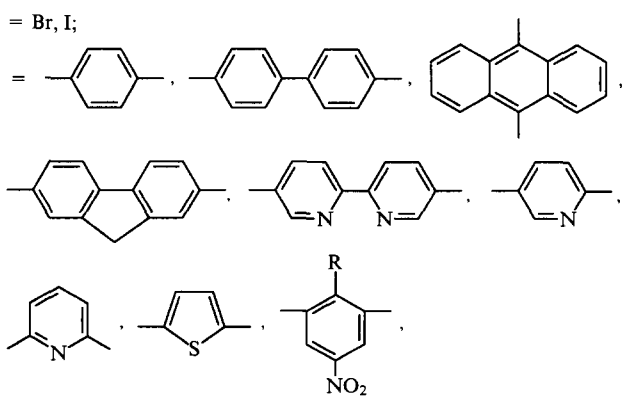
A = Li, MgBr; B = σ-bond, ferrocenylene;

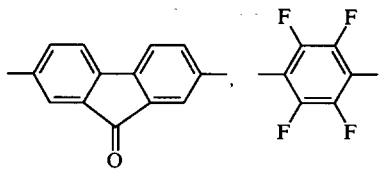
R = H, Me, CH_2=CH, Ph, ferrocenyl.

The palladium chloride-catalysed cross-polycondensation of dihaloarenes with diethynylsilanes affords a large series of silicoethyne polymers with arylene or heteroalylene fragments in the chain.[40]



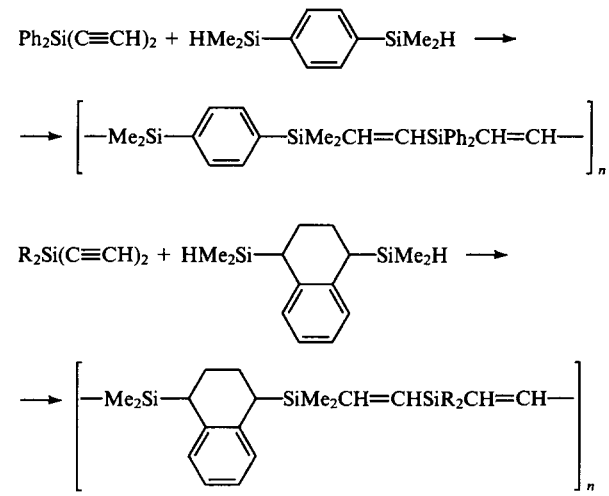
X = Br, I;

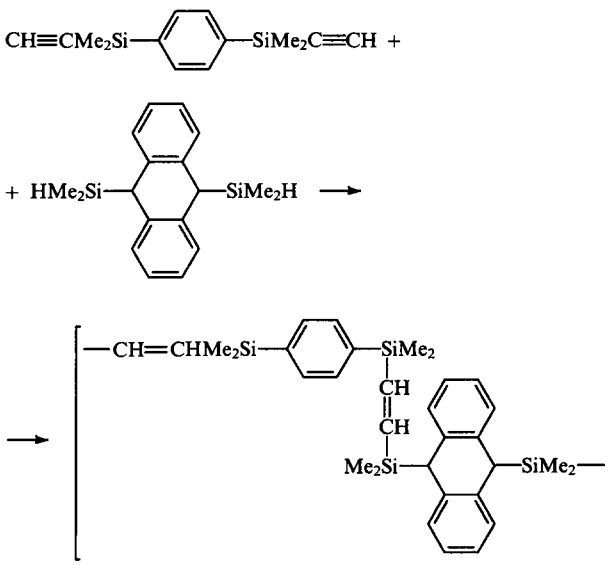
Z = 



R = NH_2, NMe_2, OH.

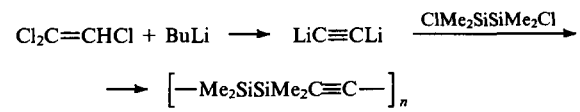
Polymers containing double bonds C=C and arylene fragments in the main chain have been obtained by hydrosilylating diethynyldiorganylsilanes with 1,4-bis-(dimethylsilyl)benzene [41] and 1,4-bis(dimethylsilyl)tetralin [42] and also by hydrosilylating 1,4-bis(ethynyldimethylsilyl)benzene with 9,10-bis(dimethylsilyl)dihydroanthracene.[43]



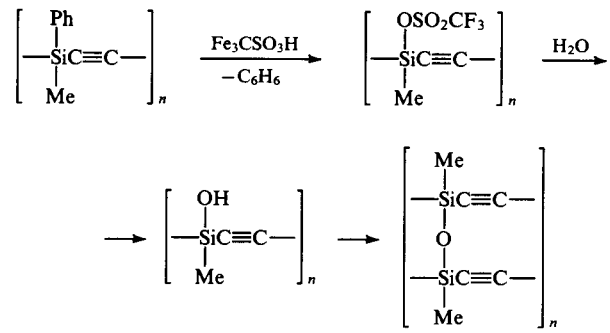


5. Polymers containing the C≡C and $(R_2Si)_n$ groups

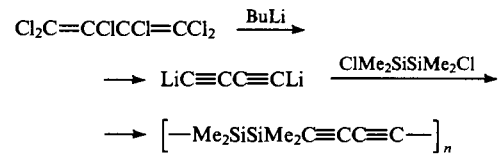
Polymers with triple bonds and disilanyl fragments in the main chain have been synthesised from dilithioethyne and 1,2-dichlorotetramethyldisilane.[44,45]



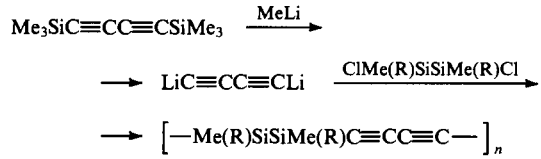
Polysilethynes have been obtained similarly.[44,45] These polymers were used to obtain fibres which were cross-linked without change in shape after treatment with F_3CSO_3H vapour and subsequent hydrolysis or UV irradiation. When they were subsequently heated to 1300 °C, silicon carbide fibres were obtained.[44,45]



Polymers of the butadiyne series have been synthesised by the same procedure from dilithiodiethyne and 1,2-dichlorotetramethyldisilane.[46,47]

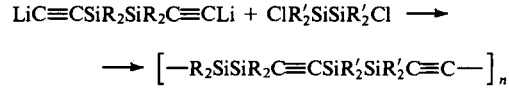


The same polymers have been obtained from bis(trimethylsilyl)butadiyne.[48]



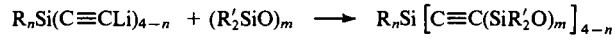
R = Et, Ph.

The reaction of tetraalkyl-1,2-bis(lithioethynyl)disilanes with tetraalkyl-1,2-dichlorodisilanes leads to polymers containing methyl and butyl groups at the silicon atom.[49]

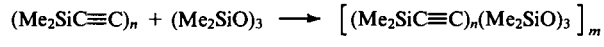


R, R′ = Me, Bu.

Finally, polymers containing the R_2SiO groups in addition to the triple bonds C≡C have been synthesised from dialkylbis(lithioethynyl)silanes and cyclodialkylsiloxanes.[50]



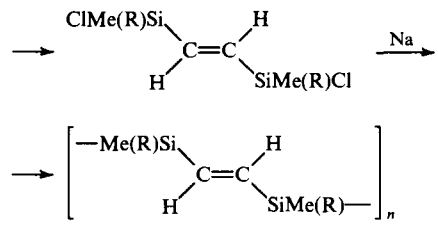
Polymers of this type are also formed from permethylcyclosilethynes $(Me_2SiC{\equiv}C)_n$, where n = 5 or 6 (see Section III), and hexamethylcyclotrisiloxane in the presence of BuLi, MeLi, $Ph_2Si(OLi)_2$, $Me_2Si(C{\equiv}CLi)_2$, and $Ph_2Si(C{\equiv}CLi)_2$ as the catalysts.[51]



The polymers obtained from 1,4-diethynylbenzene and dichloro-1,2-dimethyl-1,2-diphenyldisilane have been recommended as photo- and radiation-sensitive materials.[52]

The reaction of (*E*)-1,2-bis(chlorodiorganylsilyl)ethenes with metallic sodium in benzene leads to polymers which contain simultaneously the CH=CH and R_2SiSiR_2 fragments.[53]

$$ClMe(R)SiC{\equiv}CH + HMe(R)SiCl \longrightarrow$$



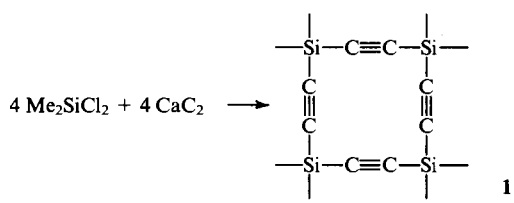
R = Me, Ph.

III. Macrocyclic polyunsaturated silicohydrocarbons

1. Cyclosilethynes

It has been suggested that the term cyclosilethynes be given to the cyclic polyethyne silicohydrocarbons made up of alternating $-R_2SiC{\equiv}C-$ groups and corresponding to the general formula $(R_2SiC{\equiv}C)_n$.[11] Compounds of this type, in which the $R_2SiC{\equiv}C$ fragments differ in the substitution at the silicon atom, have to be named in accordance with the extremely cumbersome oxa-aza nomenclature. For example, the macrocycle $(Me_2SiC{\equiv}C)_4$ is octamethylcyclotetrasilethyne, while $[Me_2SiC{\equiv}CSiMe(CH{=}CH_2)C{\equiv}C]_2$ is 1,4,4,7,7,10,10-hexamethyl-1,7-divinyl-1,4,7,10-tetrasilacyclododeca-2,5,8,11-tetrayne.

The first macrocyclic (12-membered) silicohydrocarbon made up of four alternating $Me_2SiC{\equiv}C$ fragments — 1,1,4,4,7,7,10,10-octamethyl-1,4,7,10-tetrasilacyclododeca-2,5,8,11-tetrayne or octamethylcyclotetrasilethyne **1** — was synthesised by Voronkov and Pavlov[54] in 1973 by the reaction of dichlorodimethylsilane with calcium carbide in a fused LiCl–KCl eutectic mixture at 400 °C.†



1

The great importance of this study has been noted in the literature.[55]

This silicohydrocarbon as well as decamethylcyclopentasilethyne **2** were later obtained by the reaction of the potassium–sodium alloy with ethyne and dichlorodimethylsilane in tetrahydrofuran (THF).[56,57]

$$Me_2SiCl_2 + Na/K + HC{\equiv}CH \longrightarrow (Me_2SiC{\equiv}C)_n$$

1, 2

n = 4 (**1**), 5 (**2**).

The reaction of bis(lithioethynyl)dimethylsilane with dichlorodimethylsilane affords dodecamethylcyclohexasilethyne **3**.[58]

$$Me_2Si(C{\equiv}CLi)_2 + Cl_2SiMe_2 \longrightarrow (Me_2SiC{\equiv}C)_6$$

3

Compounds belonging to the homologous series of permethylcyclosilethynes $(Me_2SiC{\equiv}C)_n$, n = 4–10, have been synthesised by Voronkov and Yarosh.[59,60] Thus octamethylcyclotetrasilethyne **1** and hexadecamethylcyclooctasilethyne **4** have been obtained by the reaction of bis(bromomagnesioethynyl)dimethylsilane (EDMS) with (chlorodimethylsilylethynyl)dimethylsilane (CDMS).[59,60]

† In this and a number of subsequent structural formulae, the methyl groups surrounding the macrocyclic silicon are not shown but are only indicated by valence bonds.

$$Me_2Si(C{\equiv}CMgBr)_2 + (ClMe_2SiC{\equiv}C)_2SiMe_2 \longrightarrow$$

$$\longrightarrow (Me_2SiC{\equiv}C)_n$$

1, 4

n = 4 (**1**), 8 (**4**).

Similarly the interaction of bis(bromomagnesioethynyldimethylsilyl)ethyne (BESA) with bis(chlorodimethylsilylethynyl)silane affords decamethylcyclopentasilethyne **2** and eicosamethylcyclodecasilethyne **5**.[59,60]

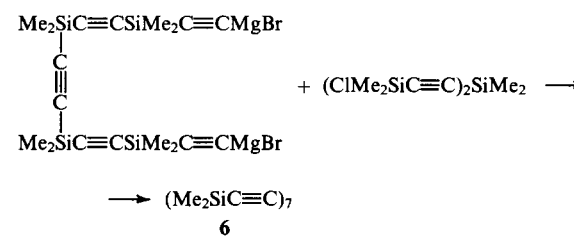
$$BrMgC{\equiv}CMe_2SiC{\equiv}CSiMe_2C{\equiv}CMgBr +$$

$$+ (ClMe_2SiC{\equiv}C)_2SiMe_2 \longrightarrow (Me_2SiC{\equiv}C)_n$$

2, 5

n = 5 (**2**), 10 (**5**).

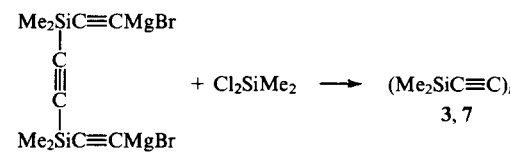
The reaction of bis(bromomagnesioethynyldimethylsilylethynyl)dimethylsilylethyne (DBES) with CDMS led to tetradecamethylcycloheptasilethyne **6**.[59,60]



$$\longrightarrow (Me_2SiC{\equiv}C)_7$$

6

Dodecamethylcyclohexasilethyne **3** and octadecamethylcyclononasilethyne **7** have been synthesised by the reaction of BESA with Me_2SiCl_2.[60]



3, 7

n = 6 (**3**), 9 (**7**).

Octamethylcyclotetrasilethyne **1**, dodecamethylcyclohexasilethyne **3**, and hexadecamethylcyclooctasilethyne **4** were isolated from the products of the reaction of EDMS with Me_2SiCl_2.[59,60]

$$Me_2Si(C{\equiv}CMgBr)_2 + Cl_2SiMe_2 \longrightarrow (Me_2SiC{\equiv}C)_n$$

1, 3, 4

n = 4 (**1**), 6 (**3**), 8 (**4**).

Voronkov and Yarosh[59,60] also synthesised cyclosilethynes containing the substituents H, $CH{=}CH_2$, (*E*)-$CH{=}CHSiMe_3$ and $C{\equiv}CSiMe_3$ at certain silicon atoms in addition to methyl groups. Thus the cyclosilethynes **8** and **9** were obtained by the reaction of EDMS with dichloromethyl(vinyl)silane.[59,60]

$$Me_2Si(C{\equiv}CMgBr)_2 + Cl_2Si(CH{=}CH_2)Me \longrightarrow$$

$$\longrightarrow [-Me_2SiC{\equiv}CSiMe(CH{=}CH_2)C{\equiv}C-]_n$$

8, 9

n = 2 (**8**), 3 (**9**).

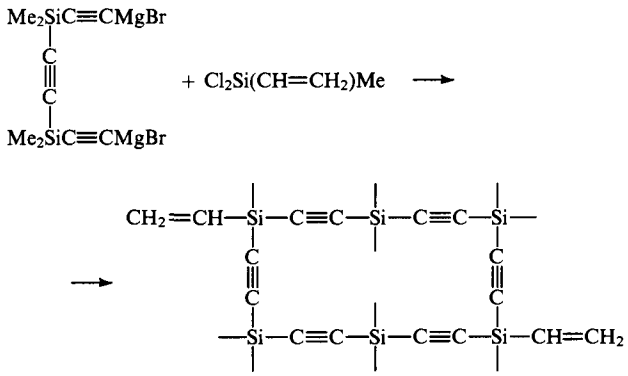
1,4,7,10-Tetramethyl-1,4,7,10-tetravinyl-1,4,7,10-tetrasilacyclododeca-2,5,8,11-tetrayne **10** has been synthesised by the reaction of bis(bromomagnesioethynyl)methyl(vinyl)silane with dichloromethyl(vinyl)silane.[59,60]

$$Me(CH_2{=}CH)Si(C{\equiv}CMgBr)_2 + Cl_2Si(CH{=}CH_2)Me \longrightarrow$$

$$\longrightarrow [Me(CH_2{=}CH)SiC{\equiv}C]_4$$

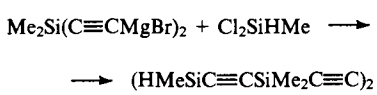
10

The interaction of BESA with dichloromethyl(vinyl)silane led to 1,4,4,7,7,10,13,13,16,16-decamethyl-1,10-divinyl-1,4,7,10,13,16-hexasilacyclooctadeca-2,5,8,11,14,17-hexayne **11**.[59,60]



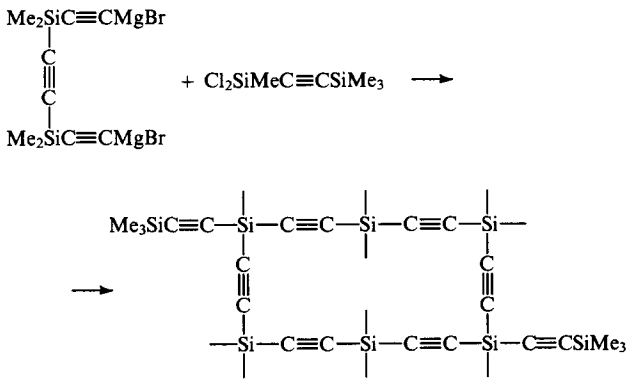
11

The reaction of EDMS with $MeHSiCl_2$ led to the isolation of 1,4,4,7,10,10-hexamethyl-1,7-dihydro-1,4,7,10-tetrasilacyclododeca-2,5,8,11-tetrayne **12**.[59,60]



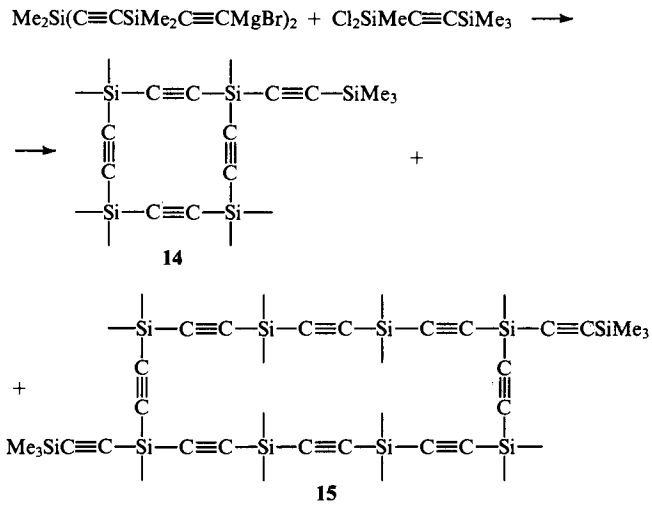
12

The interaction of BESA with dichloromethyl(trimethylsilylethynyl)silane (TMSA) affords under the same conditions with disubstituted 18-membered macrocycle **13**.[61]



13

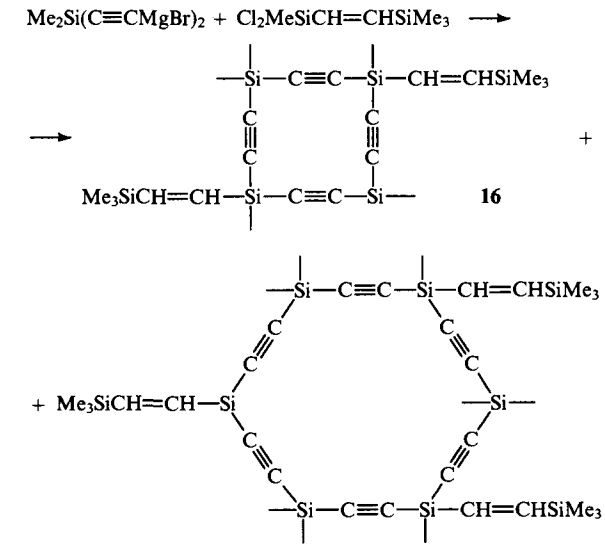
Bis[(bromomagnesioethynyldimethylsilyl)ethynyl]dimethylsilane (DMDS) reacts similarly with $Cl_2SiMe(C{\equiv}CSiMe_3)$ to form substituted macrocyclic ethyne silicohydrocarbons — the heptamethyl derivative **14** of 1-(trimethylsilylethynyl)-1,4,7,10-tetrasilacyclododeca-2,5,8,11-tetrayne and the tetradecamethyl derivative **15** of 1,13-bis(trimethylsilylethynyl)-1,4,7,10,13,16,19,22-octasilacyclotetracosa-2,5,8,11,14,17,20,23-octayne.[61]



14

15

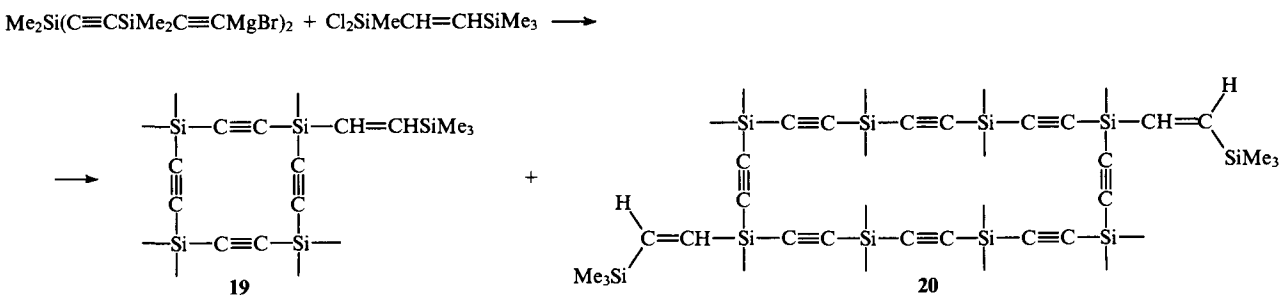
The interaction of EDMS with (*E*)-dichloro(methyl)-2-trimethylsilylvinylsilane (ETMS) afforded the cyclosilethynes **16** and **17**.[62]



16

17

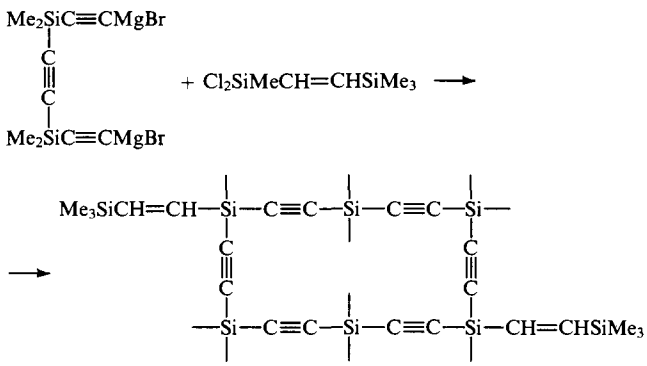
Scheme 1



19

20

Compound **18**, the product of the reaction of BESA with ETMS, is an analogue of compound **13**.[62]



18

The analogues of compounds **14** and **15** — the heptamethyl derivative **19** of 1-[(*E*)-2-trimethylsilylvinyl]-1,4,7,10-tetrasilacyclododeca-2,5,8,11-tetrayne and the tetradecamethyl derivative **20** of 1,13-bis[(*E*)-2-trimethylsilylvinyl]-1,4,7,10,13,16,19,22-octasilacyclotetracosa-2,5,8,11,14,17,20,23-octayne — were synthesised in their turn by the interaction of DMDS with ETMS (Scheme 1).[62]

Compounds **1**–**20** were obtained under the conditions of high dilution in THF and were isolated by fractional distillation or sublimation in a high vacuum (10^{-4}–10^{-5} Torr). Their yields were low and amounted to 4%–13%.

2. Macrocycles containing simultaneously triple and double bonds

Voronkov and Yarosh [63–69] synthesised by methods of fine organosilicon synthesis a series of polyunsaturated macrocyclic silicohydrocarbons containing simultaneously triple and double bonds with different numbers and orders of alternation of the latter (the silicohydrocarbons **21**–**42**). They also include compounds containing exocyclic unsaturated groups (compounds **37**–**42**).[67–69]

The reaction of the Iotsich reagent with (*E*)-1,2-bis(fluorordimethylsilyl)ethene [(*E*)-FSE] produced the 12-, 18-, and 24-membered macroheterocycles **21**–**23** with alternating double and triple bonds.[63,64]

$$BrMgC{\equiv}CMgBr + FMe_2SiCH{=}CHSiMe_2F \longrightarrow \longrightarrow [-Me_2SiCH{=}CHSiMe_2C{\equiv}C-]_n$$

21–**23**

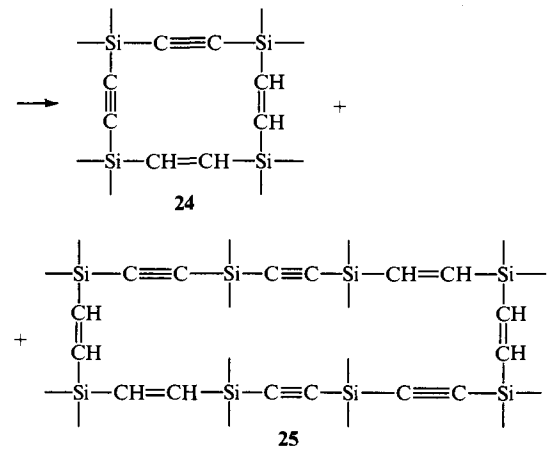
n = 2 (**21**), 3 (**22**), 4 (**23**).

The macrocyclic silicohydrocarbons **24** and **25** with alternating double and triple bonds have been synthesised by the reaction of EDMS with (*E,E*)-bis(2-chlorodimethylsilylvinyl)-dimethylsilane (BCVS).[63,64]

The interaction of EDMS with (*E*)-FSE led to the isolation of 1,1,4,4,7,7,10,10,13,13,16,16-dodecamethyl-1,4,7,10,13,16-hexasilacyclooctadeca-2,11-diene-5,8,14,17-tetrayne **26**.[64,65]

The polyunsaturated macrocycles **27** and **28** were synthesised similarly from bis(bromomagnesioethynyldimethylsilyl)ethyne and (*E*)-FSE.[64,65]

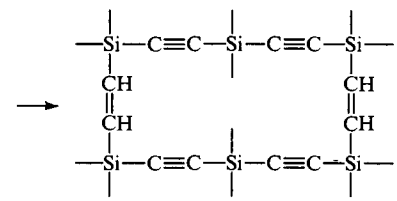
$Me_2Si(C{\equiv}CMgBr)_2$ + $(ClMe_2SiCH{=}CH)_2SiMe_2$ ⟶



24

25

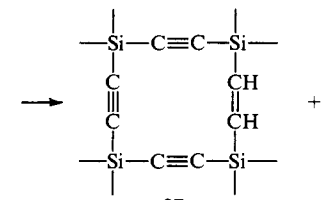
$Me_2Si(C{\equiv}CMgBr)_2$ + $FMe_2SiCH{=}CHSiMe_2F$ ⟶



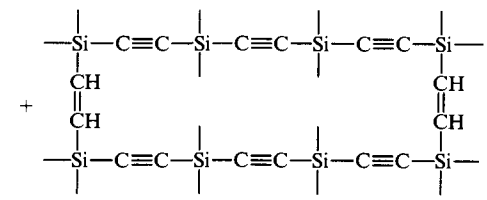
26

$BrMgC{\equiv}CSiMe_2C{\equiv}CSiMe_2C{\equiv}CMgBr$ +

+ $FMe_2SiCH{=}CHSiMe_2F$ ⟶



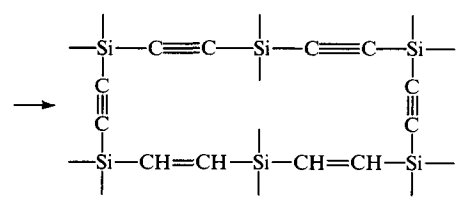
27



28

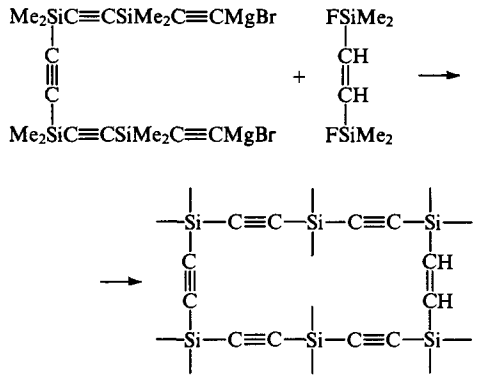
The reaction of DMDS with BCVS produced the dodecamethyl derivative **29** of 1,4,7,10,13,16-hexasilacyclooctadeca-2,5-diene-8,11,14,17-tetrayne.[64,65]

$Me_2Si(C{\equiv}CSiMe_2C{\equiv}CMgBr)_2$ + $(ClMe_2SiCH{=}CH)_2SiMe_2$ ⟶



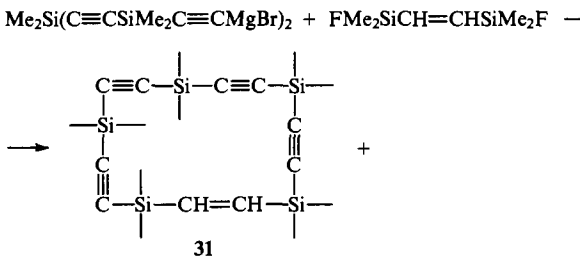
29

The product of the reaction of DBES with (*E*)-FSE is 1,1,4,4,7,7,10,10,13,13,16,16-dodecamethyl-1,4,7,10,13,16-hexasilacyclooctadeca-2-ene-5,8,11,14,17-pentayne **30**.[64,65]

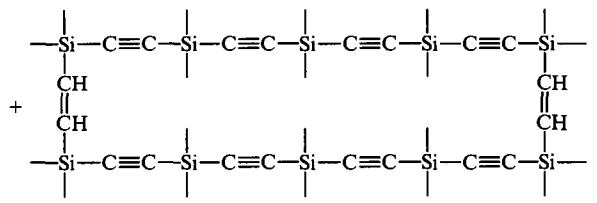


30

The interaction of DMDS with (*E*)-FSE affords the macrocycles **31** and **32**.[64,66]

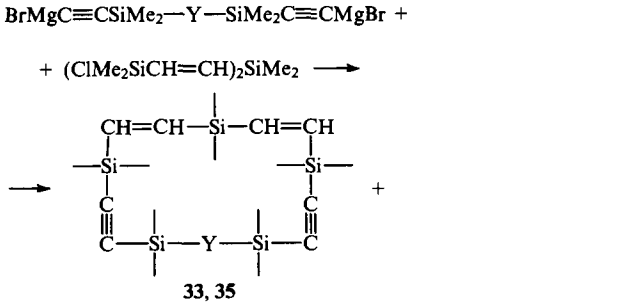


31

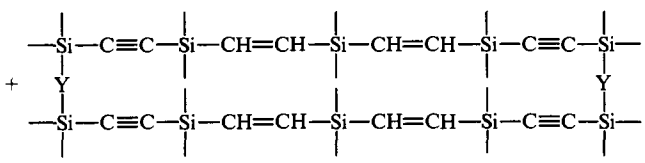


32

The highly unsaturated cyclic systems **33**–**36** were obtained similarly by the reaction of bis(bromomagnesioethynyldimethylsilyl)ethyne or (*E*)-1,2-bis(bromomagnesioethynyldimethylsilyl)ethene with BCVS.[64,66]



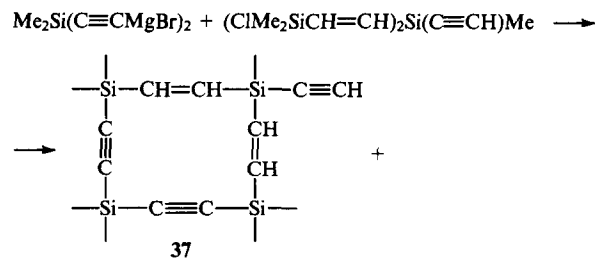
33, 35



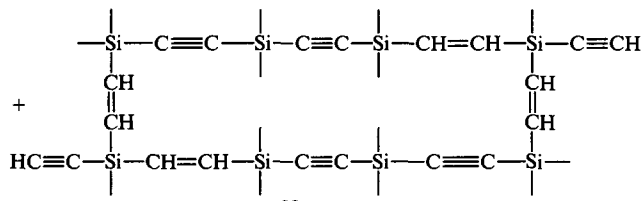
34, 36

Y = C≡C (**33**, **34**), CH=CH (**35**, **36**)

The condensation of EDMS with (*E,E*)-bis(2-chlorodimethylsilylvinyl)ethynylmethyl silane (BCVES) results in the formation of the heptamethyl derivative **37** of 1-ethynyl-1,4,7,10-tetrasilacyclododeca-2,11-diene-5,8-diyne and the tetradecamethyl derivative **38** of 1,13-diethynyl-1,4,7,10,13,16,19,22-octasilacyclotetracosa-2,11,14,23-tetraene-5,8,17,20-tetrayne containing exocyclic HC≡C groups.[67]

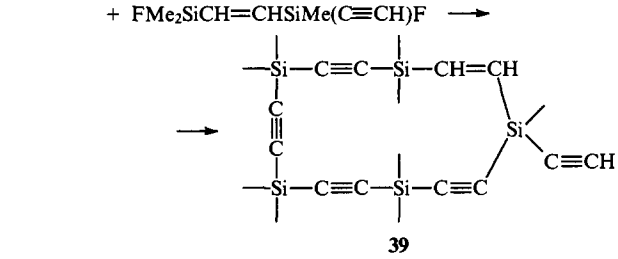


37



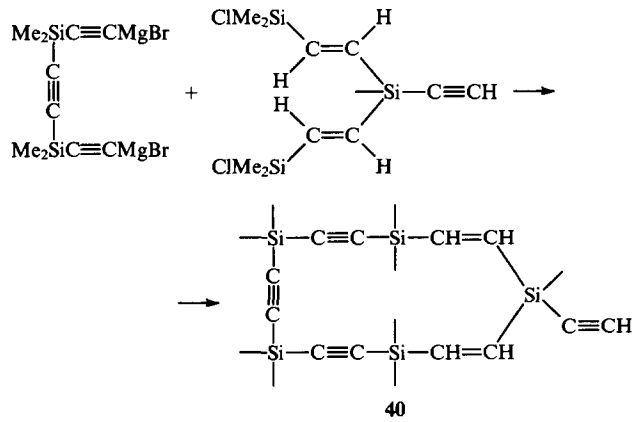
38

Similarly the reaction of DMDS with (*E*)-1-fluorodimethylsilyl-2-ethynylfluoro(methyl)silylethene produced 1-ethynyl-1,4,4,7,7,10,10,13,13-nonamethyl-1,4,7,10,13-pentasilacyclopentadeca-2-ene-5,8,11,14-tetrayne **39**.[68]

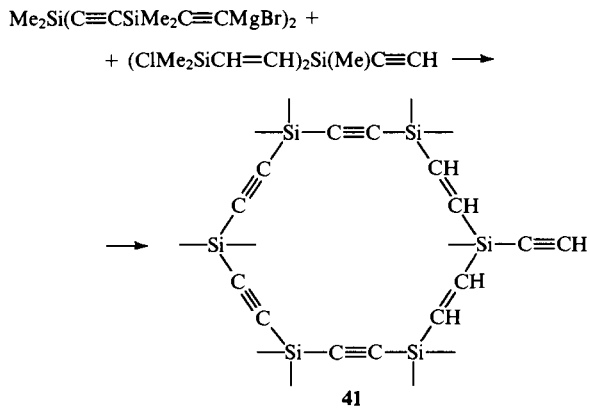


39

The reaction of BESA or DMDS with BCVES led to 1-ethynyl-1,4,4,7,7,10,10,13,13-nonamethyl-1,4,7,10,13-pentasilacyclopentadeca-2,14-diene-5,8,11-triyne **40** and a derivative of 1-ethynylundecamethyl-1,4,7,10,13,16-hexasilacyclooctadeca-2,17-diene-5,8,11,14-tetrayne **41**.[68]

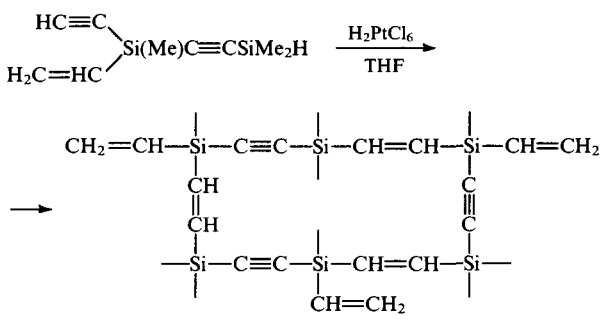


40



41

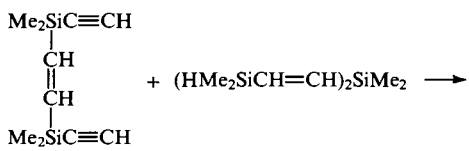
In the H_2PtCl_6-catalysed autohydrosilylation of 1-ethynyl-methylvinylsilyl-2-dimethyl silylethyne at high dilution in THF, only the ethynyl group reacts. The product of this reaction is 1,4,4,7,10,10,13,16,16-nonamethyl-1,7,13-trivinyl-1,4,7,10,13,16-hexasilacyclooctadeca-2,8,14-triene-5,11,17-triyne **42**.[69]



42

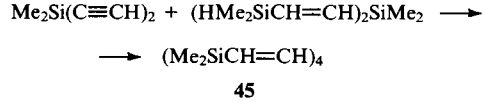
3. Cyclosilethenes

It has been suggested that the polyunsaturated macrocyclic silicohydrocarbons made up of alternating SiCH=CH fragments be called cyclosilethenes or, more precisely, cyclosil-1,2-ethenes.[11] Silicohydrocarbons of this type were first synthesised by Voronkov and Yarosh[70] by means of the autohydrosilylation reaction in the presence of H_2PtCl_6 at high dilution. The *Si*-permethylcyclosilethenes $(Me_2SiCH{=}CH)_n$ (**43**: $n = 5$; **44**: $n = 6$) were obtained in this way from ethynyldimethylsilane.[70] In addition, the specific synthesis of *Si*-decamethylcyclosilethene **43** has also been achieved by hydrosilylating (*E*)-1,2-bis-(ethynyldimethylsilyl)ethene with (*E,E*)-bis(2-dimethylsilylvinyl-dimethyl)silane.[71]



43

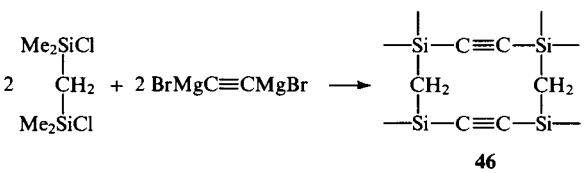
Si-Octamethylcyclotetrasilethene **45** was obtained in the same way — by the addition of (*E,E*)-bis(2-dimethylsilyl-vinyl)dimethylsilane to diethynyldimethyl silane.[71]



45

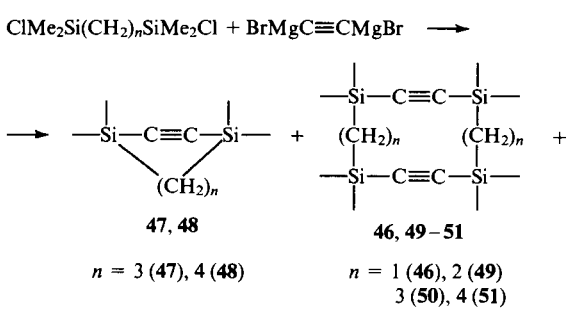
4. Macrocycles containing endocyclic $(CH_2)_n$ ($n = 1-4$) fragments

The first cyclic (10-membered) silicohydrocarbon — 1,1,4,4,6,6,9,9-octamethyl-1,4,6,9-tetrasilacyclodeca-2,7-diyne **46** — was synthesised as early as 1970 by Fritz and Schober[72] by condensing the Iotsich reagent with bis(chlorodimethyl-silyl)methane.



46

A series of cyclic and macrocyclic silicohydrocarbons (compounds **47**–**55**), containing saturated $(CH_2)_n$ ($n = 1-4$) fragments in the ring as well as the triple bonds, have been synthesised by the interaction of the Iotsich reagent with bis-(chlorodimethylsilyl)methane, 1,2-(chlorodimethylsilyl)methane, 1,3-bis(chlorodimethylsilyl)propane, or 1,4-bis(chloro-dimethyl-silyl)butane.[73]

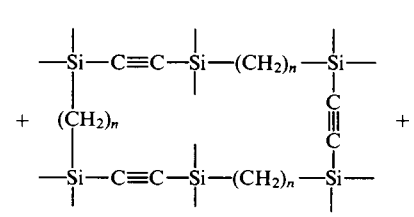


47, 48

n = 3 (**47**), 4 (**48**)

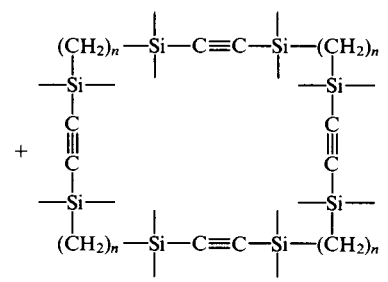
46, 49–51

n = 1 (**46**), 2 (**49**) 3 (**50**), 4 (**51**)



52, 53

n = 1 (**52**), 2 (**53**)



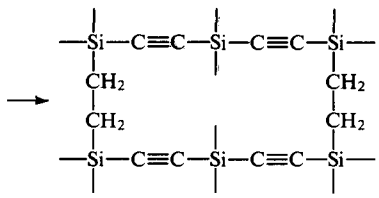
54, 55

n = 1 (**54**), 2 (**55**)

On the other hand, the 18-membered 1,1,4,4,7,7,10,10,13,13,16,16-dodecamethyl-1,4,10,13,16-hexasilacycloocta-deca-2,5,11,14-tetrayne **56** has been synthesised by the reaction of EDMS with 1,2-bis(fluorodimethylsilyl)ethane[64,74,75] (see over).

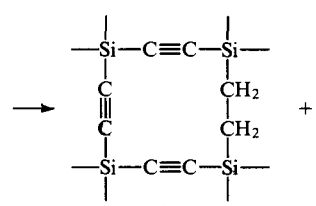
Similarly the reaction of BESA with 1,2-bis-(fluorodimethylsilyl)ethane led to macrocyclic compounds — the octamethyl derivative **57** of 1,4,7,10-tetrasilacyclododeca-2,5,8-triyne and the hexadecamethyl derivative **58** of 1,4,7-10,13,16,19,22-octasilacyclotetracosa-2,5,8,14,17,20-hexayne.[63,64]

$2\ Me_2Si(C{\equiv}CMgBr)_2 + 2\ FMe_2SiCH_2CH_2SiMe_2F \longrightarrow$

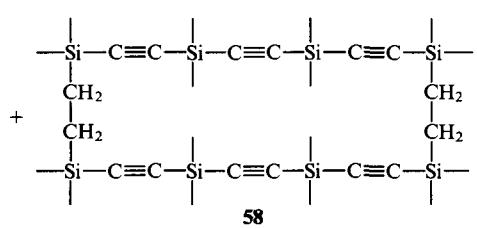


56

$BrMgC{\equiv}CSiMe_2C{\equiv}CSiMe_2C{\equiv}CMgBr +$
$+\ FMe_2SiCH_2CH_2SiMe_2F \longrightarrow$



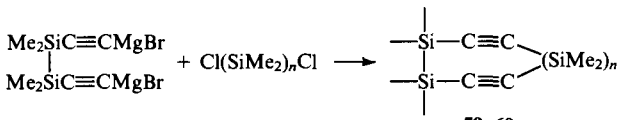
57



58

5. Macrocycles containing the $(SiR_2)_n$ (n = 2, 3) fragments

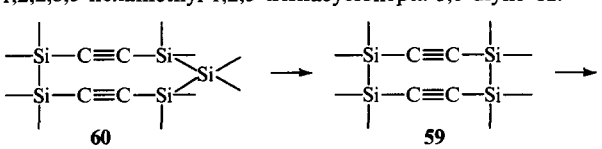
The first cyclic and macrocyclic polyunsaturated silicohydrocarbons containing simultaneously the C≡C and $(SiR_2)_n$ (n = 2, 3) groups were synthesised in 1983 by Sakurai[76-78] by means of the reaction of 1,2-bis(bromomagnesioethynyl)tetramethyldisilane with 1,2-dichlorotetramethyldisilane and 1,3-dichlorohexamethyltrisilane.



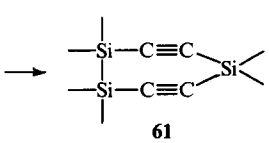
n = 2 (**59**), 3 (**60**)

59, 60

When the silicohydrocarbon **60** is heated to 680 °C under an inert atmosphere, dimethylsilylene is eliminated with formation of compound **59**, which is converted in the same way into 1,1,2,2,5,5-hexamethyl-1,2,5-trisilacyclohepta-3,6-diyne **61**.[77]



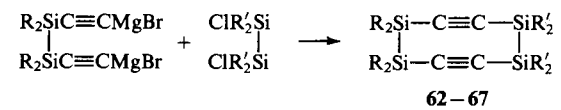
60 **59**



61

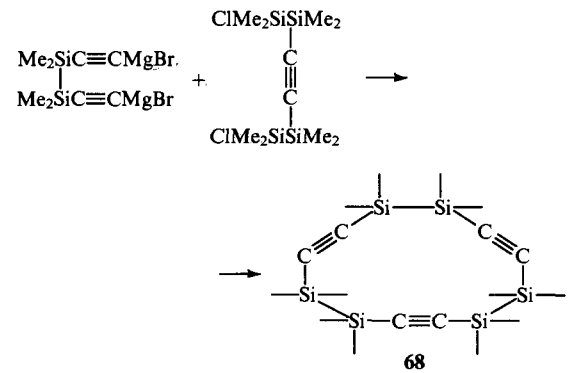
The analogous cyclic silicohydrocarbons with ethyl, butyl, hexyl, and phenyl groups were later synthesised.[78-81]

The interaction of 1,2-bis(bromomagnesioethynyl)tetramethyldisilane with bis(2-chlorotetramethyldisilanyl)ethyne led to 1,1,2,2,5,5,6,6,9,9,10,10-dodecamethyl-1,2,5,6,9,10-hexasilacyclododeca-3,7,11-triyne **68**.[82]



62-67

R = R′ = Me (**62**); R = Me, R′ = Bu (**63**); R = R′ = Bu (**64**);
R = Me, R′ = Et (**65**); R = Me, R′ = C_6H_{13} (**66**);
R = Me, R′ = Ph (**67**).



68

The same compound has been obtained in accordance with the following scheme:[83]

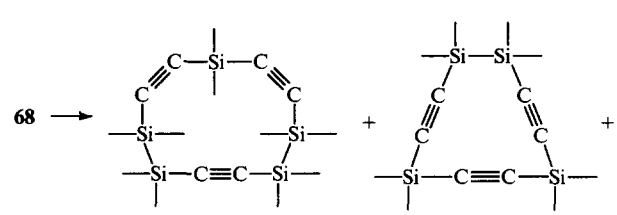
$HC{\equiv}CMgBr + (ClMe_2Si)_2 \longrightarrow$

$\longrightarrow ClMe_2SiSiMe_2C{\equiv}CH \xrightarrow{BrMgC{\equiv}CMgBr}$

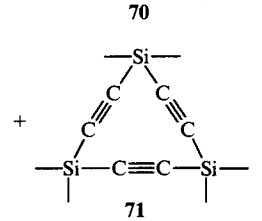
$\longrightarrow HC{\equiv}CMe_2SiSiMe_2C{\equiv}CSiMe_2SiMe_2C{\equiv}CH \xrightarrow[2.\ (ClMe_2Si)_2]{1.\ RMgBr}$

$\longrightarrow$ **68**.

When compound **68** is heated to 540 °C, a mixture of compounds **69**-**71** is obtained in 8%, 27%, and 11% yields respectively. On the other hand, heating of compound **68** to 690 °C results in the formation of only compound **71** in 68% yield.[83]

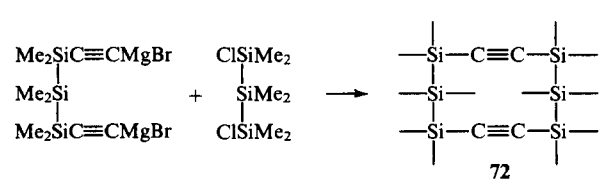


69 **70**



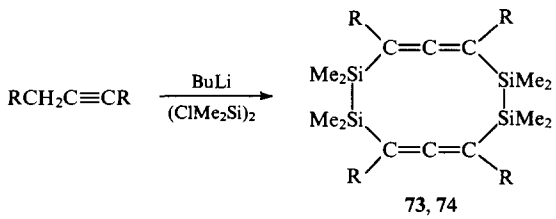
71

1,1,2,2,3,3,6,6,7,7,8,8-Dodecamethyl-1,2,3,6,7,8-hexasilacyclododeca-4,9-diyne **72** was obtained by the reaction of 1,3-bis(bromomagnesioethynyl)hexamethyltrisilane with 1,3-dichlorohexamethyltrisilane.[82,84,85]



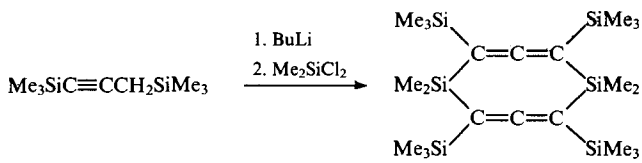
72

The reaction of 1,3-diphenylpropyne or 1,3-bis(trimethylsilyl)propyne with butyllithium and 1,2-dichlorotetramethyldisilane or dichlorodimethylsilane leads to the corresponding allene silicohydrocarbons **73**–**75**.[86,87]



73, 74

R = Ph (**73**), Me_3Si (**74**).



75

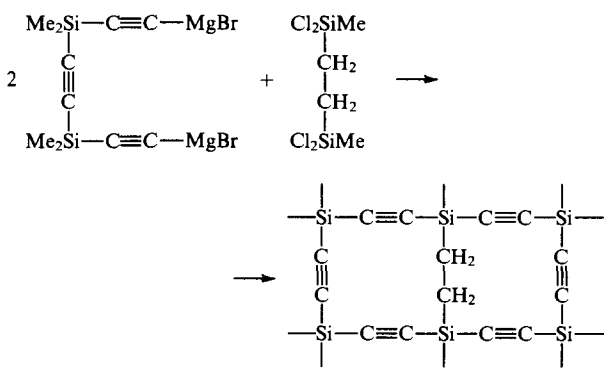
Ishikawa and coworkers[88,89] showed that, on heating to 230 °C or on treatment with a catalytic amount of butyllithium,[81,88] 1,2,5,6-tetrasilacycloocta-3,7-diynes undergo ring opening with formation of polymeric compounds:



R′ = Me, Et; R″ = Et, Ph, C_6H_{13}.

6. Bicyclic, tricyclic, and spiran systems

Bimacrocyclic trimacrocyclic and spiromacrocyclic highly unsaturated silicohydrocarbons have been obtained by methods of fine organic synthesis. Thus the first silicohydrocarbons of this type — 1,4,4,7,7,10,13,13,16,16-decamethyl-1,4,7,10,13,16-hexasilabicyclo[8′,8′,2′]eicosa-2,5,8,11,14,17-hexayne **76** — was obtained in 1988 by the interaction of BESA with 1,2-bis(chloromethylsilyl)ethane (BCSE).[64,90]

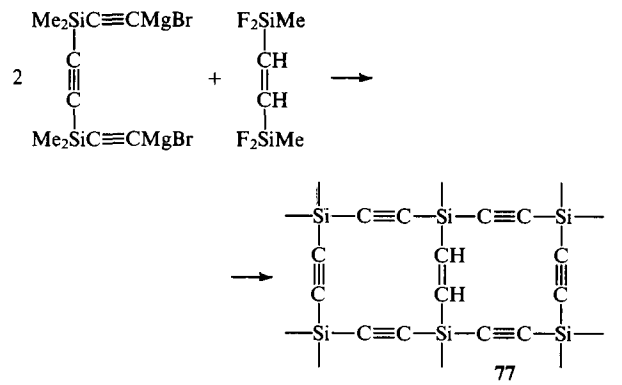


76

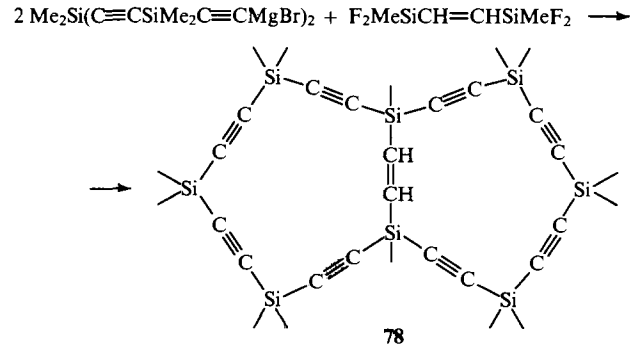
The bicyclic compound **77** was obtained similarly from BESA and (*E*)-1,2-bis(difluoromethylsilyl)ethene (DFSE).[64,65]

1,4,4,7,7,10,10,13,16,16,19,19,22,22-Tetradecamethyl-1,4,7,10,13,16,19,22-octasilabicyclo[11′,11′,2′]hexacosa-25-ene-2,5,8,11,14,17,20,23-octayne **78** was obtained in exactly the same way by the reaction of DMDS with DFSE.[64,65]

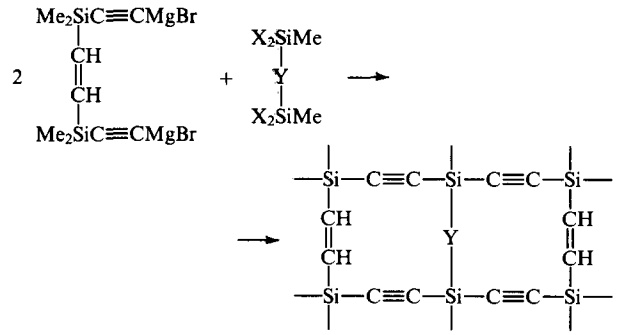
New highly unsaturated bicyclic silicohydrocarbons — the decamethyl derivative **79** of 1,4,7,10,13,16-hexasilabicyclo-[8′,8′,2′]eicosa-5,14-diene-2,8,11,17-tetrayne and the decamethyl derivative **80** of 1,4,7,10,13,16-hexasilabicyclo[8′,8′,2′]eicosa-5,14,19-triene-2,8,11,17-tetrayne — have been synthesised by the reaction of (*E*)-bis(bromomagnesioethynyldimethylsilyl)ethene (BESE) with BCSE and DFSE respectively.[91]



77



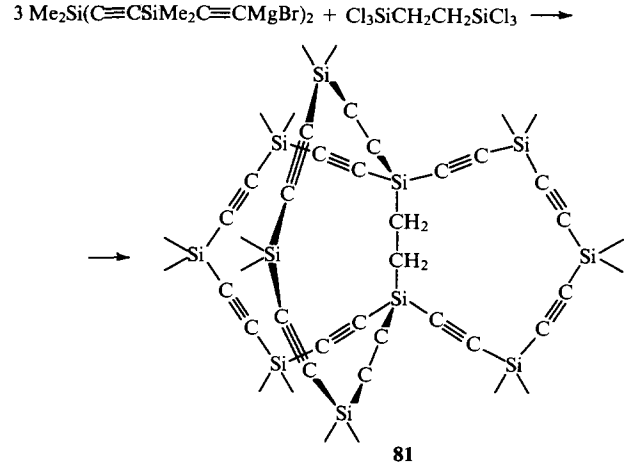
78



79, 80

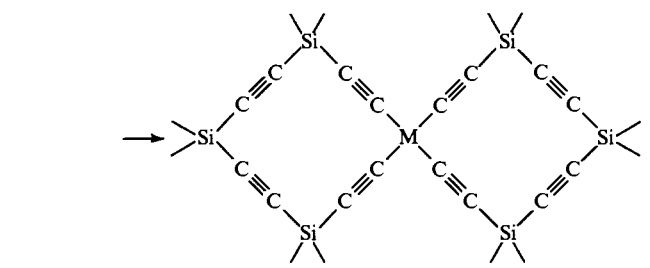
X = F, Cl; Y = CH_2CH_2 (**79**), CH=CH (**80**).

The interaction of DMDS with 1,2-bis(trichlorosilyl)ethane led to the synthesis of the first and hitherto the only trimacrocyclic silicohydrocarbon with the propellane structure — 3,3,6,6,9,9,15,15,18,18,21,21,27,27,30,30,33,33-octadecamethyl-3,6,9,12,15,18,21,24,27,30,33-undecasilatricyclo[11′,11′,11′,2′]heptatriaconta-1,4,7,10,13,16,19,22,25,28,31,34-dodecayne **81**.[92]

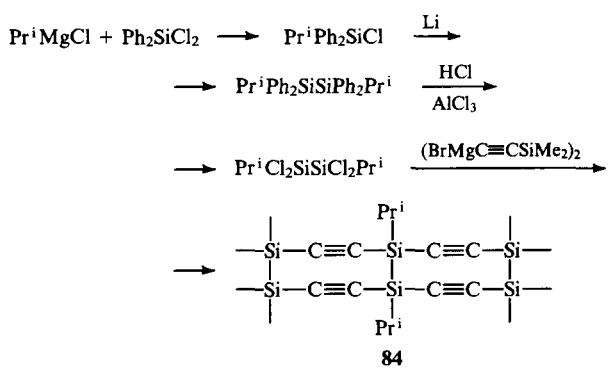


81

Finally, the first spiromacrocyclic polyethyne silicohydrocarbons — 3,3,6,6,9,9,15,15,18,18,21,21-dodecamethyl-3,6,9,12,15,18,21-heptaspiro[11′,11′]tricosa-1,4,7,10,13,16,19,22-octayne **82** and its 12-germa-analogue **83** — have been obtained by the reaction of DMDS with $SiCl_4$ and $GeCl_4$.[60,93]



M = Si (**82**), Ge (**83**).

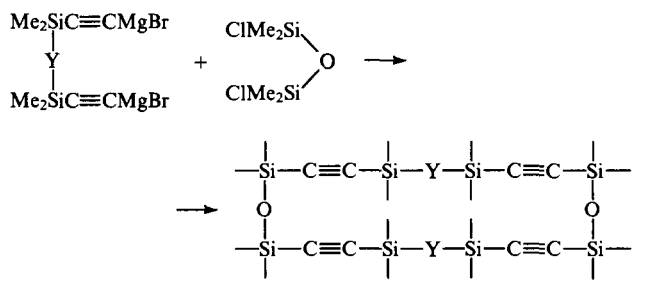


84

Compounds **5** and **15**, containing 10 triple bonds, and compound **81**, containing 12 triple bonds, are unique highly unsaturated molecular record holders. The synthesis of 1,8-diisopropyl-4,4,5,5,11,11,12,12-octamethyl-1,4,5,8,11,12-hexasilabicyclo[6′,6′,0′]tetradeca-2,6,9,13-tetrayne **84** — the only known bicyclic silicohydrocarbon containing Si–Si fragments in addition to the C≡C groups, has been achieved recently.[94]

7. Macrocycles containing endocyclic oxygen atoms

The macrocyclic polyunsaturated tetrasiloxanes **85** and **86** have been obtained by the reaction of BESA and BESE with 1,3-dichlorotetramethyldisiloxane respectively.[95,96]



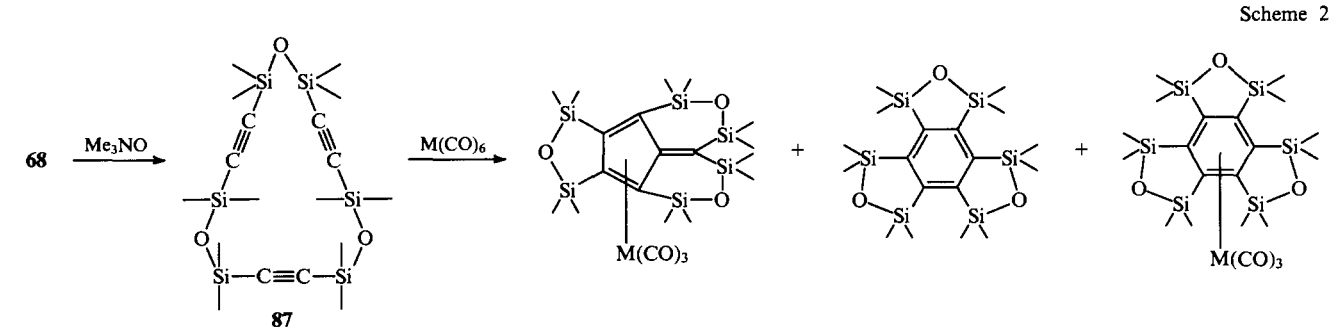
85, 86

Y = C≡C (**85**), (*E*)-CH=CH (**86**).

The oxidation of the silicohydrocarbon **68** by trimethylamine oxide leads to 1,1,4,4,6,6,9,9,11,11,14,14-dodecamethyl-1,4,6,9,11,14-hexasila-5,10,15-trioxacyclopentadeca-2,7,12-triyne **87**. The interaction of the latter with chromium molybdenum, or tungsten hexacarbonyls led to the remarkable derivatives of benzene and fulvene presented in Scheme 2.[97]

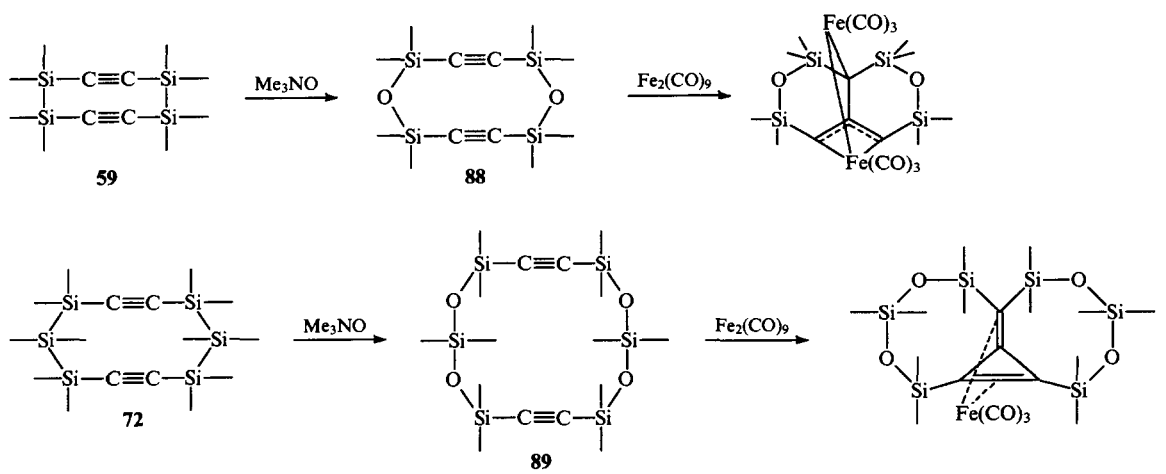
The reactions of the cyclic siloxanes **88** and **89** on treatment with $Fe_2(CO)_9$ have been investigated (Scheme 3).[84,85]

Scheme 2



M = Cr, Mo, W.

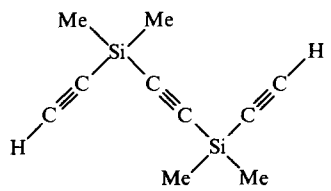
Scheme 3



IV. Physical properties

1. Molecular structure

The molecular structures of a series of polyunsaturated macrocyclic silicohydrocarbons have been established by X-ray diffraction. For a better understanding of the latter, we shall consider initially model acyclic structures:



90

and $(Me_3SiC{\equiv}C)_4Si$.

91

The molecule of compound **90** is not linear but has a zig-zag shape.[98] The Si–C(*sp*) bond lengths are 1.832 and 1.834 Å and are close to the standard Si–C(*sp*) distance of 1.837 Å.[98] The C(*sp*)–Si–C(*sp*) angles in the structure (106.6°) are smaller than the tetrahedral angle. Since there is no conformational strain in the molecule of compound **90**, the distortion of the ideal tetrahedral coordination of the silicon atoms is most probably caused by the steric interaction of the methyl substituents.

The central silicon atom in the molecule of compound **91**, surrounded by four linear $Me_3SiC{\equiv}C$ groups, has a tetrahedral configuration.[99] The C(*sp*)–C(*sp*) and Si–C(*sp*) bond lengths are respectively 1.17–1.20 and 1.840–1.871 Å, while the Si–C(*sp*)–C(*sp*) angle is close to the linear value (175–178°).[99]

The cyclic molecules of compounds **46** and **88** contain two triple bonds and have the 'chair' conformation.[100] The lengths of the bonds Si–C(*sp*) (1.839 and 1.842 Å) and C(*sp*)–C(*sp*) (1.215 and 1.216 Å) are respectively almost identical. The average Si–C(*sp*)–C(*sp*) angle is 175.5°.

The macrocyclic molecules of compounds **47**–**55** differ only in the number of methylene groups separating the $SiC{\equiv}CSi$ fragments.[101] The single unit cell of the crystal of compound **47** contains three molecules (space group *P*1), among which one is approximately at the centre of symmetry, whilst the others are in general positions and are linked by the centre of symmetry. The crystals of compound **47** contain two different conformers — the 'chair' and 'boat' conformers. The bond lengths and valence angles in compounds **46** and **49**–**51** (n = 1–4) are presented in Table 1. The rings with an even number n are more strained than those with an odd number. In all these molecules, the silicon atoms are located in one plane. The Si–C(*sp*) and C(*sp*)–C(*sp*) bond lengths in compound **62** (R = R′ = Me) are close to the standard values (1.838–1.848 and 1.182 Å respectively).[57] There are two conformers in the crystal of compound **67** (R = Me, R′ = Ph) — with the *cis,trans*- and *trans,trans*-configurations.[81] The eight-membered ring of the first conformer is planar within ±0.5 Å and has a centre of symmetry. In the first conformer, the phenyl groups are in the *trans*-positions relative to one another at each Si–Si bond and in the *cis*-positions relative to each $Si{-}C{\equiv}C{-}Si$ fragment. In the second conformer, the phenyl groups at the silicon atoms in the Si–Si and $Si{-}C{\equiv}C{-}Si$ fragments are in the *trans*-positions. Its eight-membered ring is bent (the maximum deviation from the mean square plane is 0.27 Å).[81]

The macrocyclic molecules having the general formula $(Me_2SiC{\equiv}C)_n$ (n = 4–6) (compounds **1**–**3**) have different ring conformations.[57,102] The molecule of compound **1** (n = 4) consists of a 12-membered ring with a square plane structure (D_{4h} symmetry).[57] The C(sp^3)–(Si)–C(sp^3) angles are larger than the tetrahedral angle (110.7°, 112.6°), while the C(*sp*)–(Si)–C(*sp*) angles are smaller (102.96°, 103.77°). The triple bonds are bent to the outside owing to ring strain. Compound **2** (n = 5) consists of a nonplanar ring with the envelope conformation.[57] Its triple bonds are slightly bent into the interior of the ring. As in compound **1**, the C(sp^3)–(Si)–C(sp^3) bond angles are larger than the tetrahedral value (111.4–113.5°), while the C(*sp*)–(Si)–C(*sp*) angles are smaller (104.73–106.83°). The molecule of compound **3** (n = 6) has the 'chair' conformation.[102] The C(*sp*)–C(*sp*) bond lengths in compounds **1**–**3** are 1.205–1.209, 1.210–1.220, and 1.218–1.222 Å for n = 4, 5, and 6 respectively, i.e. they increase with increase in ring size and are larger than in their C-analogues (1.18–1.19 Å), which is evidently due to their electronic interaction with the silicon atom.

The Si–C(*sp*) bond lengths (1.808–1.829 and 1.818–1.847 Å) in compound **27** are shorter[103] than in 1,1,4,4,7,7,10,10-octamethyl-1,4,7,10-tetrasilacyclododeca-2,8-diyne **47**,[101] but are approximately the same as in compound **2**.[57]

The crystal of compound **56** has C_i symmetry, although its intrinsic symmetry is C_{2h}. This 18-membered macroheterocycle has an overall 'chair' conformation and is on the whole rigid. The average Si–C(*sp*) distance (1.850 Å) differs little from the average Si–C(sp^3) distance (1.857 Å), apparently owing to failure to take into account corrections for the thermal motions of the atoms (especially the methyl groups). The length of the triple bond (1.201–1.207 Å) has the usual value. The molecules of compound **56** form stacks in the crystal, the outer surfaces of which are made up of the $Si{-}C{\equiv}C{-}Si$ fragments.[75]

A characteristic feature of the macrocyclic silicohydrocarbons with endocyclic $Si{-}C{\equiv}C{-}Si$ and Si–CH=CH–Si groups is a tendency towards disorder in the crystal structure.[95,103,104] This is frequently caused by their great flexibility combined with an appreciable looseness of the crystal structure — which is a consequence of the noninvolvement of the endocyclic $-C{\equiv}C-$ and CH=CH– bonds in the intermolecular contacts, which leads to the coexistence in the crystal of two or more conformers with different orientations.[75,95]

The molecular structure of compound **85** with endocyclic Si–O–Si (two) and $Si{-}C{\equiv}C{-}Si$ (six) groups is ordered.[95] The molecule of compound **86** differs from the structurally similar molecule of compound **85** by the presence of the CH=CH groups instead of the two $C{\equiv}C$ groups.[96] The Si–O bond lengths (1.630 Å) in compound **85** are greater than in compound **86** (1.605 Å), which is due to the greater strain in compound **85**. The latter leads in its turn to a decrease in the Si–O–Si bond angle in compound **85** (148.9°) compared with compound **86** (156.9°). The remaining bond lengths and bond angles in compound **85** are close to those observed in compound **86** [the Si–C(*sp*) bond lengths are 1.839 and 1.834 Å respectively].

The overall configuration of the bicyclic molecule of compound **78** ('butterfly'), determined primarily by the tetrahedral valence environment of the 'bridging' Si atoms, is the most compact.[104] The *trans*-structure of the Si–CH=CH–Si bridge disturbs the symmetry of this molecule. The disorder is comparatively small and is associated with the presence of

Table 1. The bond lengths (Å) and bond angles (deg) in compounds **46** and **49**–**51**.[101]

Compound	n	Si–C(*sp*)	Si–C(sp^2)	Si–C(sp^3)	C≡C	Si–C(*sp*)–C(*sp*)
46	1	1.867	1.872	1.842	1.216	176.9
49	2	1.866	1.879	1.844	1.213	173.7
50	3	1.862	1.877	1.851	1.216	179.5
51	4	1.867	1.877	1.843	1.220	178.1

two enantiomers at each crystallographic site. In the ordered fragments of the molecule of compound **78**, the bond lengths and bond angles have the usual values. Thus the average Si–C(*sp*) distance is the same as the value observed in other silicohydrocarbons.[101] A similar type of disorder has been observed also in the crystals of the macrocyclic compounds **24**, **27**, **49**, and **54** with four silicon atoms in the ring and an asymmetric distribution of the C≡C, CH=CH, and CH_2-CH_2 groups.[103]

The structure of compound **31** can be regarded as the same as one of the condensed heterocycles in the molecule of compound **78**.[103] The macrocycle **31** with five silicon atoms exists in the crystal in the form of three conformers, which is manifested by a pronounced structural disorder. All three conformers of this heterocycle have virtually the same, almost symmetrical, 'large envelope' configuration.

2. Melting points

The melting points of the cyclodimethylsilethynes $(Me_2SiC{\equiv}C)_n$ (n = 3–10) exceed 140 °C and oscillate markedly as the ring size varies. The compounds with an even number n have higher melting points (the melting point is a maximum for n = 6). Among the compounds with an odd number n, the minimum melting point is observed for n = 3 (Fig. 1).[59,60,83] A similar behaviour is manifested by the first three known analogues of these compounds containing only one double bond, namely $(Me_2SiC{\equiv}C)_{n-1}(Me_2SiCH{=}CH)$, the melting points of which are 228, 198, and 257 °C for n = 4, 5, and 6 respectively;[64–66] this also applies to cyclodimethylsilethenes $(Me_2SiCH{=}CH)_n$, the melting points of which are 158, 110, and 230 °C for n = 4, 5, and 6 respectively.[71]

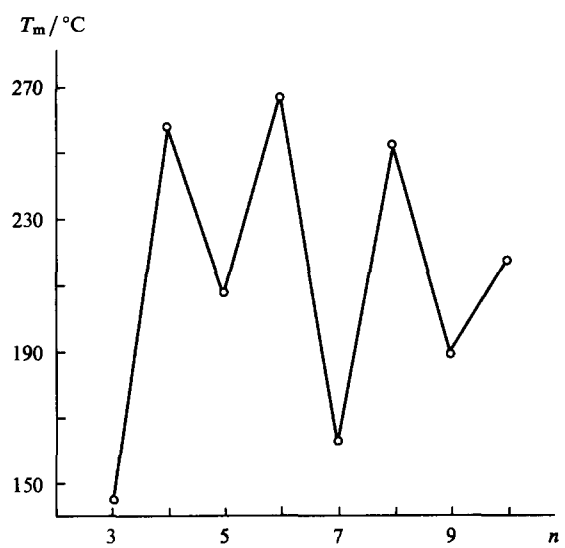


Figure 1. Melting points of the cyclodimethylsilethynes $(Me_2SiC{\equiv}C)_n$ (n = 3–10).[59,60,83]

The replacement of the methyl groups in the polyunsaturated macrocyclic silicohydrocarbons by substituents such as H, C_2H_5, $CH{=}CH_2$, C≡CH, $CH{=}CHSiMe_3$, and $C{\equiv}CSiMe_3$, leading to a decrease in ring symmetry, diminishes the melting point.[59–62] A decrease in the degree of unsaturation of the macrocycle also entails a decrease in the melting point.

The bicyclic and tricyclic as well as spirocyclic polyunsaturated silicohydrocarbons differ from the monocyclic ones by higher melting points (Table 2). A decrease in the melting point with decrease in the degree of unsaturation is also observed for these substances.

Table 2. The melting points of the bicyclic, tricyclic, and spirocyclic macrocycles.[61,65,66,90–92]

Compound	Cyclic system	T_m/°C	Compound	Cyclic system	T_m/°C
76	bicycle	277	**80**	bicycle	274
77	"	305	**81**	tricycle	269
78	"	280	**82**	spiran	293
79	"	255	**83**	"	299

3. NMR spectra

The chemical shifts of the protons in the methyl groups at the silicon atom in the polyunsaturated macrocyclic silicohydrocarbons are determined by the nature of the neighbouring endocyclic bonds and are almost independent of the size of the macroring (Table 3).

Table 3. The chemical shifts (δ) of the methyl protons in the ^{1}H NMR spectra of macrocyclic polyunsaturated silicohydrocarbons.

Fragment	δ/ppm	Ref.
$Me_2Si(C{\equiv})_2$	0.26–0.32	59–71
$Me_2Si(C{\equiv})(CH{=})$	0.23–0.24	74
$Me_2Si(CH{=})_2$	0.16–0.19	75
$Me_2Si(C{\equiv})(CH_2{-})$	0.15–0.16	90–93

The chemical shifts of the protons in the endocyclic CH=CH and CH_2-CH_2 groups have the usual values for the acyclic SiCH=CHSi and $SiCH_2CH_2Si$ groups (6.0–7.10 and 0.62 ppm respectively).

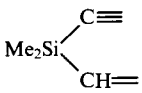
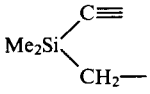
On the other hand, in the ^{13}C NMR spectra the chemical shifts of the carbon atoms of the methyl groups are determined both by the ring size and by the nature of the neighbouring bonds. With increase in the size of the macrocycle, the ^{13}C signal arising from Me_2Si undergoes a downfield shift. Thus the ^{13}C chemical shift of Me_2Si in the NMR spectra of the cyclodimethylsilethynes **1**, **2**, and **3** (n = 4–6) varies in the following sequence: −0.80 to −0.69, 0.12–0.15, and 0.62–0.87 ppm respectively.[59,60]

In the NMR spectrum of the $Me(CH_2{=}CH)Si(C{\equiv})_2$ fragment, the signal due to the methyl carbon atom undergoes an upfield shift (δ = −2.10 to −2.21 ppm).[59,60] The shift of the methyl carbon atom in the $Me(H)Si(C{\equiv})_2$ (δ = −3.89 ppm) [59,60] and $Me_2Si(CH{=})_2$ (δ = −3.37 to −3.80 ppm) fragments[63,65] is even more pronounced. The $^{13}C(sp^3)$ chemical shift is −2.43 to −2.57 ppm for the $Me_2Si(C{\equiv})(CH{=})$ fragment and −4.01 to −4.90 ppm for the $Me(HC{\equiv}C)Si(C{\equiv})(CH{=})$ fragment, depending on the ring size. The ^{13}C chemical shift of the ^{13}C atom in $-CH_2-$ in the endocyclic $Me_2Si(CH_2)(C{\equiv})$ fragment is 8.10 ppm.[63,75]

The chemical shifts of the C(sp) atoms in the endocyclic $SiC{\equiv}CSi$ fragment are in the range 105.1–117.2 ppm [$\delta(^{13}C)$ = 113.02 ppm for $Me_2SiC{\equiv}CSiMe_3$ [105]]. The ^{13}C chemical shifts for the exocyclic ethynyl groups linked to the silicon atom have the following values: 84.60–86.30 ppm (C≡) and 95.51–95.76 ppm (≡CH).

The ^{13}C signal for the endocyclic SiCH=CHSi fragment is at 146.15–150.45 ppm (for comparison, we may note that the signal for $Me_3SiCH{=}CHSiMe_3$ is at 150.0 ppm[106]). The ^{13}C chemical shifts for the exocyclic vinyl groups linked to the silicon atom are at 130.70–132.85 ppm (CH=) and 135.60–136.25 ppm ($=CH_2$).

Table 4. The chemical shifts of the silicon atoms (δ_{Si}) in the ^{29}Si NMR spectra of highly saturated macrocyclic silicohydrocarbons.

Fragment	δ_{Si}/ppm	Ref.
$Me_2Si(C\equiv)_2$	−40.1 to −42.7	59–71
	−26.1 to −27.6	74
$Me_2Si(CH=)_2$	−14.7 to −17.4	75
$Si(C\equiv)_4$	−66.9 (in spiran)	90–93
$MeSi(C\equiv)_3$	−69.0 to −70.0 (in monocycle)	
$Me(HC\equiv C)Si(CH=)_2$	−32.1	
	−14.5	
$Me(CH_2=CH)Si(C\equiv)_2$	−48.5 to −49.0	
$CH_3Si(C\equiv)_3$	−54.6 (in tricycle)	

The silicon chemical shifts in the ^{29}Si NMR spectra are independent of the size of the macrocycle and are determined exclusively by the nature of the endocyclic and exocyclic substituents (Table 4).

4. UV, Raman, and photoelectron spectra

The silicohydrocarbons containing the $SiC\equiv CSi$ fragment absorb in the near ultraviolet. A maximum at 215 nm and a shoulder at 228 nm are observed in the UV spectrum of $(Me_2SiC\equiv C)_4$ **1**, while the spectrum of $(Me_2SiC\equiv C)_5$ **2** has only a shoulder at 230 nm.[57] Quantum-chemical calculations by the semiempirical AM1 method for the molecule of compound **2** indicate a marked conjugation between the π MO of the $C(sp)-C(sp)$ bond and the π MO of the silicon atom, which leads to the splitting of the corresponding molecular orbitals to the extent of 1.73 eV. According to UV spectroscopic data, conjugation in the molecules increases from compound **24** to compound **21** and to compound **19**.[107] This is accompanied by a bathochromic shift of the bands (210, 217, and 223 nm respectively), compared with $(Me_2SiC\equiv CSiMe_2O)_2$ **88** (202, 207, and 215 nm).[101]

The linear (disilanylene)ethynylene polymers of the type $(SiR_2SiR_2C\equiv C)_n$ (R = alkyl) absorb in the range 241–244 nm with an extinction coefficient of 13 000–17 000 litre mol^{-1} cm^{-1} per unit.[49,82] An electron is transferred from the MO involving the Si–Si σ-bond. Quantum-chemical calculations (CNDO/2) show that the highest occupied and the lowest unoccupied MO are σ-type orbitals.[108] This agrees with the finding that the polymer of the type $(Et_2SiOSiEt_2C\equiv C)_n$, not containing the Si–Si group, absorbs at shorter wavelengths (at 216 nm).[82]

As a consequence of the symmetry of the triple bond in the $SiC\equiv CSi$ fragment in macrocyclic ethyne hydrocarbons, the stretching vibrations of the triple bond are inactive in the IR spectra, while the Raman spectra show an intense $C\equiv C$ stretching vibration band. The $\nu(C\equiv C)$ band in the Raman spectra of cyclodimethylsilethynes $(Me_2SiC\equiv C)_n$ with $n = 4-6$ undergoes a slight hypsochromic shift (2132, 2134, and 2137 cm^{-1} respectively).[57] The band due to the stretching vibration of the triple bond in the Raman spectra which we obtained for crystalline cyclodimethylsilethynes ($n = 4-10$) is located in the lower-frequency range 2110–2120 cm^{-1} and decreases slightly with increase in n from 5 to 10 (Table 5). The lower $\nu(C\equiv C)$ frequency for $n = 4$ (2113 cm^{-1}) is apparently due to the 'rigid' molecular structure (see above). The Raman spectra of the spirocyclic compounds **82** and **83** show two lines characteristic of the triple bond vibration (2116, 2122, and 2116, 2127 cm^{-1} respectively). The doublet nature of the lines is apparently associated with the resonance of the triple bonds in the orthogonal rings. The triple bond vibration appears in the Raman spectra of the model compounds $(Me_3SiC\equiv C)_4E$ (E = Si, Ge) by a single line (2114.5 and 2118.5 cm^{-1} respectively).

Table 5. The stretching vibration frequency of the triple bond in the Raman spectra of compounds of the type $(Me_2SiC\equiv C)_n$.

Compound	n	$\nu(C\equiv C)$/cm^{-1}	Compound	n	$\nu(C\equiv C)$/cm^{-1}
1	4	2113	**6**	7	2115
8	4	2118	**4**	8	2112.5
2	5	2119	**7**	9	2113, 2109 sh.
3	6	2118.5	**5**	10	2113

The He(I) photoelectron spectra of compounds **59**, **68** and **71** have been obtained. The interpretation of the first bands in these spectra is based on a comparison with the orbital energies calculated by the semiempirical MINDO/3 and MNDO methods.[109,110] The Si–Si bonds have very low ionisation energies and may therefore destabilise the π orbitals of the ethyne fragments.[109] An interaction via the σ-bonds between the out-of-plane π orbitals and the Si–Si σ-bonds, leading to a marked destabilisation of the $a_g(\pi)$ orbital (8.13 eV), has been observed in compound **59**. A similar interaction via σ-bonds has also been noted for compound **68**.

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The spatial organisation of macromolecular metal chelates

A D Pomogailo, I E Uflyand, E F Vainshtein

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Abstract. The spatial organisation of metallopolymers (macromolecular metal chelates) is analysed on three levels; local, molecular, and supermolecular. The thermodynamic features of the formation of chelates with polymeric ligands are examined and data are presented concerning the dependence of the structure of the chelate units on various factors. The principal changes which the macrochain may undergo on formation of metal chelate centres are considered. The behaviour of the macromolecular ligands and their low-molecular-mass analogues is compared on the molecular level. The principal characteristics of the formation of intramolecular and intermolecular complexes are listed and the causes of their stability are examined. The bibliography includes 125 references.

I. Introduction

The problems of the chemistry of macromolecular metal chelates (MMC)† have attracted increased attention by investigators during recent years.[1–9] As a result of the efforts of specialists in various fields (polymer, coordination, bioinorganic, and analytical chemistry, catalysis, etc.), considerable advances have now been achieved in the MMC chemistry. Thus numerous MMC containing virtually any metals in the Periodic System have been obtained, their physicochemical properties have been investigated, and their principal structural characteristics have been elucidated. However, the quantitative parameters of the chelate formation process involving macromolecular ligands have so far been studied inadequately,[11] in contrast to the low-molecular-mass metal chelates‡ (LMC). This has been explained by the need to take into account a whole series of additional factors, in the first place those arising from the chain nature of the ligand. It is useful to examine three levels of the spatial organisation of the MMC:

1. the local level, which reflects the chemical structure of a single chelate unit in the chain molecule (the nature of the complex forming metal and of the electron-donating atoms, the ring size, the steric structure of the ring, etc.);
2. the molecular level, which is determined by the chemical structure of the polymer chain (the chain length, the elemental composition of the repeat units, the shape and conformation of the chain, etc.);
3. the supermolecular level, which reflects the nature of the intermolecular interaction of the macromolecules and the degree of their mutual order.

Taking these three levels of the spatial organisation of the MMC into account, the free energy of formation of the chelates involving macroligands can be represented (on the assumption that its components are additive) by the equation[12]

$$\Delta G = \Delta G_1 + \Delta G_2 + \Delta G_3 , \quad (1)$$

where ΔG_1, ΔG_2, and ΔG_3 are the free energy changes for the local, molecular, and supermolecular levels respectively. Under certain conditions, the free energy change for a particular level may be neglected, which makes it possible to analyse in detail the enthalpy (ΔH) and entropy ($T\Delta S$) contributions to ΔG for each level.

$$\Delta G = \Delta H - T\Delta S \quad (2)$$

Taking this into account, the characteristics of the steric structure of the MMC on each level are analysed in the present review.

II. The local level of the structural organisation of metallopolymers

Initially we shall consider dilute solutions of polymers, i.e. solutions in which chain association may be neglected. Then $\Delta G_3 \to 0$ and Eqn (1) can therefore be expressed in the form

$$\Delta G = \Delta G_1 + \Delta G_2 . \quad (3)$$

† A characteristic feature which makes it possible to identify fairly reliably chemical compounds of this class in the presence of a polymer chain and of metal chelate rings.

‡ The chelate effect in the LMC is one of the most interesting phenomena in the thermodynamics of intermolecular interactions.[10]

A D Pomogailo Institute of Chemical Physics in Chernogolovka, Russian Academy of Sciences, 142432 Chernogolovka, Moscow Region, Russian Federation. Fax (7-096) 515 35 88
I E Uflyand Rostov Pedagogical University, ul. Engel'sa 33, 344082 Rostov-on-Don, Russian Federation
E F Vainshtein Semenov Institute of Chemical Physics, Russian Academy of Sciences, ul. Kosygina 4, 117947 Moscow, Russian Federation. Fax (7-095) 265 51 74. Tel. (7-095) 121 09 42

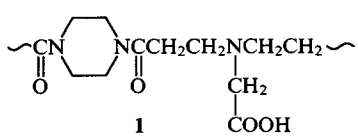
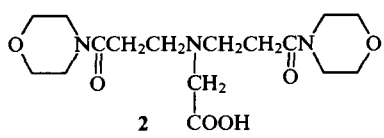
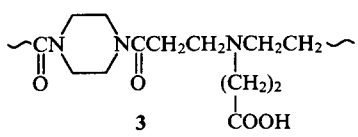
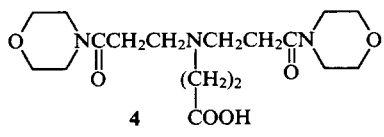
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In the case of infinitely long chains ($l \to \infty$) and low degrees of conversion§ with respect to the chain molecule ($\alpha \to 0$), the chelation process may not exert a significant influence on the form and conformation of the macromolecule, so that $\Delta G_2 \to 0$ and hence

$$\Delta G = \Delta G_1 \ . \qquad (4)$$

Thus, in the case of dilute solutions with $l \to \infty$ and $\alpha \to 0$ the chelating macroligand behaves similarly to its low-molecular-mass analogue and the familiar Flory principle then operates: when the components of the model reaction are chosen correctly, the reactivity of the binding centres is independent of whether they belong to the polymer chain or to the low-molecular-mass analogue. This makes it possible to exclude from consideration the molecular and supermolecular levels and to analyse only the local chelate units. The entropy and enthalpy components of ΔG in the case of MMC are determined mainly by the same contributions as in the case of LMC. Since the nature of the complex-forming metal and the electron-donating groups is the same in both cases, the enthalpy of chelate formation changes little on passing from LMC to MMC. For example, ΔH for the chelation of copper(II) ions by type **1** and **3** poly(amido-amines) and their type **2** and **4** low-level-mass analogues are similar (Table 1),[13] which indicates a similar steric structure of the chelate units in these compounds. Therefore, for both MMC and LMC ΔG is determined by the entropy component. This is indicated by the isotypical nature of the dependences of ΔG and ΔS in chelation processes on the degree of conversion (Fig. 1) and also by the independence of ΔH of α (Table 1).

Table 1. Thermodynamic functions for the formation of copper(II) complexes (in kJ mol^{-1} and J mol^{-1} K^{-1}).

Ligand	ΔG	$-\Delta H$	ΔS
 **1**	51.5–47.3[a]	30	72–58[a]
 **2**	57.0	30	90
 **3**	37.2–33.1[b]	16	71–58[b]
 **4**	34.5	17	58

[a] Degree of conversion $\alpha = 0.45-0.85$.
[b] Degree of conversion $\alpha = 0.18-0.88$.

Formally the chelation reaction can be divided into several hypothetical elementary stages and the entropy of the entire process can be expressed as follows:

$$\Delta S_1^0 = \Delta S_{solv} + \Delta S_4^0 = \Delta S_2^0 + \Delta S_3^0 + \Delta S_5^0 + \Delta S_4^0 \ ,$$

§ The degree of conversion α is defined as the ratio of the actual number of metal ions bound to one chain and the maximum possible number.

where ΔS_1^0 is the experimental entropy of the reaction in solution, ΔS_4^0 is the calculated theoretical entropy of the reaction in the gas phase, ΔS_{solv} is the entropy of solvation of the metal ion (ΔS_2^0), of the ligand (ΔS_3^0), and of the complex formed (ΔS_5^0), which is determined as the difference between the entropies in solution and in the gas phase.

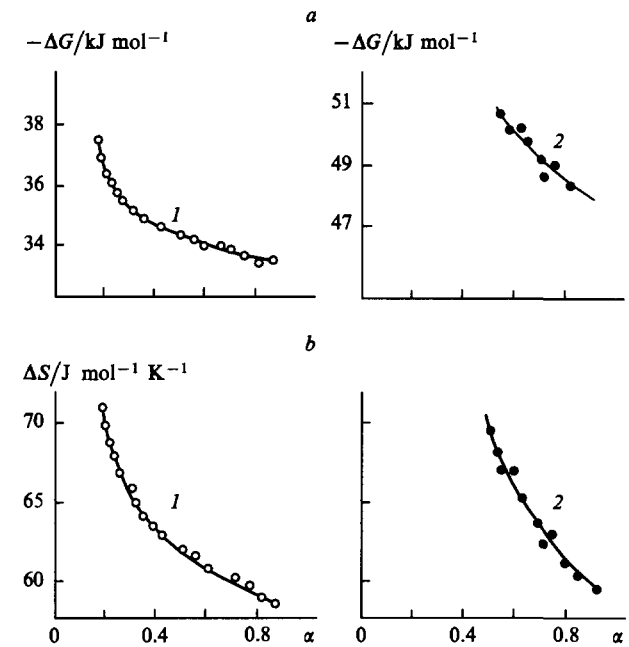


Figure 1. Dependence of ΔG (*a*) and ΔS (*b*) for the formation of copper(II) chelate complexes of poly(amidoamines) of types **1** (curve *1*) and **3** (curve *2*) on the degree of conversion.

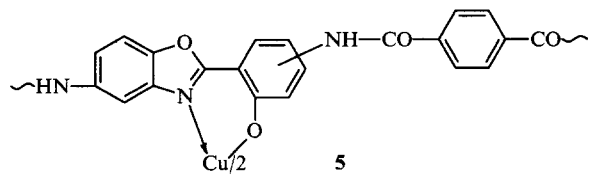
ΔS_4^0 represents in its turn the sum of the entropies of transfer (ΔS_t), internal rotation ($\Delta S_{int.rot}$), symmetry (ΔS_{sym}), isomerisation (ΔS_{isom}), vibration (ΔS_{vib}), and rotation (ΔS_{rot}).[14]

$$\Delta S_1^0 = \Delta S_{solv} + \Delta S_t + \Delta S_{int.rot} + \Delta S_{sym} + \Delta S_{isom} + \Delta S_{vib} + \Delta S_{rot} \ .$$

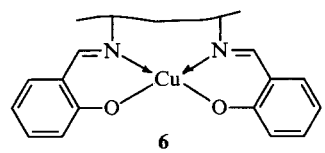
It is assumed[14] that the positive contributions to the entropy component of ΔG come from ΔS_t, ΔS_{rot}, ΔS_{sym}, and ΔS_{isom}. The contribution of ΔS_t, due to the change in the number of species on chelation, apparently changes little on passing from LMC to MMC. Consequently the entropies of chelation are similar in the two cases, since the contribution of the transfer process is the main one. ΔS_{rot} makes a definite contribution to the entropy component. It is smaller in the case of MMC than in the reaction with monodentate ligands because the initial macroligand and the MMC formed are nonrotating species. The symmetry groups for the low- and high-molecular-mass compounds are significantly different and the number of possible isomers of polymeric chelates may be smaller, so that the contribution of isomerisation is in this case reduced. Thus the nickel(II) chelate complexes with salicylaldimine ligands exist in two isomeric forms: planar (green) and tetrahedral (brown). Only a paramagnetic pseudo-tetrahedral form has been obtained on a polymer base[15] even under conditions where the diamagnetic isomer is formed preferentially in the low-molecular-mass system.[16]

ΔS_{vib}, $\Delta S_{int.rot}$, and ΔS_{solv} makes negative contributions to the entropy component.[14] It is postulated that the contributions by the vibration and internal rotation are much lower in the case of the high-molecular-mass system than in the case of the LMC. If the monomeric and polymeric chelating ligands form structurally identical chelate units, then the contribution of solvation is approximately the same in both cases. However, as a rule such cases are rare and the polymer chain exerts a significant influence

on the structure of the local chelate unit with the possibility of the formation of structures which are both less and more distorted than the LMC. As an example, one may quote the copper(II) chelate complex of poly(hydroxyphenylbenzoxazole-terephthalamide) **5**, which has a distorted tetrahedral structure like its low-molecular-mass analogue. However, a somewhat higher value of A and a lower value of g in the EPR spectra compared with the LMC are characteristic of the MMC, which indicates a smaller dihedral angle.[17] On the other hand, in the case of the salicylaldimine ligands the structures of the chelate units are different in the LMC and MMC: planar in the LMC and distorted tetrahedral in the MMC (complex **6**).[15] In conformity with the change in the stereochemistry of the chelate unit, an increase or a decrease in the contribution of solvation is observed.

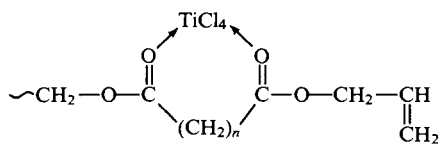


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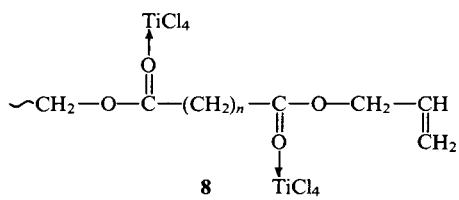


6

As for the LMC, the free energy ΔG in the case of polymeric ligands depends to a large extent on the size of the chelate ring. The familiar Chugaev ring rule holds for the MMC: five- and six-membered rings prove to be the most stable. The influence of ring size on the mechanism of the binding of metal ions by polymers can be illustrated in relation to the formation of complexes between $TiCl_4$ and the copolymers of styrene and the diallyl esters of dicarboxylic acids.[18] For n = 1 or 2, a mixture of complexes with the *cis*-disposition (complex **7**) or *trans*-disposition (complex **8**) of the carbonyl groups is formed. Both in the initial ligand and in the MMC, there are two nonequivalent carbonyl groups, but the difference between the vibrational frequencies $\Delta\nu$(C=O) for the *cis*- and *trans*-forms increases from 10–15 to 40–45 cm^{-1}. This indicates a more rigid fixation of the isomers on complex formation. The increase in the size of the separating bridge ($n > 3$) precludes the formation of chelates.



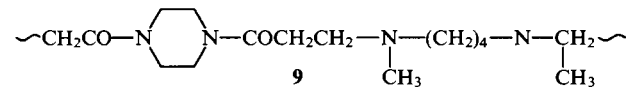
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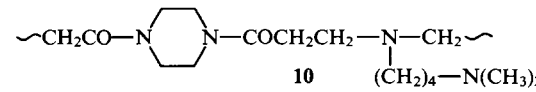
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The study of copper(II) complexes of poly(amidoamines) showed that an increase in the chelate ring size from five-membered to six-membered entails a significant decrease in the stability constants or even precludes the chelation of copper(II) with formation of stable complexes. In this case, the decrease in stability is accounted for mainly by the decrease in enthalpy, since conformational freedom is reduced to a much greater extent in polymers than in low-molecular-mass compounds.[19,20]

The ligands **9** and **10**, which should form seven-membered chelate rings, do not give rise to stable complexes. Thus an increase in the length of the aliphatic chain, linking the nitrogen atoms of the monomer unit, greatly diminishes the complex forming capacity of poly(amidoamines)[19]

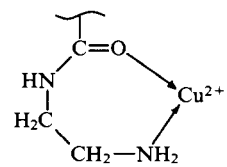


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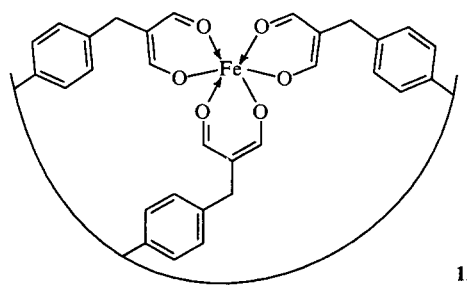
10

However, since the polymer chain determines the steric structure of the chelating fragment while the metal ion selects sections of the macromolecular chain with the preferred conformation, there is a possibility of the formation of analogues of metallocycles different from the low-molecular-mass ones. For example, the interaction of copper(II) ions with vinyl polymers containing aminoalkylamide units in the side chain results in the formation of the seven-membered chelate rings **11**, the amine nitrogen atom and the amide C=O groups participating in the coordination to the metal.[21] On the other hand, in the copper(II)–glycylglycine low-molecular-mass system, five-membered rings are formed.[22] Thus, knowing the conformation of the local chelating fragment, it is possible to predict the formation of MMC with metallocycles having a particular size.



11

As well as the contributions from the entropy and enthalpy of chelating common to low- and high-molecular-mass metal chelates, a series of specific contributions are characteristic of the MMC. They include a contribution reflecting the 'adjustment' of the local chelating fragment because the interaction of metal ions with the chelating macroligand is accompanied not only by direct chemical steps (the formation of the metallocycle) but also by a change in the 'local rigidity' ¶ at the reaction site, which is determined by the change in the interaction of the valence-nonbonded chain atoms. The energy of this 'adjustment' is much smaller for soluble macroligands than the energy of chelation, so that the structure of the coordination centres is usually determined by the nature of the complex-forming metal. For example, in the interaction of an iron(III) salt with polystyrene, containing acetylacetone (acac) groups, the 'adjustment' of the polymer chain takes place in such a way that the octahedral structures **12** are formed without appreciable strain.[24]



12

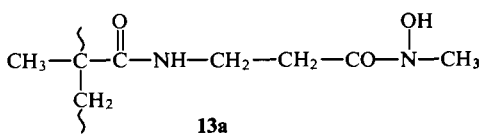
¶ In conformity with the definition given by Landau and Lifshitz,[23] the 'local rigidity' is understood as the resistance to bending of a uniform straight linear filament.

Table 2. Spectroscopic and magnetic characteristics of the monomeric and polymeric nickel and cobalt chelates with ligands of the Bipy and Phen types.

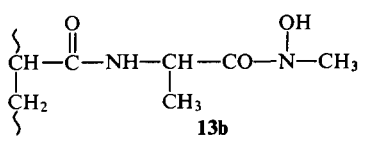
Complex	M	L	IR spectrum (principal frequencies)/cm^{-1}			Dq/cm^{-1}	B'/cm^{-1}	β	μ_{ef}/B.M.
			ν(C=C)	ν(heterocycle)	ν(COO$^-$)				
Monomer	Ni	Bipy	1635	1605	1565	1134	773	0.743	3.16
Polymer	Ni	Bipy	1639	1606	1560	1028	837	0.804	2.96
Monomer	Co	Bipy	1637	1610	1560	1152	834	0.859	4.53
Polymer	Co	Bipy	1638	1608	1560	1018	883	0.909	4.75
Monomer	Ni	Phen	1637	1600	1565	1166	830	0.797	3.17
Polymer	Ni	Phen	1640	1600	1560	990	857	0.823	2.95
Monomer	Co	Phen	1635	1605	1565	1163	849	0.874	4.75
Polymer	Co	Phen	1639	1608	1565	1016	884	0.911	4.87

The change in the 'local rigidity' can influence significantly the stereochemistry of the chelate unit formed. Thus the monomeric and polymeric nickel(II) and cobalt(II) chelates with ligands (L) of the type of 2,2'-bipyridyl (Bipy) and 1,10-phenanthroline (Phen) have similar spectroscopic and magnetic characteristics (Table 2), indicating the same steric structure of the chelate units.[25] On the other hand, a decrease in the splitting parameter Dq and an increase in the Racah interelectron repulsion parameter B' have been observed on passing from LMC to MMC. Bearing in mind[26] that $Dq \sim 1/a$,[6] one can assume that the decrease in the splitting parameter indicates an increase in the metal–ligand distance a in the given series. Furthermore, the nephelauxetic parameter β increases in the same series, which indicates a decrease in the degree of covalence in the metal–ligand bond. A consequence of this is, for example, a weakening of the exchange interactions on passing from low-molecular-mass dinuclear nickel(II) chelate complexes of *N*-acylsalicylamides[27] to their polymeric analogues.[28,29] It is known[30] that the bond lengths are altered less than the bond angles, so that a more pronounced distortion of the bond angles compared with the bond lengths can be expected in the MMC.

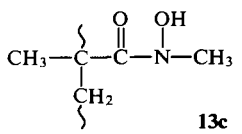
A contribution arising from the 'neighbouring groups' effect also appears in the case of the MMC. This contribution is associated with the influence of both reacted and unreacted units on the free energy of formation of the chelating fragment and hence on the structure of the chelate unit. This effect, which is explained mainly by steric factors, leads to the repulsion of the chelate units and their deformation, hindering chelate formation as the degree of conversion increases. For example, the octahedral iron(III) complexes of hydroxamic acid copolymers **13a–c** are formed without appreciable strain only when the chelating fragments are separated by 11 atoms (compounds **13a**).[31] When the number of atoms between the hydroxamic groups is $t = 7$, a slight strain arises, whereas in the case where $t = 1$ (compound **13c**) the complexes are not formed at all (Fig. 2).



13a



13b



13c

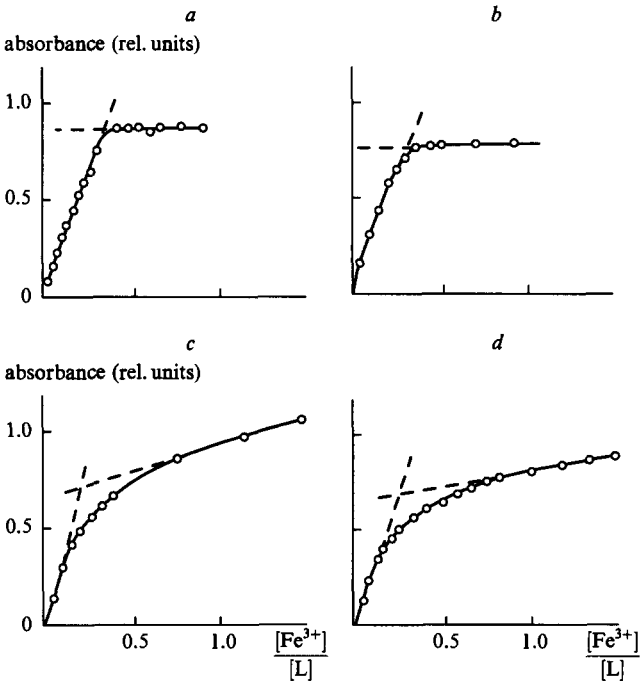
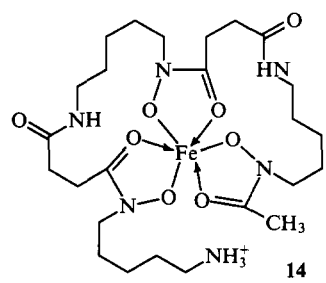


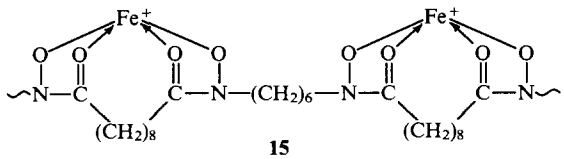
Figure 2. Determination of the composition (inflexion point) of the iron(III) complexes of deferrioxamine (*a*) and poly(hydroxamic acids) **13a** (*b*), **13b** (*c*), and **13c** (*d*).

It is noteworthy that the hydroxamic groups in deferrioxamine **14** [a low-molecular-mass ligand with a high selectivity with respect to iron(III) ions] are separated by nine atoms.



14

In contrast to copolymers containing hydroxamic groups, the formation of complexes with [M]:[L] = 1:3 is not characteristic of the homopolymer — poly(hydroxamic acid).[32] In the presence of the $-(CH_2)_8-$ bridge, the 1:2 complexes **15** are formed preferentially, whereas in the case of the bridge having the composition $-(CH_2)_6-$ a considerable strain arises, as a consequence of which the formation of octahedral complexes becomes impossible.



15

Bulky chelating ligands arranged side by side in the polymer chain preclude exchange interactions between metal ions even at a high concentration of the latter. For example, an increase in the number of copper(II) ions bound to poly(hydroxyphenylbenzoxazole-terephthalamide) (complex **5**) leads to a broadening of the EPR spectral lines as a consequence of magnetic dipole–dipole interaction between the paramagnetic centres (Fig. 3) due to the decrease in the distance between them.[17]

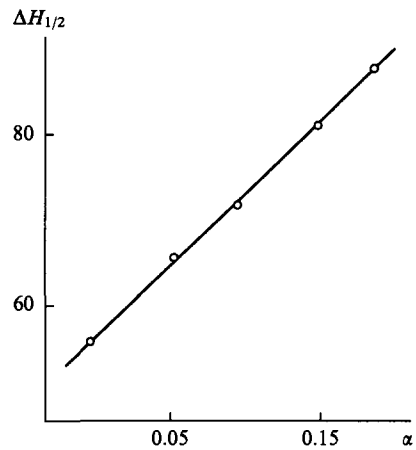


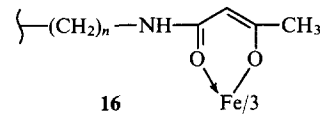
Figure 3. Dependence of the line half-width ($\Delta H_{1/2}$) on the degree of conversion for the copper(II) complex of poly(hydroxyphenylbenzoxazole-terephthalamide) **5**.

However, even for the minimum binding of copper(II) ions to the polymer, the spectrum is not fully converted into a singlet, which indicates the occurrence of exchange interactions between the metal ions. It is known[33] that cooperative effects begin to be manifested over distances of 6–9 Å; consequently the minimum distances between neighbouring copper(II) ions in such MMC exceed this quantity. This distinguishes such complexes from, for example, the copper complexes of linear polyethyleneimine (PEI), in which there is no steric hindrance to exchange interactions between the metal ions.[34] On the other hand, the uncoupling of the chelating fragments leads to the appearance of unfavourable entropy factors. In particular, a decrease in the stability constant ($\lg K$) is observed on passing from the picolinic acid-based LMC to its macromolecular analogue (the copolymer of styrene and vinylpicolinic acid [M = Cu, Ni, Co, Zn, or Mn (Table 3)].[35]

Table 3. The values of $\lg K$ for metal complexes of picolinic acid (A) and its polymeric analogue (B) (dioxane–water).

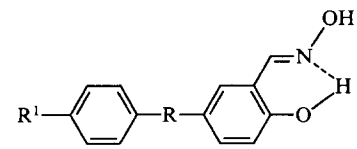
Ligand	Cu^{2+}	Ni^{2+}	Co^{2+}	Zn^{2+}	Mn^{2+}
A	12.80	12.70	12.50	12.72	9.50
B	9.88	9.56	8.28	8.44	8.44

If the chelating fragment is in a side chain, the influence of the main chain depends on the length of the connecting bridge and when the latter increases the difference between the LMC and the MMC vanishes. For example, for type **16** MMC, starting with $n = 2$, the stability of the complexes becomes virtually the same.[36]



16

The chelation process is greatly influenced also by the nature of the connecting bridge between the chelating fragment and the polymer chain. For example, the transfer of copper(II) ions from the aqueous to the organic phase (chloroform, toluene) in the formation of a complex with a hydrophobic low-molecular-mass ligand (compound **17a**) takes place very readily. On the other hand, chelation by its polymeric analogue **17b** takes place ineffectively and only the replacement of the short and hydrophobic methylene bridge in compound **17b** by the long hydrophilic ethylenediamine (compound **17c**) or methylamine (compound **17d**) unit imparts appreciable hydrophilicity and spatial mobility to the chelating fragments, which promotes the diffusion of ions in the polymeric medium and renders the ligands bound to the polymer more mobile.[37]



17a–d

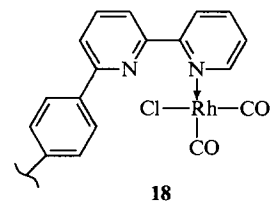
R = CH_2, R^1 = CH_3 (**a**)

R = CH_2, R^1 = polystyrene (**b**)

R = $NHCH_2CH_2NH$, R^1 = polystyrene (**c**)

R = CH_2NH, R^1 = polystyrene (**d**)

On the other hand, if the polymer chain gives rise to hindrance to the formation of chelate complexes, as in the case of polystyrene with bipyridyl groups fixed in the 4-position in the benzene ring,[38] then monodentate binding of the metal with formation of compound **18** is observed.



18

In other words, the selection of the macroligand makes it possible to follow the multistage mechanism of the formation of the MMC, to isolate the intermediates, and to stabilise the unstable (in the case of low-molecular-mass analogues) complexes.

Thus on the local level the free energy changes are similar when the components of the model reaction involving the LMC and the MMC are chosen correctly. However, it is then necessary to take into account the polymeric nature of the chelating ligand and the contributions arising from this factor to the entropy of chelation. If one considers the reaction

$$[CuX]^+ + Y^- \rightleftharpoons [CuY]^+ + X^-, \quad (5)$$

where Y = poly(amidoamine) and X = its low-molecular-mass analogues, the contribution of the transfer process is zero (the number of species remains unchanged). The free energy change can then be found from the equation

$$\Delta G = -2.303\,RT \lg K = -A_{es} - TS_{st}\,, \quad (6)$$

where A_{es} is the loss of electrostatic energy when the positively charged cation moves away from the negatively charged heteroatom on the polymer to infinity, S_{st} is a statistical factor, and $\lg K$ is defined by the expression

$$\lg K = \lg K_{[CuY]^+} - \lg K_{[CuX]^+} \quad . \tag{7}$$

The enthalpy and entropy of the ligand exchange process (5) are estimated by means of the equations

$$\Delta H = -A_{es}\left[1 + \frac{T}{\varepsilon}\frac{\delta\varepsilon}{\delta T}\right] , \tag{8}$$

$$\Delta S = -A_{es}\left[\frac{1}{\varepsilon}\frac{\delta\varepsilon}{\delta T}\right] + S_{st} , \tag{9}$$

where ε is the effective relative permittivity. As was in fact to be expected, ΔH for this process is zero,[39,40] which indicates an isotypical ligand environment of the copper(II) ions in the LMC and the MMC. On the other hand, the entropy component varies with increasing degree of conversion from positive to negative values (Table 4). It attains zero (i.e. the ΔG for the LMC and the MMC are equal) when half of the negative charges on the polymer are bound to the copper(II) ions or, in other words, when the numbers of the positive and negative charges on the polymer are found to be equal. On the other hand, further addition of copper ions results in the preferential concentration of positive charges on the polymer.

Table 4. Thermodynamic functions of the ligand exchange reaction (5).

$\Delta(\lg K)$	$-\Delta G$/kJ mol^{-1}	TS_{st}/kJ mol^{-1}	S_{st}/J mol^{-1} K^{-1}
0.65	3.72	3.72	12.5
0.45	2.55	2.55	8.6
0.31	1.76	1.76	5.9
0.22	1.26	1.26	4.2
0.06	0.33	0.33	1.1
0.01	0.74	0.04	0.1
−0.02	−0.13	−0.13	−0.4
−0.10	−0.59	−0.59	−2.0
−0.13	−0.75	−0.75	−2.5
−0.20	−1.13	−1.13	−3.8
−0.40	−2.30	−2.30	−7.7
−0.49	−2.80	−2.80	−9.4
−0.73	−4.18	−4.18	−14.0

III. The molecular level of the structural organisation of metallopolymers

With increase in the degree of conversion and/or decrease in the length of the polymer chains, it is necessary to take into account the molecular level of the spatial organisation of the MMC. We shall analyse initially the influence of the degree of conversion on the chelation process for a fixed length of the polymer chains.

The effect consisting in the change of the chain conformation, which is observed after the attainment of a certain degree of conversion and involves different numbers of monomer units, is most frequently manifested. There is then a possibility of both a helix–coil transition, characteristic of charged chains, and of a change in the preferential conformation of the statistical coil.[41] Conformational transitions have been detected in linear poly(amidoamines) on protonation and complex formation.[19] Thus viscometric titration showed that the viscosity of the linear polymer **19** decreases monotonically with increase in the pH (Fig. 4). Analysis of the superposition of the distribution curve on the pH dependence of the viscosity shows that the ratio of the specific viscosity and the concentration (η_{sp}/c) decreases on completion of the formation of the complex CuL and then remains virtually constant until the deprotonation of the ligand is completed. The second small jump corresponds to the formation of HL_2^+ and can be explained by a conformational transition.[39]

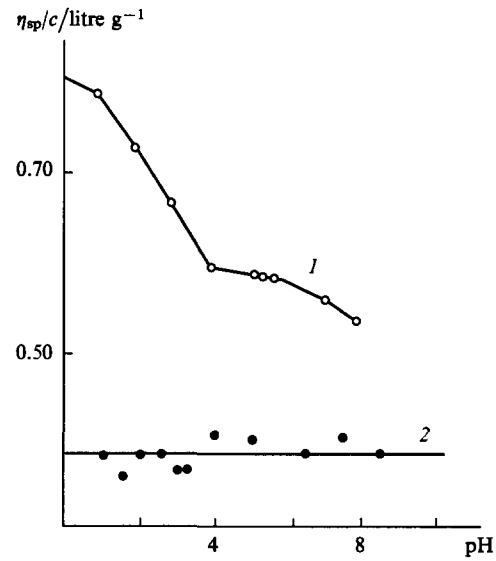
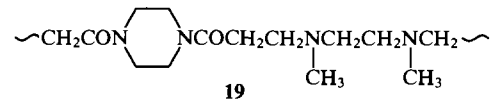
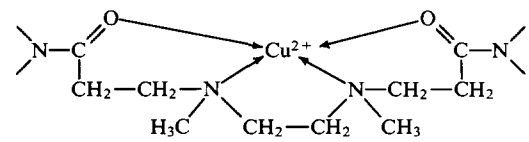


Figure 4. The viscosity and the distribution curves as a function of pH for the copper (II) complexes of linear (compound **19**, curve *1*) and branched (compound **21**, line *2*) poly(amidoamines).

In other words, the involvement in the reactions of the nitrogen atoms of the main chain is accompanied by conformational transitions which influence the properties of the entire macromolecule, since the junctions between different monomer units (six-membered diacylpiperazine chelate rings in complex **20**) are very rigid.

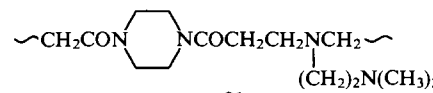


19



20

In the case of the branched polymer **21**, appreciable deviations of η_{sp}/c from a constant value are not observed over the entire pH range (Fig. 4).[40] The weak dependence of the viscosity on the pH and on the degree of conversion for this polymer is unusual and is probably due to the fact that the conformational transition associated with complex formation involves only the side substituents and does not affect significantly the characteristics of the main chain.



21

It has been established[42] that, for the poly-L-lysine.heme and poly-L-lysine.hemin complexes at low degrees of conversion, the fraction of the α-helical structure and the viscosity of the solution do not change. This result shows that the MMC obtained is intramolecular and that the helical structure can be represented schematically in the form of complex **22**. If the degree of conversion exceeds 0.1, then the fraction of the helical structure diminishes, which indicates the existence of steric hindrance to its establishment owing to the coordination of the bulky complexes **23**.

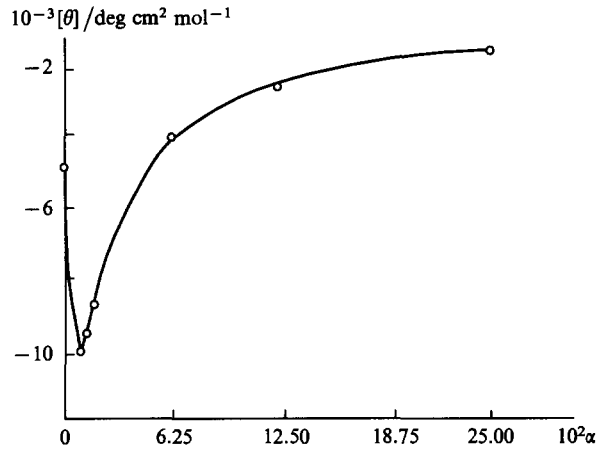
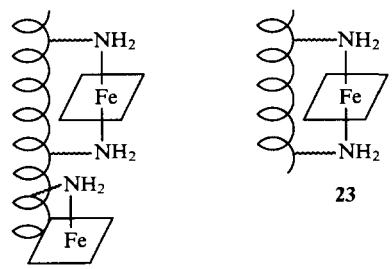


Figure 5. Dependence of the ellipticity θ of poly-*N*(5)-(3-hydroxypropyl)-L-glutamine on the degree of conversion of the Cu^{2+} ions.



In the interaction of copper(II) ions with poly-*N*(5)-(3-hydroxypropyl)-L-glutamine up to a degree of conversion of 6.25×10^{-2}, the α-helical conformation predominates, whilst above this conversion the chain conformation changes (Fig. 5).[43]

The helix – coil transition may be observed in the copper(II) – poly-L-glutamic acid system when a change takes place both in the ratio $[M^{2+}]/[L]$ (Fig.6) and in the pH of the solution for a fixed $[M^{2+}]/[L]$ ratio (Fig.7).[44] If the degree of neutralisation is

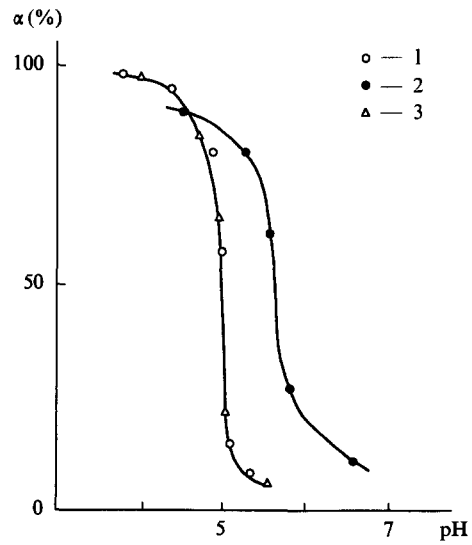


Figure 6. Dependence of the content of the α-helium (α) in poly-L-glutamic acid (*1*) and in its copper complex on pH for $[Cu^{2+}]/[L] = 0.1$ (*2*) and 0.02 (*3*).

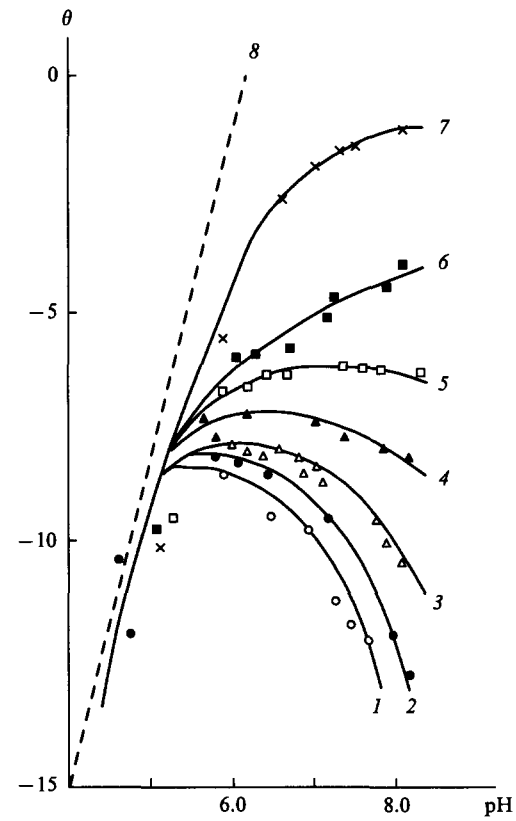


Figure 7. Relation between the molar ellipticity at 222 nm and the pH of Cd^{2+} – polyglutamic acid solutions for different ratios $[Cd^{2+}]/[L]$: (*1*) 1.5; (*2*) 1.0; (*3*) 0.77; (*4*) 0.5; (*5*) 0.4; (*6*) 0.3; (*7*) 0.15; (*8*) 0.0.

less than 0.2, i.e. the polyaminoacid has a helical structure, then the Cu^{2+} ions are hardly bound by the polymer. On the other hand, the interaction of these ions with poly-L-lysine leads to the formation of complexes containing a polymer in the α-helical conformation.[45,46] It is interesting to note that, when Cu^{2+} ions are added, poly-D-lysine undergoes a conformational transition, whereas the addition of other ions, for example, Zn^{2+}, Mg^{2+}, Mn^{2+}, or Ca^{2+}, has no effect whatever on the polymer conformation.[47]

Electrostatic, hydrophobic, or hydrophilic interactions between the components may exert an appreciable influence on the chelation of metal ions. On formation of charged chains, the macromolecules is stretched as a result of the reaction with the metal ion as the degree of conversion increases. Thus the introduction of metal cations into the cavity within the macrocycles of the homopolymers of vinylcrown-ethers may alter significantly the conformation of the polymer chain. In the initial state, such polymers are typical micelles, in which the nonpolar hydrocarbon 'tails' are collected in a coil, whilst the polar 'heads' (crown ethers) emerge into the solution surrounding the micelle. On complex formation, the polymeric crown-ethers are converted into polyelectrolytes, which leads to electrostatic repulsion of the monomer units. This interaction results in the uncoiling of the coil and the assumption by the polymer of the extended chain conformation.[48]

The formation of a complex between uncharged polyvinylpyrrolidinone and copper(II)-chlorophyllin is accompanied by the formation of hydrogen bonds, which leads to a sharp increase in the viscosity of the solution.[49]

The hydrophobic interaction of the LMC with the macroligand is also important. This has been clearly shown in relation to the formation of complexes between heme and water-soluble polmers — poly(ethylene oxide), poly(vinyl alcohol), and polyvinylpyrrolidinone.[50] It was found that the equilibrium between

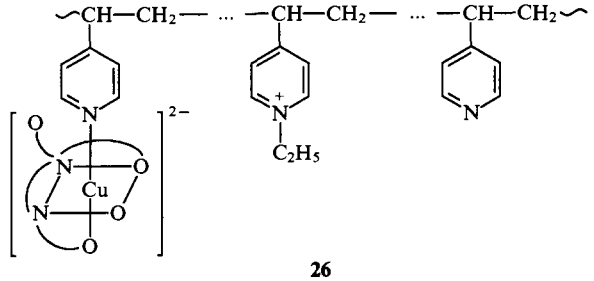
the monomeric and dimeric forms of heme, which obtains in aqueous solution, is fully displaced towards the monomeric form at a high concentration of the polymeric ligand. This effect increases with increasing hydrophobicity of the polymer in the series polyvinylpyrrolidinone > poly(ethylene oxide) > poly-(vinyl alcohol), which led to the conclusion that there is a hydrophobic interaction between heme and the polymer.

Table 5. Stability constants of complexes **26**.

CuX^{n-}	Ligand				
	4-ethyl-pyridine	P4VP	QP4VP (20)[a]	QP4VP (25)[a]	QP4VP (61)[a]
24	72	60	123	–	240
25	70	48	–	870	1100

Note. Reaction conditions: aqueous methanol (1:1 by volume), ionic strength of solution 0.1 M, pH 8, T = 298 K.
[a] Here and in Table 6 the numerals in brackets denote the degree of quaternisation.

The macroligand may contain positively or negatively charged atoms, which either promote or interfere with its interaction with metal ions (although they do not in fact influence significantly the formation of a direct chemical bond involving them). This has been noted in a study of the interaction of CuX^{n-}, where X = ethylenediaminetetraacetate (complex **24**) or *N*-(2-hydroxyethyl)ethylenediamine-*N,N',N'*-triacetate (complex **25**), with quaternised poly-4-vinylpyridine (QP4VP) in the formation of type **26** complexes.[51] The stability constants of these complexes (Table 5) increase with increase in the degree of quaternisation despite the fact that steric hindrance should increase in this case. Evidently this is caused by an electrostatic effect; the local concentration of CuX^{n-} should increase with increasing degree of quaternisation by virtue of the Coulombic interaction between the polycation and CuX^{n-}. An increase in the charge on the initial LMC increases its affinity for the polycation and the stability constants also increase in the same sequence.



26

The degree of conversion of metallochlorophyllins (M = Co^{3+}, Fe^{3+}, Ni^{2+}, Cu^{2+}, or Zn^{2+}) in the interaction with QP4VP proved to be unity.[52] The stability constants of these complexes were $\sim 10^3$ litre kg mol^{-1}, i.e. were greater than for the low-molecular-mass analogues. In all probability, the stability of the complexes of the metallochlorophyllins with QP4VP is determined by the electrostatic binding of the carboxylate anion of the LMC to the quaternary pyridinium cation in the polymer chain.

Similar conclusions were reached[51] also in a study of the formation of complexes of methylaquocobaloxime† with pyridine-containing ligands [reaction (10)]. In this case, the stability constants decreases in the sequence 4-ethylpyridine > P4VP > QP4VP(25) > QP4VP(61). The steric hindrance exerted by the polymeric ligand and the positive charge density increase in the same sequence.

† MeCo(dimethylglyoxime monoanion)$_2H_2O$ (Ed. of Translation).

Table 6. The stability constants and rates of formation of complexes by reaction (10).

Constant (method of determination)	Ligand			
	4-ethyl-pyridine	P4VP	QP4VP (25)	QP4VP (61)
K/litre mol^{-1} (a)	3.5×10^3	1.7×10^3	5.3×10^2	95
K/litre mol^{-1} (b)	3.3×10^3	1.8×10^3	4.9×10^2	1.4×10^2
k_1/litre mol^{-1} (a)	20	18	8.4	2.5
k_{-1}/s^{-1} (b)	5.3×10^{-3}	1.0×10^{-2}	1.6×10^{-2}	2.6×10^{-2}
k_{-1}/s^{-1} (a)	6.0×10^{-3}	9.9×10^{-3}	1.7×10^{-2}	1.8×10^{-2}

Note. Method: (*a*) kinetic [aqueous methanol (3:7 by volume), ionic strength of solution 0.05 M, pH 8, T = 298 K]; (*b*) spectrophotometric.

$$CH_3Co(DH)_2H_2O + L \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} CH_3Co(DH)_2L + H_2O \quad (10)$$

(DH = dimethylglyoxime)

Chelation makes it possible comparatively frequently to stabilise conformational and tautomeric forms uncharacteristic of the initial polymer. Thus the addition of the [(2,2',2'',2'''-tetrapyridyl)iron]$^{3+}$ ions to solutions of sodium poly(L-glutamate) increased the content of the α-helical form at pH values where the coil usually predominates.[53] In other words, the metal ion selects the polymer chain conformation which it prefers most.

The chain conformation is determined by many factors (for example, the nature of the solvent) which exerts a significant influence on the entire chelation process. Thus, in the interaction of poly(2-methyl-*N*-vinylimidazole) with the $CoCl_3(en)_2$ system, where en = ethylenediamine, in $H_2O-C_2H_5OH$ mixture, an increase in the ethanol content from 0 mass% to 10 mass% entails a decrease in thermodynamic parameters: from 46.5 to 43.6 kJ mol^{-1} in ΔG, from 97.2 to 41.5 kJ mol^{-1} in ΔH, and from 164.3 to 47.3 J K^{-1} mol^{-1} in ΔS.[50] The solvent also significantly influences the rate constants for forward (k_1) and reverse (k_{-1}) ligand exchange reactions [reactions (11)] (Fig. 8).[54] This can be accounted for by the variation of the conformation of the polymeric ligand as a function of the nature of the solvent; the rate of the ligand exchange reaction of cobaloximes with polymeric ligands, such as the styrene–4-vinylpyridine copolymer, may be controlled by varying the conformation of the macroligand.

$$K = \frac{[ClCo(DH)_2L][DMF]}{[ClCo(DH)_2DMF][L]}$$

$$ClCo(DH)_2DMF + L \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} Cl \cdot Co(DH)_2L + DMF \quad (11)$$

The rate constants for the chemical decomposition (k_{decomp}) of the complex between cobaloxime and the styrene–chloromethylstyrene copolymer proved to be smaller by a factor of 4 than the low-molecular-mass benzylcobaloxime (Table 7).[55] This can be explained by the fact that the diffusion of divalent cobalt complexes, formed in the homolytic photochemical decomposition, proceeds less easily as a consequence of steric hindrance by the polymer chain. Furthermore, the alkyl radicals formed are retained by the polymer; the probability of their recombination thus increases compared with the monomeric analogues. However, this type of effect has not been observed in dimethyl sulfoxide (Table 7), because in this solvent cobaloximes are

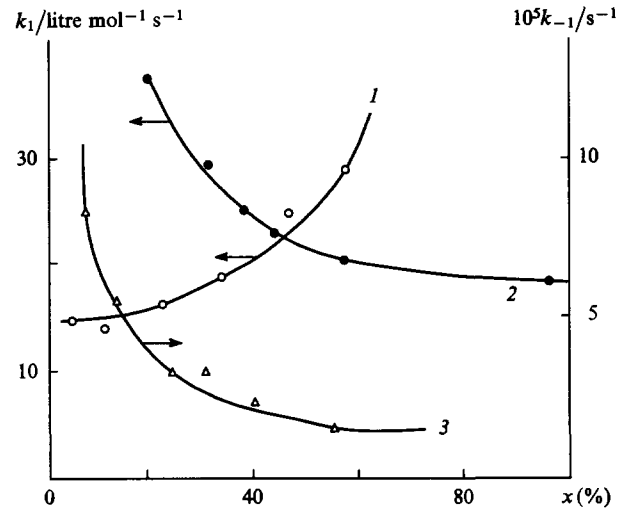


Figure 8. Dependence of the rate constants for the forward (k_1) and reverse (k_{-1}) reactions on the content (x) of 4-vinylpyridine units in the copolymer: (*1*) in benzene; (*2*) and (*3*) in DMF.

localised on the surface of the polymer coil and are not subjected to steric hindrance due to the polymer chain. In mixed solvents (DMSO–benzene), the ratio of the rate constants for the decomposition of the polymer (k^P) and the monomer (k^m) diminishes with increase in the benzene content (Fig. 9). It follows from measurements of the viscosity of the polymer to which cobaloxime is attached that the polymer chain becomes 'extended' with increase in the benzene content in the solvent. Thus the decrease in the rate constant for the photochemical decomposition of the polymer-bound cobaloxime with increase in the benzene content in the solvent is apparently caused by the extension of the polymer chain.

One of the characteristic features of the chelation reaction involving polymeric ligands on the molecular level is the 'neighbouring group' effect caused both by the interaction of the neighbouring chelating fragments and by the statistical nature of the entire chelation process.[56] If blocks containing a smaller number of active centres (functional groups) than required for

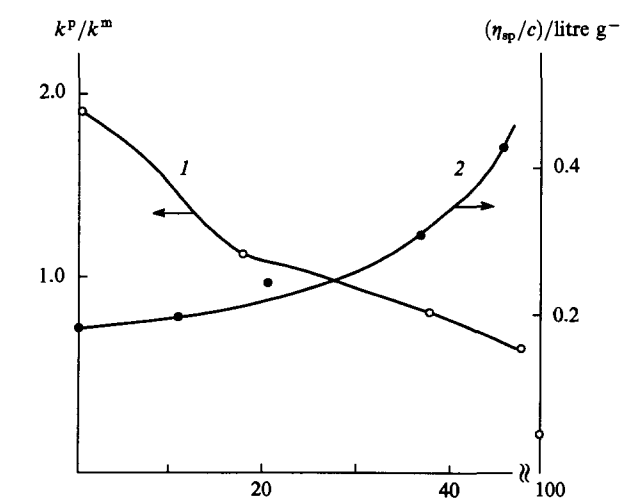


Figure 9. Variation of the relative rate constant (k^P/k^m) for the photochemical decomposition of alkylcobaloximes (curve *1*) and of the ratio η_{sp}/c (curve 2) for MMC as a function of the benzene content in the solvent.

Table 7. Rate constants for the photochemical decomposition of alkylcobaloximes[a]

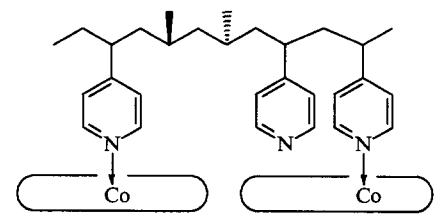
$$RCo(DH)_2L \overset{h\nu}{\rightleftharpoons} R^{\cdot} + Co(DH)_2L$$ [a]

R	Solvent	Irradiation region/nm	$10^2 k_{decomp}$/ s^{-1} [b]
Benzyl	benzene	entire region	4.6
	DMSO	"	1.0
	DMSO	> 350	1.1
	DMSO	> 450	1.1
	DMSO	> 550	< 0.1
Polymer [c]	benzene	entire region	1.1
Polymer [d]	DMSO	entire region	1.4
	DMSO	"	1.4
	DMSO	> 350	1.0
	DMSO	> 450	0.9
	DMSO	> 550	< 0.1

[a] L = Py, C_6H_6, or DMSO.
[b] k_{decomp} was measured on irradiation with light from a tungsten lamp with a constant photointensity.
[c] Contained 8.1 mol% of the cobaloxime.
[d] Contained 2.1 mol% of the cobaloxime.

chelation to the metal ion remain unreacted during the chelation process, then such blocks no longer participate in the coordination, i.e. the concentration of the unreacted centres is not equal to the active concentration of the reacting species. Here it is necessary to take into account the fact that the fraction of the monomer units capable of coordination, among all the unreacted monomer units, depends on the degree of conversion. Various ways of binding the metal to the macroligand are possible.[41] Thus, if there are q metal ions on the chain containing m active centres, then the number of complexes formed, having different structures, is c_m^q (the number of combinations of q molecules with m chain centres).

Low-molecular-mass cobalt(II) chelates, for example of ethylenediamine, have a fairly large volume (diameter about 10 Å), so that during their coordination, even when a close packing is produced, some P4VP units remain uncoordinated for steric reasons (complex **27**).



27

The calculated maximum degree of conversion of P4VP is in this case 0.63, which is close to the experimental values (Fig. 10, see over). A complex of this kind has a rigid rod-shaped structure, in which the mobility of the Co^{2+} chelate is much smaller than that of the monomeric analogues. The decrease in the g-factor in the EPR spectrum of the complex *cis*-$[Cr(en)_2(P4VP)Cl]Cl_2$ with increase in the degree of conversion indicates a decrease in the symmetry of the Cr^{3+} complex (D_{4h}).[8] Such disburbance of the anisotropy is caused by the steric hindrance generated both by the P4VP ligands and the fixed chelates.

For the vinyl imidazole copolymers, the number of ligands axially coordinated to heme is about two, decreasing with decrease in the 1-vinylimidazole content in the copolymer (Table 8, see over). A favourable contribution by the entropy factor, associated according to the authors[57] with the high apparent concentration of the functional groups in the polymer

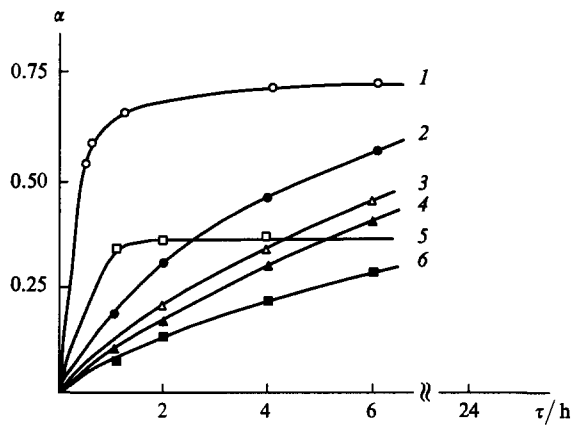


Figure 10. Kinetic curves for the formation of MMC; [chelate] = 0.05 M, [chelate]:[L] = 1, solvent $C_2H_5OH-H_2O$, 353 K: (*1*)Co(acac)$_2$.(P4VP)NO_2; (*2*) $[Co(en)_2(PEI)Cl]Cl_2$; (*3*) $[Co(en)_2(P4VP)Cl]Cl_2$; (*4*) $[Co(en)_2(QP4VP)Cl]Cl_2$ (R = CH_3); (*5*) $[Cr(en)_2(P4VP)Cl]Cl_2$; (*6*) $[Co(en)_2(QP4VP)Cl]Cl_2$ (R = $CH_2C_6H_5$).

Table 8. Parameters of the formation of complexes between heme and the polyvinylimidazole homopolymer and the vinylimidazole–vinylpyrrolidinone copolymer.

Ligand	α	K/litre mol^{-1}	ΔH/kJ mol^{-1}	ΔS/J mol^{-1} K^{-1}
Homopolymer	1.6	1.6×10^4	–	–
Copolymer (50)[a]	1.3	3.1×10^4	−16.8	30.7
Copolymer (20)[a]	1.2	3.2×10^4	–	–
Copolymer (10)[a]	0.9	4.1×10^4	−22.6	13.0
1-Ethylimidazole	1.3	4.8	−23.0	−42

[a] The numerals in brackets denote the vinylimidazole content in the copolymer.

matrix, is observed. Therefore in most cases the stability constant of the MMC is higher by a factor of 10^2-10^4 than the corresponding constant for the low-molecular-mass analogues.

The pyridine-containing ligands can be arranged in the following sequence in terms of the calculated equilibrium constant (Table 9) of the ligand exchange reaction

Table 9. Equilibrium constants of the ligand exchange reaction (11) as a function of the ligand composition.

Ligand	$10^{-5}K$/litre mol^{-1}
Pyridine	0.68
Styrene–4-vinylpyridine copolymer with different contents of 4-vinylpyridine units (%)	
9.8	0.45
13	1.0
24	1.2
32	1.4
41	1.9
53	1.5
100	0.085

Note. Solvent–DMF (at 20 ± 0.5 °C).

Table 10. Thermodynamic parameters of the ligand exchange reaction (11).

Ligand	ΔG/kJ mol^{-1}	ΔH/kJ mol^{-1}	ΔS/J mol^{-1} K^{-1}
Pyridine	−27.2	−14.2	42
P4VP	−22.2	−8.0	50.4
Styrene–4-vinylpyridine copolymer[a]	−29.3	−6.3	79.8

Note. Solvent–DMF (at 20 ± 0.5 °C).
[a] Content of 4-vinylpyridine units 32%.

[Eqn (11)]: styrene–4-vinylpyridine copolymer (13%–53% of 4-vinylpyridine) > Py > styrene–4-vinylpyridine (10% of 4-vinylpyridine) copolymer > poly-4-vinylpyridine.[54] The distance between the pyridine fragments in P4VP is so short that not all the 4-vinylpyridine groups can function as ligands owing to the steric hindrance generated by the coordinated cobaloximes. In the case of the copolymer containing 13%–53% of 4-vinylpyridine fragments, where the steric hindrance between the cobaloxime moieties may be neglected, the equilibrium constant is higher than for the low-molecular-mass analogue (Py). This is also indicated by the calculated thermodynamic parameters of the ligand exchange reaction (Table 10).

The rate of formation of the cobalt chelates with the partly quaternised P4VP diminishes in the following sequence of groups R (the group in the quaternising agent): H > CH_3 > $CH_2C_6H_5$ (Fig. 10), which is due to the steric hindrance arising from the polymeric ligands.[58]

The use of polymeric crown-ethers for the formation of [L]:[M] = 2:1 complexes with a sandwich structure (Fig. 11), i.e. in those cases where the size of the cavity within the macrocycle is too small for the formation of 1:1 complexes, proved to be effective. This is clearly seen in relation to the interaction of the potassium ion with the 15-crown-5-ether (the constant for the extraction of potassium picrate is 0.42×10^3 mol^{-2}) and with its polymeric analogue (extraction constant 2.3×10^3 mol^{-2}). The greater effectiveness of the polymeric crown-ethers in the formation of the 2:1 complexes is caused by the high local concentration of the macrocycles in the polymer chain, which entails the single-stage binding of the metal ion by two neighbouring fragments (Fig. 11). However, one should note that the examination of the macromolecular models of the complexes indicates that the involvement in complex formation of, not neighbouring, but alternate monomer units is preferable.[59]

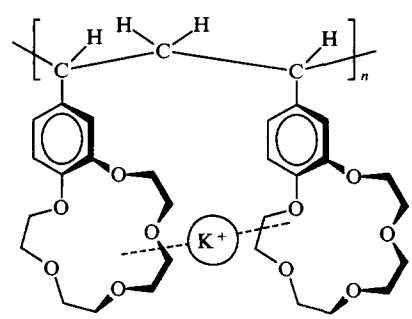


Figure 11. The structure of the sandwich type complex formed by the K^+ ion and the polyvinylbenzo-15-crown-5.

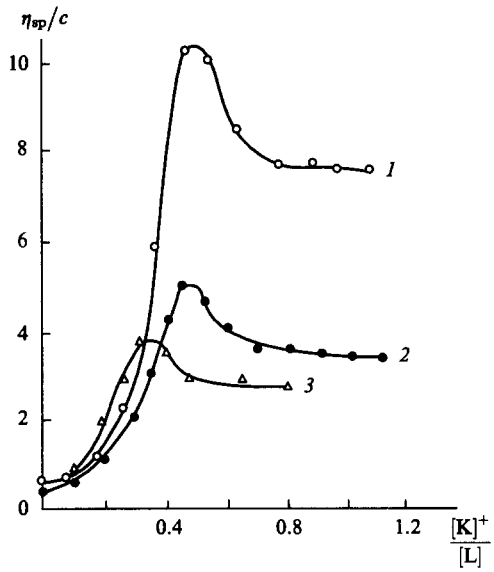
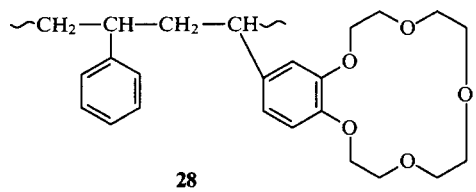


Figure 12. Dependence of the viscosity of the styrene–vinylbenzo-15-crown-5 copolymer on the ratio $[K^+]:[L]$ for different contents of the chelating fragments (%): (*1*) 18; (*2*) 11.8; (*3*) 5.8.

The results of viscometric measurements have shown (Fig. 12) that the maximum values of η_{sp}/c in the potassium ion–copolymers **28** system corresponds to the 2:1 complex and that the content of the crown-ether units does not exceed 20%. In other words, intramolecular metal chelates are formed only when the chelating fragments are separated by less than four (on average) styrene units.[60]



28

In the formation of the MMC, the first step may be regarded as a second-order reaction (first-order with respect to each component), while all the subsequent steps (with formation of the chelate rings) may be regarded as first-order reactions. The overall formation of metal chelates with a single chain is a second-order reaction. Since the rates of complex formation reactions are ususally high, it is difficult to distinguish experimentally the consecutive stages of the process. However, in those comparatively rare cases where this has been achieved the successive stability constants K_i as a rule increase with increase in the degree of conversion. Low-molecular-mass ligands behave differently. Thus, in the case of the low-molecular-mass pivaloylacetone and methacryloylacetone the ratio $K_1/K_2 = 1.08$ and 1.12 respectively (copper complexes are considered). On the other hand, the analogous ratio for polymethacryloylacetone[61] is 0.84, i.e. the stability constants increase with increase in the degree of conversion. This is a consequence of the cooperative 'chain effect', which involves a change in the shape of the macromolecule without change in the contour length on complex formation.[41,59] In particular, the interaction of metal ions with soluble polymers decreases the flexibility of the polymer chains with increase in the degree of conversion. This effect is manifested particularly clearly in the case of polymers containing biypyridyl units in the main chain.[62,63] Appreciable changes in the shape of the macromolecules of poly-2-vinylpyridine have been observed[64] in its interaction with cobalt acetylacetonate. The stability constant of the MMC in the case of polymeric ligands can be expressed in the form

$$K = \prod_{i=1}^{i=N} K_i = \sigma K_j ,$$

where $\sigma = K_i/K_{i-1}$ is the parameter of the cooperative effect, showing by what factor the stability constant increases as a result of each successive addition compared with the previous value. It has been postulated that all the consecutive stability constants, other than the first, are the same (since virtually the entire entropy is lost in the first step, the subsequent stages represent intramolecular cyclisation). The 'chain effect' is manifested by the high local concentration of the functional groups, so that the stability constant is not determined by the average concentrations of the components but by their local concentrations in the coils (as in microreactors).[65] After entering a region of a high local concentration of the functional groups, the metal ion immediately forms coordinatively saturated complexes, whilst the groups which remain free participate in the formation of a small number of coordinatively unsaturated structures.

The constancy of the composition of the complexes for different ratios of the reacting components (within wide limits) is a distinctive feature of the reactions of macroligands compared with their low-molecular-mass analogues: it is thermodynamically easier for a macromolecule to form coordinatively saturated complexes (even if their amount is smaller) than the unsaturated complexes. Thus a study of copper(II) complexes of a polymer aminated by ethylenediamine, diethylenetriamine, and trimethylenediamine demonstrated[66] small differences between the values of $A_{||}$ and $g_{||}$ as well as α^2 (the unpaired electron density on the coordination ion) for the LMC and the MMC (Table 11). These differences indicate the existence of some steric hindrance to the formation of the tetracoordinate complex CuN_4 in the case of the polymer. When the content of copper ions in the MMC is <0.05 mmol g^{-1}, the EPR spectrum is satisfactorily resolved and corresponds to isolated mononuclear complex species having the same composition. When the copper concentration increases, the EPR spectrum represents the superposition of an anisotropic multiplet (due to the isolated complexes) and a singlet with a g-factor of about 2.08–2.10. The amplitude of the latter increases with increase in the copper content in the MMC. The singlet is evidently due to the existence of regions with a higher local concentration of copper ions, where the distance between neighbouring ions does not exceed 7–9 Å and where there is a strong spin-exchange interaction between them. The composition of the copper complexes in such regions apparently correspond to the formulae CuN_4, CuN_3, CuN_2, or CuN—i.e. in the course of chelation coordinatively saturated complexes are formed initially as the degree of conversion increases and then coordinatively unsaturated complexes are produced.

In the case of an acrylic acid copolymer containing phenanthroline units, a 1:1 complex (this complex has the highest stability constant) and then a 1:2 complex are formed in succession with increase in the degree of conversion.[67] On passing from the

Table 11. Parameters of the EPR spectra of the copper complexes of a polymer aminated by polymethylene amines and of its low-molecular-mass analogues at 77 K.

Complex	$A_{\|} \pm 3$/G	$g_{\|} \pm 0.005$	$g_{\perp} \pm 0.005$	α^2
MMC	180	2.214	2.050	0.79
MMC[a]	175.5	2.205	2.049	–
Cu(en)	184	2.235	–	0.81
$Cu(en)_2$	190	2.201	2.045	0.80

[a] Temperature—298 K.

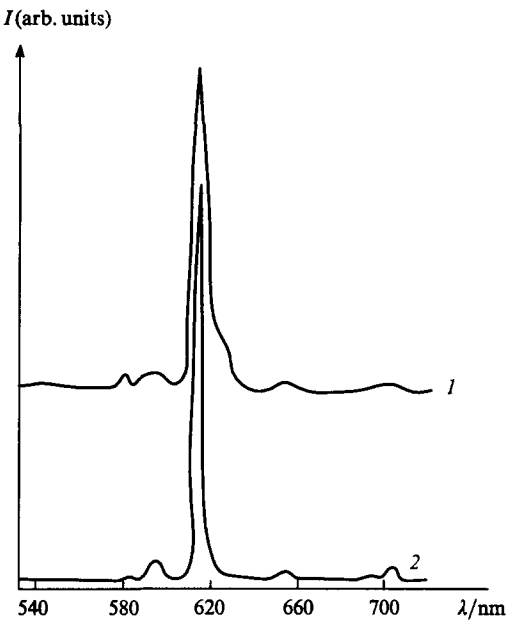
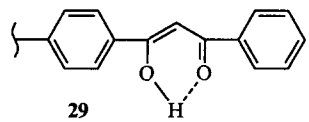


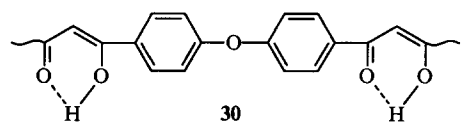
Figure 13. Emission spectra of the europium(III) complexes of poly-*p*-benzoylacetylstyrene (curve *1*) and dibenzoylmethane (curve *2*).

first complex to the second, a slight increase in $A_{||}$ and an appreciable decrease in α^2 (by 0.05) are observed, which indicates slight tetrahedral distortions of the coordination unit. This can be explained by the steric hindrance arising when four coordinated nitrogen atoms are located in a single plane.

Together with the main peak at 613 nm due to the $^5D_0 \rightarrow {}^7F_2$ transition (as in the low-molecular-mass analogue dibenzoylmethane), an additional peak at 580 nm, corresponding to the forbidden $^5D_0 \rightarrow {}^7F_0$ transition,[68] appears in the emission spectrum of the Eu^{3+} complex of poly(*p*-benzoylacetylstyrene) **29** (Fig. 13). The appearance of this peak is associated with the decrease in symmetry around the Eu^{3+} ion (owing to the steric hindrance arising in the formation of the polycyclic complex). An increase in the degree of conversion in this instance leads to the formation of 1:2 and 1:1 complexes with the [M]:[L] = 1:3 complex. The fluorescence intensity remains almost constant until the attainment of the maximum at low Eu^{3+} concentrations (Fig. 14). In other words, the maximum intensity corresponds to the 1:3 complex. When the β-diketone fragment is introduced into the main chain (the ligand **30**), the formation of 1:3 complexes becomes more difficult and the 1:2 complex, characterised by a low fluorescence intensity, becomes the main product.



29



30

The reaction of iron(III) ions with the low-molecular-mass ligand bipyridyl produced an equilibrium mixture of 1:1, 1:2, and 1:3 complexes, whereas the formation of only 1:1 chelate is characteristic of poly(6-vinyl-2,2′-bipyridyl).[69] Thus the polymeric ligand makes it possible to stabilise complexes having a specified composition.

One of the manifestations of the chain effect in metallopolymer systems is also the independence of the thermodynamic parameters of the chelation process of the chain length (molecular mass) of the polymeric ligand.[70] Thus, in the formation of copper(II) complexes of poly(hydroxamic acids), the stability constants of the latter diminish with increase in the molecular mass of the polymer (from 3000 to 15 000).[71] Fig. 15 presents the spectra of the copper complexes of methylhydroxamic acid and its polymeric analogues in the far infrared. In this case, the absorption band at 550 cm^{-1} in the IR spectrum of the LMC refers to the Cu–O and C–N bond vibrations. This band undergoes a bathochromic shift with increase in the molecular mass of the polymer. The band at 516 cm^{-1}, assigned to the deformation vibration of the ring and the O=C–C– group, shifts in the same direction. Bearing in mind that the order in which the frequencies of the stretching vibrations and their force constants vary corresponds to the order of the variation of the stability constants of the complexes of β-diketones, one may postulate that the stability of the copper complexes of poly(hydroxamic acid) diminishes with increase in molecular mass.[72]

The formation of low-molecular-mass chelates involving cobalt(II) and P4VP with a lower degree of polymerisation also proceeds more readily.

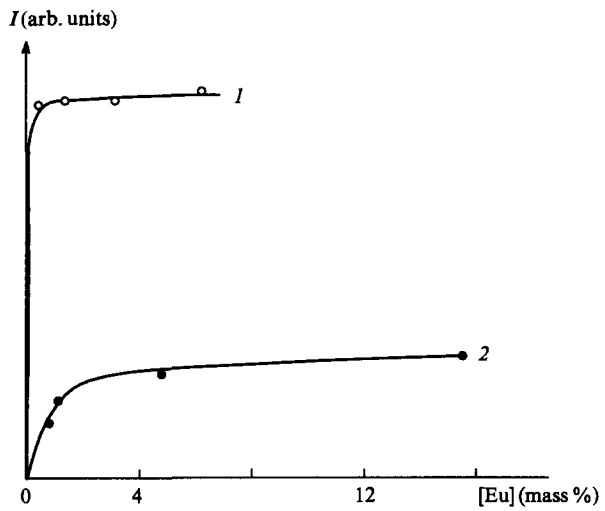


Figure 14. Dependence of fluorescence intensity at λ = 613 nm on the europium content in the macrocomplexes of **29** (curve *1*) and **30** (curve *2*).

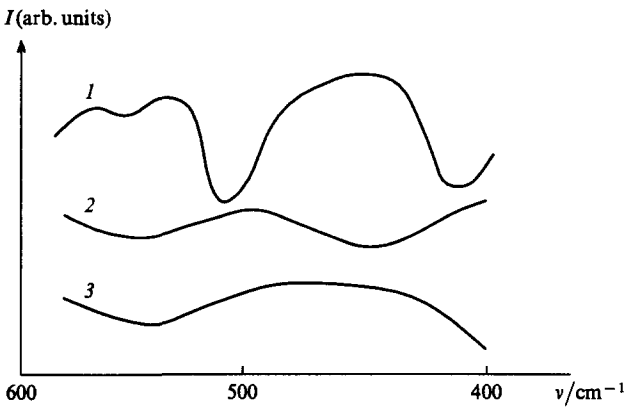


Figure 15. IR spectra of the copper(II) complexes of methylhydroxamic acid (curve *1*) and poly(hydroxamic acids) with M_n = 640 (curve *2*) and 17 000 (curve *3*).

The chelating fragments of one (intramolecular metal chelates) or two polymer chains (intermolecular metal chelates) may participate in the formation of macromolecular metal chelates. A typical manifestation of the chain effect is intramolecular (and not intermolecular) cyclisation in dilute solutions. For example, the interaction of poly(6,6'-dimethyl-5-vinyl-2,2'-bipyridyl) with cobalt(II), copper(II), and zinc(II) chlorides in ethanol at 298 K results in the formation of 1:1 complexes with M←N bonds.[73] The decrease in the viscosity of the solutions of the MMC in dimethylformamide (DMF) on dilution (Fig. 16) indicates their polyelectrolyte nature. The solubility of these compounds indicates the absence of intermolecular cross-linking, i.e. the bipyridyl groups behave like the usual chelating ligands in the side chains of the polymer. Similar results have also been obtained for the VO^{2+} and Co^{2+} complexes of polyureas incorporating the bipyridyl group.[74]

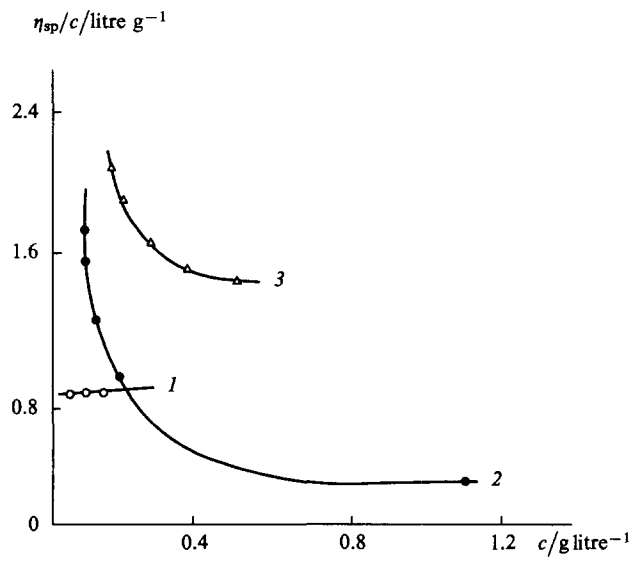
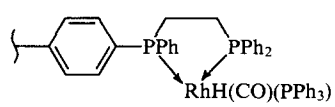


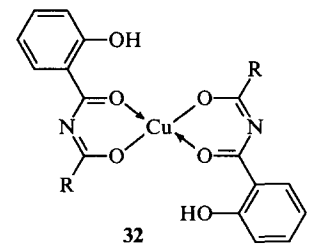
Figure 16. Concentration dependences of the ratio η_{sp}/c for poly-4-methyl-4'-vinyl-2,2'-bipyridyl (curve 1) and its complexes with $ZnCl_2$ for [Zn]:[L] = 0.3 (curve *2*) and 0.6 (curve *3*).

The features of the formation of chelates with participation of polymeric ligands noted above may lead both to the appearance of new reactions, uncharacteristic of the low-molecular-mass compounds,[75] and to a change in the mode of the complex formation reactions known for the LMC.[76] Thus it has been shown that the polymer modified by 1,2-bis(diphenylphosphino)ethane forms the mononuclear complex **31** on interaction with $RhH(CO)(PPh_3)_3$,[77] whereas the low-molecular-mass analogues — 1,3-bis(diphenylphosphino)propane and 1,4-bis(diphenylphosphino)butane — give rise to dimeric rhodium complexes.

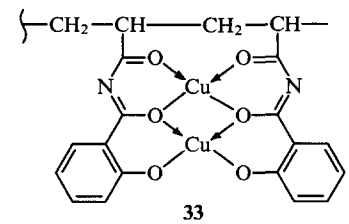


31

The low-molecular-mass chelating ligands *N*-acylsalicylamides afford mononuclear metal chelates on interaction with copper(II) ions and, of the two possible coordination centres, the diacylamine fragment participates in the complex formation reaction (complex **32**).[27] However, the *N*-acylsalicylamide on the polymer base immediately gives rise to the dinuclear copper complexes **33**.[78]



32



33

Another characteristic example is the shift of the monomer ⇄ dimer equilibrium in solution of metallophthalocyanines towards the monomeric form on formation of complexes with polymeric ligands, which is indicated, for example, by the increase in the intensity of the monomer peak with a simultaneous decrease in the intensity of the dimer peak in the UV spectra of the metallophthalocyanines (Fig. 17).[79] This shows that the large size of the polymer chain prevents the aggregation of the metallophthalocyanine units. Evidently the dimer cannot arise if only one metal chelate molecule is present in each polymer coil. The mole fraction X_i of the metal chelate bound to the polymer chains, each of which contains k metal chelate molecules, may be calculated by the equation[79]

$$X_i = \frac{k(1-p^2)(p\alpha)^{k-1}}{(1-p+p\alpha)^{k+1}}, \qquad (12)$$

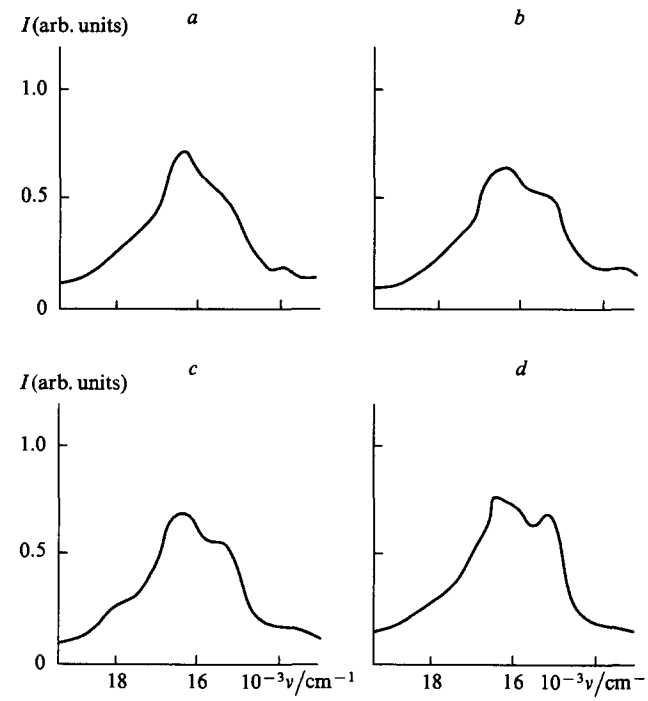


Figure 17. Absorption spectra in the visible region of complexes of cobalt-tetrasulfophthalocyanine (concentration 2.5 μM) with PVA at different concentrations of the latter (mM): (*a*) 2.5; (*b*) 5.9; (*c*) 10.0; (*d*) 25.0.

where $p = 1 - 1/P_n$ (P_n is the number-average degree of polymerisation). Calculations showed (Table 12) that, in the case of a polymer with a relatively low molecular mass (P_n = 50), X_i for isolated (k = 1) metal chelate molecules is extremely large and diminishes slowly with increase in α. On the other hand, in the case of a polymer with a high molecular mass (P_n = 1680), the fraction of polymer chains containing only one metal chelate molecule attains high values at low degrees of conversion.

Table 12. Calculated amounts (in mol%) of isolated molecules of metallophthalocyanines bound to polyvinylamine.

$10^2\alpha$	P_n = 50	P_n = 1680
1	45.04	0.32
0.2	82.95	5.27
0.1	90.88	13.93
0.02	98.07	56.04
0.01	99.03	73.31

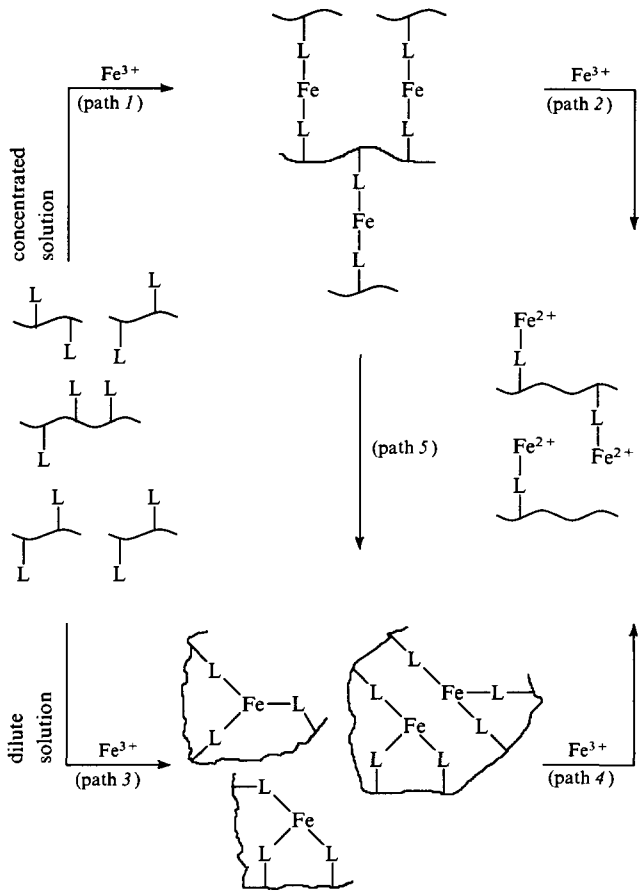
At the molecular level there are spatial organisation requirements which distingish macromolecular metal chelates from their low-molecular-mass analogues. The principal polymer chain effects are fully manifested on this level: the changes in the conformation of the chain, neighbouring groups, etc. In certain cases, these effects can be separated, which makes it possible to discover their characteristic features.

IV. The supermolecular level of the structural organisation of metallopolymers

On passing from a dilute to a concentrated solution and further to a massive specimen, there is a significant increase in the extent of the intermolecular interaction of both the initial polymers and of the metal chelates based on them, which makes it necessary to take into account a third (supermolecular) level of the spatial organisation of the MMC. Studies have shown that the reactions of metal ions with concentrated solutions of macroligands, cross-linked or graft polymers, are distinguished primarily by the greater free energy changes in the process. In concentrated solutions, the polymeric nature of the ligands considered should be manifested more strongly than in dilute solution and the characteristics of the chelation process associated with their polymeric character should be more pronounced. Therefore, in considering the kinetic and thermodynamic features of the chelation process on the supermolecular level, one has to take into account all the principal effects of the polymer chain.

With increase in the macroligand solution concentration, there is an appreciable increase in the probability of the formation of intermolecular (and not intramolecular) metal chelates.[80,81] By varying the degree of conversion, it is possible to observe the reversible transition between the intermolecular and intramolecular metal chelates. We shall demonstrate this with the aid of the scheme, presented below, for the formation of complexes between iron(III) ions and poly(hydroxamic acids) (Scheme 1).[82] At high polymer concentrations, the hydroxamic groups from different polymer chains are disposed closer to one another than the chelating fragments in the same chain. This increases the probability of the formation of intermolecular bonds (path *1* in Scheme 1), whereupon cross-linking becomes a significant feature of the process. The cross-linking of the polymer chain is accompanied by an increase in the viscosity of the solution (Fig. 18). Increase in viscosity by virtue of intermolecular cross-linking via the formation of metal chelates has been observed[60] after the addition of alkali metal salts to styrene–crown-ether copolymers. As a result of further addition of iron(III) ions, the cross-linked complexes with the composition [L]:[M] = 3:1 are converted into 1:1 complexes (path *2*) and, by virtue of the rupture of

Scheme 1



the cross-links, each iron ion is bound to only one hydroxamic group (path *4* also leads to the same products).

At low concentrations of the chelating macroligand, where the neighbouring hydroxamic acid groups in the same chain are disposed closer to one another than the groups from different polymer chains, the iron complex is formed intramolecularly (path *3*, Fig. 18), which diminishes the limiting size of the disordered polymer coil and hence diminishes the viscosity. With increase in polymer concentration, the change in viscosity becomes more appreciable, since the density of the cross-links

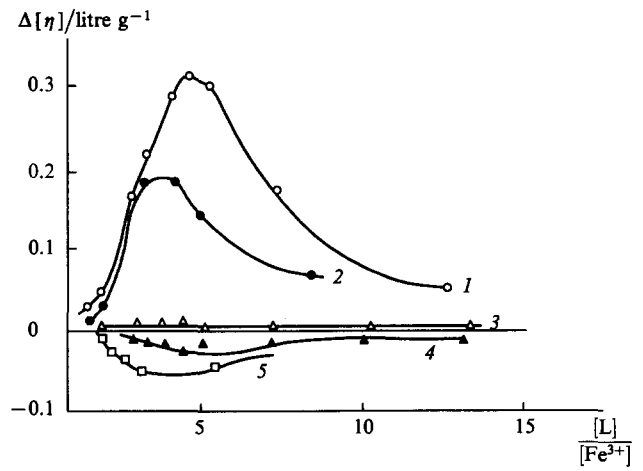


Figure 18. Dependence of the change in the intrinsic viscosity of the polymer containing 0.749 mol% of hydroxamic acid units on the ratio [L]:[Fe] for different concentrations of the polymer (g litre^{-1}): (*1*) 4.90; (*2*) 3.25; (*3*) 1.0; (*4*) 0.75; (*5*) 0.50.

increases. It is noteworthy that the molecular mass of the polymer has a greater influence on the viscosity than the content of the chelating fragments.[82]

The cross-linked polymers formed at high concentrations are 'kinetic' products, which after a time are converted into thermodynamically more stable intramolecular complexes (path *5*). The transition between the intramolecular and intermolecular complexes is reversible

Since the chemical bond is the same in both cases, the enthalpy of the transition ΔH should be zero and hence the transformation is determined by entropy factors. The conversion of intermolecular chelates into intramolecular ones is a first-order reaction, the rate constants for which are 5.21×10^{-6} s^{-1} at 303 K and 49.7×10^{-6} s^{-1} at 333 K. The activation energy and the entropy are 63.3 kJ mol^{-1} and 4.2 J mol^{-1} K^{-1} respectively.

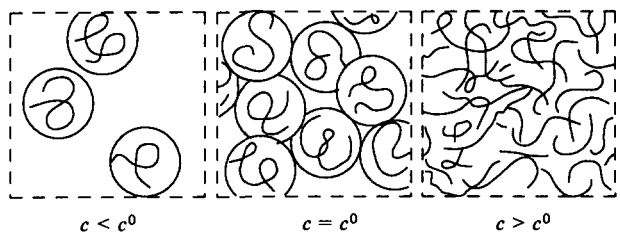


Figure 19. Schematic representation of the polymer at different concentrations of the latter.

The following two parameters are most important for the formation reactions of intermolecular metal chelates: the critical polymer concentration c^0 and the temperature T_t of the liquid ⇄ gel transition.

The quantity c^0 represents the concentration above which the intermolecular interaction becomes significant (Fig. 19).[83] It is noteworthy that the critical concentration of the polymer is inversely proportional to its molecular mass.[84] Above the critical concentration, the transition temperature T_t is almost independent of the concentration and molecular mass of the polymer (Fig. 20). It has been suggested that Eqn (13), obtained from the classical theory of gel formation, be used to calculate T_t.[85] This equation shows that T_t is determined mainly by the thermodynamic characteristics associated with the formation of metal–polymer bonds (i.e. ΔH and ΔS).

$$T_t = \frac{\Delta H}{\Delta S - R \ln[(c - c^0)/c^0]} \tag{13}$$

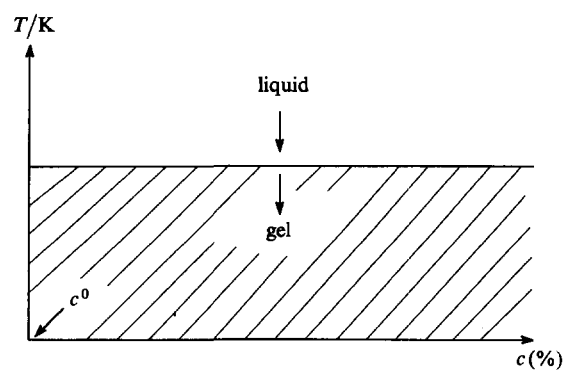


Figure 20. Liquid ⇄ gel phase diagram.

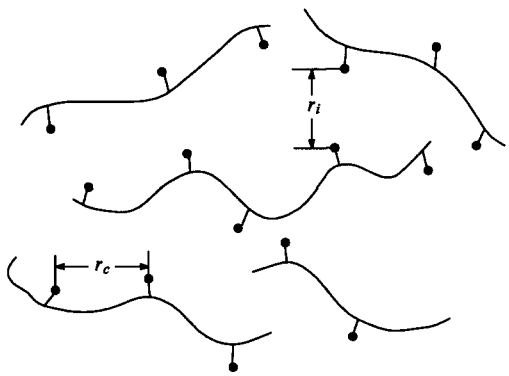


Figure 21. Schematic illustration of the formation of intramolecular (r_c) and intermolecular (r_i) chelates.

The distance between the chelating fragments on formation of the intramolecular (r_c) and intermolecular (r_i) metal chelates (Fig. 21) can be determined by means of statistical analysis, adopting the spheres in contact model. The distance r_i is determined from the equation

$$r_i = \frac{S}{(N_c/2)^{1/3}} , \tag{14}$$

where S is the length of the side of a box made up of close-packed spheres (1 cm) and N_c is the number of chelating fragments in 1 cm^3. The latter quantity is calculated as follows:

$$N_c = \frac{c_p}{100\, M_s} X N_A , \tag{15}$$

where c_p is the polymer concentration at the gel formation point (g litre^{-1}), M_s the average molecular mass of the elementary unit, X the mole fraction of the chelating fragments in the polymer, and N_A the Avogadro number.

The distance between the chelating fragments in one chain (r_c) is a function of the mole fraction of the chelating unit in the polymer and of the size of the polymer, which are determined by the solvent. Assuming that the polymer in solution consists of a disordered coil, r_c can be calculated by the equations

$$r_c = r_0 \beta , \tag{16}$$

$$r_0^2 = c_\infty t l^2 , \tag{17}$$

where r_0^2 is the mean square of the distance between neighbouring chelating fragments; t the average number of chemical bonds separating the chelating fragments, l the bond length (0.154 nm), c_∞ the characteristic ratio taking into account the increase in the size of the polymer as a result of short-range effects in the disordered coil model, and β the expansion factor taking into account the increase in the size of the polymer by virtue of its interaction with the solvent.

As an example, one may quote the results of the calculation of the quantities r_c and r_i for hydroxamic acid copolymers (Table 13).[82] Analysis of these data indicates that the hydroxamic acid groups of the polymer react in a 'disordered' fashion and

Table 13. Comparison of the values of r_c and r_i for hydroxamic acid copolymers.

Content of hydroxamic fragments in the copolymer (mol %)	r_c/nm	r_i/nm	Difference (%)
0.259	12.8	11.2	13
0.749	6.8	6.4	6
1.80	4.2	4.9	15

form infinite networks only when the probability of the intermolecular binding of the metal exceeds 50%.

In the analysis of the kinetics of reactions involving insoluble polymers, one must take into account both diffusional (transfer of the functional groups after the system has passed through the glass point) and topological (virtually complete absence of the translational diffusion of the functional groups grafted to the polymer skeleton) difficulties. In comparatively early studies,[86] it was shown that the rate-limiting stage of chelation by cross-linked macroligands is diffusion. Because of this, the surface chelating groups are the first to react and the access of metal ions to the interior of the block is restricted. In particular, the study of the kinetics of the chelation of metal ions by cross-linked polyamine ligands confirmed the appreciable influence of diffusion on this process: for polymer particles whose size is up to 0.1 mm, external diffusion is rate-limiting, whilst for particles with sizes in excess of 0.1 mm internal diffusion into the deep layers is rate-limiting.[87] In the case of linear polymers, the rate of complex formation is appreciably higher than for cross-linked polymers because it is determined by the rate of diffusion of the metal ions to the functional groups. The formation of chelates is preceded by the formation of outer-sphere complexes and their transformation into inner-sphere complexes with subsequent diffusion of the metal to the second ligand of the polymer, and so on. As a consequence of the lower metal concentrations at the reaction site, the overall composition of the complex may be different from that in the case of linear polymers and low-molecular-mass analogues. The significant difference in the binding of metal ions by the soluble and cross-linked macroligands also consists in the fact that in the latter the overall macroligand concentration is constant and independent of the dilution of the suspension by the solvent.

The small difference between the stability constants of the low-molecular-mass and high-molecular-mass hydroxyquinoline metal chelates indicates isotypical spatial environments of the metal ion in these compounds. Polymers with 8-hydroxyquinoline groups have been obtained by the polymerisation of[88] or polycondensation[89] method. The composition of the complexes corresponds in this case to the ratio [M] : [L] = 1 : (1.5 – 2.0), which is close to the ratio 1 : 2 corresponding to the stoichiometry of divalent metal complexes. On the other hand, the formation of 1 : 1 complexes is characteristic of cross-linked polymers.[90] Furthermore, the stability constants of complexes based on cross-linked polymers are lower than those of the low-molecular-mass analogues (Table 14).[91]

Table 14. *Stability constants of 8-hydroxyquinoline complexes.*

Metal	MMC			LMC		
	$\lg K_1$	$\lg K_2$	$\lg K_3$	$\lg K_1$	$\lg K_2$	$\lg K_3$
Cu	7.45	6.65	14.10	13.49	12.73	26.22
Ni	5.60	5.35	10.96	11.44	9.94	21.38
Mg	3.18	2.82	6.00	6.38	5.43	11.81

In terms of the stability of the complexes with 8-mercaptoquinoline polymer, divalent metals can be arranged in the sequence Hg > Cu > Ni > Co > Zn > Pb, which is the same as the stability series of the 8-mercaptoquinoline chelate complexes of these metals. However, in contrast to low-molecular-mass analogues, the macroligands form 1 : 1 complexes and the selectivity of 8-mercaptoquinoline in relation to certain metal ions is retained when this group is introduced into the polymer.[92]

The composition and stability of the MMC formed are also influenced by the physical state of the macroligand. As a result, their transition from the nonporous (gel) to porous structures is accompanied by a decrease in the overall stability constant of the complexes owing to the closer packing of the chains and the lower mobility of the functional groups, which leads to appreciable free energy losses on complex formation.

It is interesting to note that the time required for the saturation of the macroligand by the metal increases with increase in the size of grains in the latter.[93]

An increase in the degree of cross-linking leads, on the one hand, to a decrease in stability of the macrocomplexes as a consequence of the increase in strain in the twisted chain on formation of the second and subsequent coordination centres and, on the other, to a change in the nature of the intermolecular interaction. In particular, the rate of interaction of vanadyl acetylacetonate with the chloromethylated styrene–divinylbenzene copolymer modified by catechol groups is much lower when the degree of cross-linking of the polymer is 20% than when it is 2%. The rate increases if the polymer with a 20% degree of cross-linking is ground (Fig. 22).[94] The ratio of the initial rates of absorption of vanadyl ions from a solution of the polymers with 2% and 20% degrees of cross-linking is ~3.9.

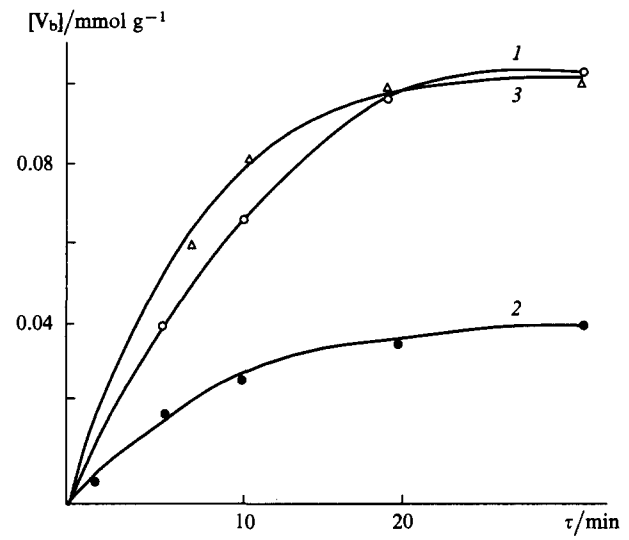


Figure 22. Absorption of vanadyl ions from a solution by a polymer containing catechol groups; (*1*) degree of cross-linking of the polymer 2%; (*2*) degree of cross-linking of the polymer 20%; (*3*) ground polymer with a degree of cross-linking of 20%.

An increase in the degree of cross-linking of the polymeric ligand may alter the steric configuration of the chelate unit: thus it changes from square planar to tetrahedral in the nickel complexes.[15]

The intermolecular interaction in a polymer is known[95] to be much more pronounced than in the analogous low-molecular-mass compounds. Apparently in the MMC it is still stronger than in the initial ligands. This happens both as a consequence of the decrease in chain flexibility on formation of the complex and as a result of the increase in the energy of the local intermolecular interaction. The parameters of the intermolecular interaction in the MMC are influenced by the electron-donating capacity of the functional groups, their distance from the main chain, and also the presence and size of other substituents which do not participate in the complex formation reaction. As a result of these factors, the polymeric complexes frequently give rise to more ideal morphological structures than the original macroligand. Thus the structural changes in the styrene–divinylbenzene copolymer during its alkylation by 5-chloromethyl-8-hydroxyquinoline in nitrobenzene in the presence of $AlCl_3$ have been elucidated in detail.[96] In the stage involving the attachment of the complex to the polymer, the latter undergoes a reorganisation — micronetwork rearrangements and twisting of

the polymer. The structural changes in the polymer obey the steric requirements of the complex-forming metal (minimum free energy loss) and in all cases the capacity of the chain molecules for twisting depends on the rigidity of the chain, the nature of the solvent, etc. By operating with these factors, it is possible to weaken or, conversely, to intensify the twisting or extension of the chain. It is then necessary to take into account the increase in the rigidity of the chain at the binding sites with increase in the degree of conversion.

In particular, the change in the chain rigidity, which depends on the number of bound functional groups, affects the stability of the complexes: the most stable complexes are formed for low degrees of conversion and the least stable are formed for higher conversions. With increase in the degree of conversion, the stability constants of the copper(II) chelate complexes of poly(acrylohydroxamic acid) pass through a maximum (Table 15): they increase with increase in η in the region of low conversions and diminish in the region of high values of η.[97]

Table 15. Stability constants of copper(II) chelate complexes of poly(acrylohydroxamic acid) {293 K, [$NaNO_3$] = 0.2 M}.

α	B_1	B_2	B
0.087	−1.9	−2.9	−4.8
0.26	−0.75	−1.85	−2.6
0.43	−1.1	−2.4	−3.5
0.69	−1.0	−2.8	−3.8

Note. $B_1 = K_1K_a$; $B_2 = K_2K_a$; $B = B_1B_2 = KK_a^2$.

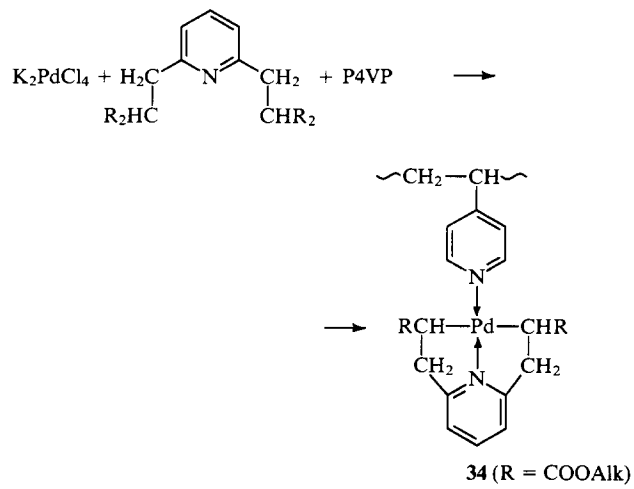
The stability of the MMC is influenced significantly also by the valence of the metal. Thus the stability of poly(enol-ketone) chelates based on oxidised poly(vinyl alcohol) films increases in the following sequence of ions: $M^+ > M^{2+} > M^{3+}$.[98] An important factor is that oxidation of the films promotes the permeation of the metal ions into their deep layers.

The dependence of the properties of the complexes formed and of the degree of conversion on the method of preparation of the complexes is characteristic of the MMC based on cross-linked macroligands.[99-101] As was to be expected, if the polymer does not swell in the given solvent, then the chelation reaction either does not occur or proceeds with a very low percentage binding of the metal.[102] This conclusion has been confirmed yet again by a study of the interaction of transition metal compounds with polymers based on 2,2′-dipyridylmethane.[103] The composition of the complexes formed with participation of this polymer also depends on the nature of the metal and the ligands bound to it.

The influence of temperature on the chelation process may be demonstrated in relation to the interaction of K_2PdCl_4 with 2,6-derivatives of pyridine[104] in the presence of P4VP or the styrene–4-vinylpyridine copolymer. The interaction results in the formation of complex **34** (Scheme 2).

Macromolecular metal chelates have been obtained at 298 and 360 K. It was found that the P4VP-based MMC, obtained at 298 K, are bright yellow in colour and dissolve readily in ethanol, while the polymer obtained at 360 K is dark yellow and is only slightly soluble in ethanol. This can be explained by the different conformations of P4VP in ethanol at different temperatures. On the other hand, the palladium chelate based on the styrene–4-vinylpyridine copolymer, the conformations of which are the same at these temperatures, dissolves readily both in ethanol and chloroform regardless of the temperature at which it is obtained. The degree of conversion, found from elemental analysis and NMR spectra, was 25% in all cases under these conditions. In other words, by varying the temperature, it is possible to obtain complexes having the same composition but with different steric structures.

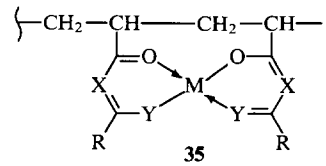
Scheme 2



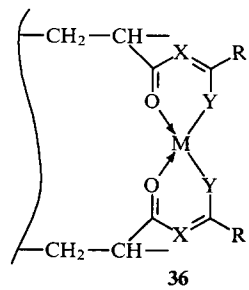
34 (R = COOAlk)

The structure of the complexes is in many respects determined by the conditions of their preparation. It is apparently necessary to take into account the relaxation time of the products formed, which are in a stationary state, and hence the dynamics of the variation of the required properties. The interchain cross-links arising in the rigid chain polymers alter appreciably their supermolecular organisation, which increases the rigidity of the chain. This should be manifested by a change in the relaxation transitions within the chains and the segments. Evidently, the α-relaxation, associated with the micro-Brownian motion of the long sections of the chains near the glass point, is more subject to such influences. For low degrees of saturation of the macroligand, the overall restriction of the chain mobility is slight. With increase in the degree of saturation, an ever increasing number of cross-links are formed between neighbouring chains, which should lead to an increase in the glass point T_g. In the region of β-relaxation, the glass point is almost independent of the metal content and intermolecular cross-linking leads to its increase. On cyclisation, T_g should increase with increasing metal content as a consequence of the increase in the rigidity of the individual sections and the decrease in the mobility of the entire chain.

Macroligands with chelating fragments grafted to the surface (the readily swelling functional group coating on an insoluble substrate) occupy an intermediate position between the soluble and cross-linked polymers.[1,65] The interaction of metal ions with such macroligands simulates to a large extent complex formation in solutions. As a rule, in both cases the free energy changes are similar.[105,106] Intramolecular cyclisation (complex **35**), and not intermolecular cyclisation (complex **36**), is characteristic of grafted macroligands, as for soluble polymers.[28,29,107]



35



36

In order to assess the interactions in transition metal ion–grafted macroligand systems, the modified Langmuir equation is usually employed:

$$\frac{c}{c_b} = \frac{1}{kf_{max}} + \frac{1}{f_{max}}, \quad (18)$$

in which c and c_b are the concentrations of the dissolved and bound metal, k is the stability constant, and f_{max} is a constant characterising the limiting degree of binding (limiting adsorption) of the metal to the functional groups of the polymer. This equation is valid only for low degrees of conversion when the concentration of the unreacted and unreactive centres may be neglected.

In particular, the adsorption of copper(II) ions on polymeric ligands with grafted iminodiacetic acid groups is described by the Langmuir equation (Fig. 23).[108] The parameters of the Langmuir equation, calculated from the relations presented in Fig. 23, are listed in Table 16. The constant f_{max} increases with increase in the degree of grafting to ~0.3. This quantity indicates that the number of centres capable of binding Cu^{2+} ions increases to 30% depending on the number of bis(carboxymethyl)amino-groups.

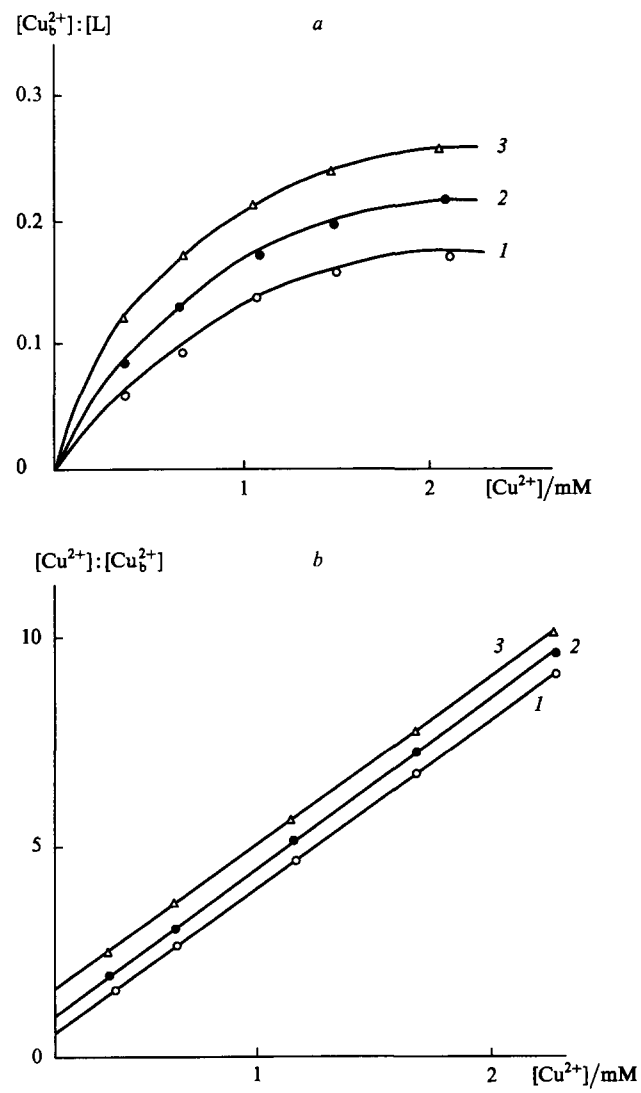


Figure 23. Relation between the amount of Cu^{2+} ions and their concentration in solution (*a*) and the corresponding Langmuir relation (*b*) for different degrees of grafting of the chelating fragments (%): (*1*) 24.4; (*2*) 31.8; (*3*) 40.5.

Table 16. Parameters of Eqn (18) for the chelation of copper(II) ions by polymers with grafted iminodiacetic acid groups.

Degree of grafting	$10^{-4}K$/litre mol^{-1}	f_{max}/mmol g^{-1}
24.0	1.8	0.24
31.8	2.2	0.26
40.5	3.1	0.29

The constant K also increases with increasing degree of grafting. These results show that the ability of the ligand groups of the grafted chains to chelate Cu^{2+} ions increases with increasing degree of grafting. The complexes formed become more stable apparently by virtue of the fact that, as soon as the Cu^{2+} ion has been coordinated to one ligand, other ligand groups coordinate to it more readily. On the other hand, the adsorption of Cu^{2+} by a polymer containing the same number of bis(carboxymethyl)-amino-groups bound directly to the main chain is described by the Langmuir equation with the parameters $K = 3.5 \times 10^3$ litre mol^{-1} and $f_{max} = 0.075$ mmol g^{-1} under the same conditions.[109] Thus the chelating capacity of the polymers improves after the introduction of a grafted chain as a bridge.

V. Conclusion

Analysis of the three levels of the structural organisation of the MMC shows that the characteristics of their formation differ significantly from those of the formation of the LMC. For the latter, the second and third levels are not as a rule considered. Therefore the methods for the estimation of the thermodynamic parameters of the MMC and the LMC should also differ. On the most thoroughly investigated local level, important information about the mechanism of the formation reaction can be obtained precisely by comparing the thermodynamic parameters.

Examination of the second level leads to the conclusion that, in the calculation of the thermodynamic parameters, account must be taken of the principal polymer effects, as for the kinetics of chemical reactions with participation of macromolecular reagents. Only this approach permits the quantitative estimation of the differences between the processes involving the formation of the LMC and of the complexes in the macrochain–MX_n systems. In ideal cases, it is possible to estimate the contribution of each effect (or at least to discover which is the dominant one) to the thermodynamics of the process, which helps in understanding the characteristic features of the formation and structure of the MMC.

The third, supermolecular level has been least investigated. This is associated, on the one hand, with the dependence of its parameters on the degree of conversion in the chelation process and, on the other, with the possibility of the occurrence of the so called 'stationary states' characteristic of long-chain molecules. The properties of the MMC obtained differ appreciably from the equilibrium ones. Unfortunately, not only the properties of the system in a specified 'stationary state' but also the very conditions of the appearance of such a state still remain uninvestigated.

In the general case, the observed equilibrium constant can be represented to a first approximation as the product of the equilibrium constants for different levels. Unfortunately, the number of kinetic studies on MMC is still insufficient for more specific generalisations.

Here we may also note that the importance of the problems under consideration is determined, firstly, by the need for a purposeful approach to the synthesis of MMC with specific homogeneous structures.[110] Secondly, there is a possibility of synthesising deliberately MMC designed for different practical applications (in the first place as metallopolymer composite materials in metal complex immobilised catalysts). Among comparatively new aspects, we may point out the use of

MMC in 'non silver' photographic processes,[111] as sensitisers of photodynamic cancer therapy,[112] and as high-temperature superconducting materials (ceramic material consisting of polymers with YBC-chelates‡).[113]

The structural organisation considered in the present review mainly in relation to polymerisation MMC is characteristic also of the MMC of the coordination and condensation types,[113-116] liquid-crystal polymeric chelates,[117-121] and also MMC obtained by methods involving the polymerisation and copolymerisation of the corresponding metal-containing monomers.[122] The formation of complexes between a metal-containing monomer of the chelate type and a template during radical copolymerisation and polymerisation makes it possible to regulate the position of the metal ion in the polymer matrix, while the high degree of cross-linking promotes the stabilisation of the functional group environment.[123] Such template polymerisation strategy is promising from the standpoint of the construction of highly specific catalysts, sorbents, and synthetic receptors for the recognition of complex biomolecules. In other words, the MMC, i.e. organised polymolecular *ensembles* (especially in thin Langmuir–Blodgett metallopolymer films),[124] are potential objects for the vigorously developing supramolecular chemistry[125]—the constructional chemistry of intermolecular bonds.

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‡ Yttrium-barium-copper chelates (Ed. of Translation).

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Heterogeneous catalytic reactions of carbon dioxide

O V Krylov, A Kh Mamedov

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Abstract. The most important classes of heterogeneous catalytic reactions involving CO_2 are examined: the incorporation of CO_2 in the C–C, C–H, and C–N bonds with formation of carbonyl- and carboxyl-containing compounds and oxidation of other compounds by CO_2. Reactions of the second class are more promising from the standpoint of the utilisation of carbon dioxide as a chemical raw material and from the standpoint of the solution of the ecological problems involving its utilisation from the gaseous waste discharged into the atmosphere.

The reactions involving the oxidation of C_1-C_7 hydrocarbons and C_1-C_2 alcohols by carbon dioxide, which have been investigated by the authors of this review, are examined in detail. Catalysts based on manganese oxides are most effective in these reactions. The bibliography includes 231 references.

I. Introduction

Considerable interest in the heterogeneous catalytic reactions of CO_2 has been aroused by two factors: (1) the need to combat the greenhouse effect and (2) the exhaustion of the available resources of carbon-based raw materials. We shall examine both these factors.

1. The ecological importance of carbon dioxide

In May 1992, 143 countries signed in Rio de Janeiro an agreement concerning the control of global warming and the reduction of the carbon dioxide waste discharged into the atmosphere. The largest emitter of carbon dioxide is the USA, where 26.7% of the entire carbon dioxide waste or about 1.6 billion tonnes annually is discharged into the atmosphere.[1]

A series of communications concerning the possible consequences of global warming have been published recently. In particular, the influence of the CO_2 waste on changes in the climatic zones on the territory of the former USSR has been considered.[2,3] At first sight, the conclusions reached do not appear very alarming. In most regions, with the exception of highly mountainous ones and possibly the very centre of European Russia, an increase in temperature by several degrees is more likely to have favourable rather than negative consequences: the amount of atmospheric precipitation and ultimately the agricultural productivity will increase; the possible flooding of coastal regions does not appear quite so alarming either.

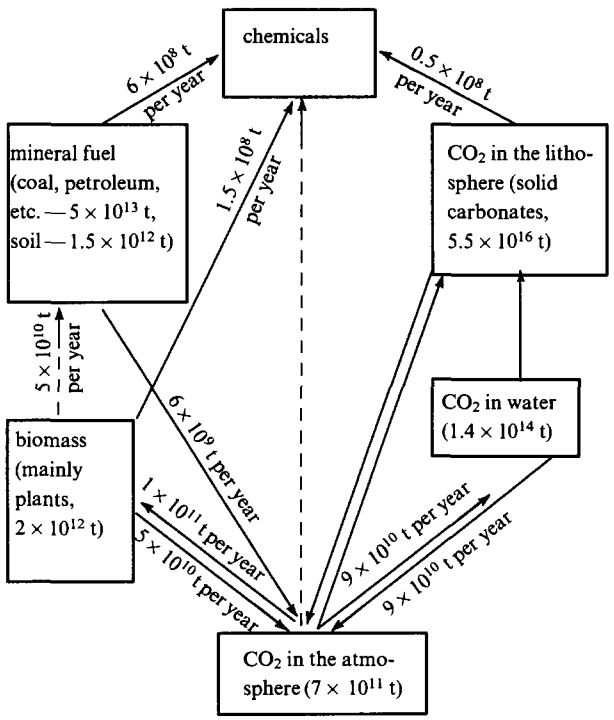
It has to be said that there exists also a different point of view on the consequences of the greenhouse effect. For example, it has been noted[4] that there have been periods during the Earth's history when the average content of CO_2 exceeded the current level by a factor of 5. The periods of the intense emission of CO_2 coincided with an intensification of volcanic activity and led to the rapid growth of numerous life forms. In discussions of this problem, Russian scientists have occupied a 'softer' position than foreign investigators. However, Russia cannot regard itself as an isolated society and if a decision has been reached at an international level (the Rio de Janeiro Conference) concerning the need to reduce the discharge of the greenhouse gases, then Russia — the third emitter of carbon dioxide after the USA and western Europe — must also inevitably participate in this process. We may likewise note that the CO_2 evolved will be partly absorbed by the hydrosphere, the lithosphere, and the biosphere (see the scheme overleaf). However, calculations have shown that such absorption will not compensate for the evolution. About 57% of the evolved CO_2 will remain in the atmosphere. A scheme illustrating the redistribution of carbon dioxide in natural objects is presented below (all the figures are quoted relative to carbon).

Carbon dioxide is not the only substance responsible for the greenhouse effect: the contribution of CO_2 is about 50%, 24% of the effect is due to the freons (chlorofluorocarbons) and N_2O, and 15% is due to methane. At the present time, vigorous research is being prosecuted throughout the world on the replacement of freons by other cooling agents, since freons decompose the ozone layer in the stratosphere. Since the methane molecule absorbs more solar radiation than the CO_2 molecule, the role of methane in the greenhouse effect may actually supercede that of CO_2 in the course of further development of industry and agriculture.

Considering the various methods for reducing the greenhouse effect, the well known Belgian scientist Delmon[5] noted that its

O V Krylov Laboratory for Complex Heterogeneous Catalysts, Semenov Institute of Chemical Physics, Russian Academy of Sciences, ul. Kosygina 4, 117977 Moscow, Russian Federation.
Fax (7-095) 938 21 56. Tel. (7-095) 939 71 68.
A Kh Mamedov Mamedaliev Institute for Petrochemical Processes, Academy of Sciences of Azerbaijan, ul. Tel'nova 30, 370604 Baku, Azerbaijan.

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diminution by 3% requires either (1) the reduction of the felling of forests by 25%, or (2) the abolition of all rice plantations, or (3) the destruction of all ruminants, or (4) the reduction of the world consumption of energy by 7%. Out of the four procedures examined, only the first and the fourth are realistic, although both are very hard to achieve. It is of interest that if one follows the third procedure, then calculations show that the aim of reducing the emission of greenhouse gases by 3% will not be attained. The reduction of the felling of forests and the development of atomic power are extremely important in this connection. One must also not fail to note that from the environmental point of view atomic power is greatly preferable to thermal power.

The waste gases from industry, electric power stations, and transport are powerful contaminants of the atmosphere. In terms of the scale of their harmful effect on the atmosphere, the automobile exhaust gases occupy the first place.[6] The most undesirable components of the exhaust gases are hydrocarbons, CO, and NO and nowadays the efforts of many scientific teams are directed to the fight against these gases. The problem of reducing the amount of CO_2 in exhaust gases is hardly considered.

Naturally, a partial solution of a large number of ecological problems, including the problem of the greenhouse effect, might be to abandon automobile transport as a means of individual mobility and to go over to collective types of transport. However, the world community is not yet ready for such a solution. One cannot rule out the possibility that this question will arise in the XXIst century if the existing trend towards the growth of population and energy consumption and also the impairment of the environmental situation continues.

2. Carbon dioxide as a raw material

The second reason for the increased interest in the chemical processing of carbon dioxide is its utilisation as a raw material. Regardless of the problem of the greenhouse effect, carbon dioxide should be regarded as an important source of chemical raw material in the future. The resources of petroleum and coal are being rapidly exhausted. At the present time, they are estimated as $(5-10)\times10^{12}$ t in terms of carbon. After petroleum and coal, the resources of natural gas are coming to an end. On the other hand, the total amount of CO_2 in the atmosphere and in the ocean is $\sim 1.5 \times 10^{14}$ t (in terms of carbon), i.e. is greater by 1.5 orders of magnitude, while its amount in the lithosphere is greater still — by two orders of magnitude (see the Scheme).

Despite the enormous amounts available, the widescale application of CO_2 as a raw material is hindered by its low concentration in the atmosphere, which is only 0.03% in the present day 'pre-greenhouse' atmosphere (338.6 ppm in 1980). In the lithosphere, CO_2 exists in a concentrated state in the form of natural carbonates, but the decomposition of carbonates requires the expenditure of large amounts of energy. The most promising source of CO_2 as a raw material are probably the waste gases as well as natural gases. The CO_2 content in the natural gas from certain deposits reaches 30%.

In order to stimulate studies on the chemical utilisation of CO_2, it has been proposed in the USA to introduce a special tax on the consumption of fuel amounting to 13 dollars (at 1992 prices) per barrel of the petroleum equivalent (or 57 dollars per tonne of conventional fuel). If the aim is to achieve a 10% reduction of the discharge of CO_2 by 2010, then for a discharge amounting to 8.17 billion tonnes the tax will have to be increased to 44 – 155 dollars per barrel, which will impose a heavy burden on tax payers.[7]

At the end of September 1991, after two year discussions, the European Community adopted a differentiated tax on energy consumption, which will continuously increase from 1993 until 2000. The aim is to stabilise the discharge of CO_2 at the 1990 level.[8]

A major programme concerning the utilisation of CO_2 has been adopted in Japan.[9] Most attention is devoted to chemical methods for the processing of CO_2. The possibility of its being pumped into subterranean strata in order to increase the extraction of petroleum and also of its pumping into the ocean is considered. The latter variant can be achieved, in particular, with the aid of CO_2-fixing microorganisms. The majority of the projects presuppose the pumping of CO_2 into deep layers of the ocean (deeper than 1000 m). Under such conditions, the hydrates $CO_2.nH_2O$ ($n = 5 - 6$), which prevent the dissolution of carbon dioxide in water, are formed at the CO_2 – oceanic water interface.[10]

Thus the need both to combat the greenhouse effect and to employ new forms of raw material in industry requires the chemical processing of large amounts of CO_2. In pure form, carbon dioxide is so far little used. It is employed as a solvent, as an extractant, as a cooling agent, and also for the generaton of a carbon dioxide atmosphere in greenhouses.

II. Utilisation of carbon dioxide

1. Carbon dioxide in the chemical industry

The largest industrial consumers of CO_2 are the producers of carbamide, calcined soda, and salicylic acid. In all these industries, CO_2 is obtained not from the atmosphere but from secondary industrial gases and from solid carbonates (mainly from limestone). The question of the utilisation of the CO_2 evolved on combustion of fuel has so far simply not been part of technological plans.

The world output in the production of carbamide (urea) is 110 million tonnes annually. Carbamide is formed when CO_2 reacts with ammonia under a pressure of 200 atm at 200 °C.

$$2NH_3 + CO_2 \rightleftharpoons NH_4COONH_2 \rightleftharpoons (NH_2)_2CO + H_2O$$

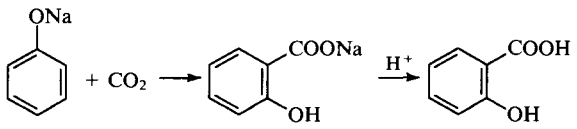
The production of carbamide is a good example of the employment of CO_2 not from an external source but from the resources of the same factory. After the conversion of CO by treatment with steam, hydrogen is used to synthesise ammonia, whilst CO_2 is directed to the manufacture of carbamide.

Another major industry involving the use of CO_2 as the raw material is the preparation of calcined soda by the Solvay method. The world production of cancined soda is about 30 million tonnes annually. Together with CO_2, the reactants are NaCl (in the form of a brine) and ammonia.

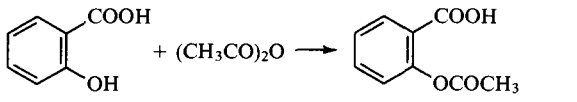
$$NaCl + NH_3 + CO_2 + H_2O = NaHCO_3 + NH_4Cl$$

Calcined soda is obtained by the heat treatment of $NaHCO_3$, whereupon CO_2 and H_2O are evolved.

The manufacture of salicylic acid is not quite such a large scale process. It is synthesised by carboxylating phenol under pressure (the Kolbe–Schmitt reaction).

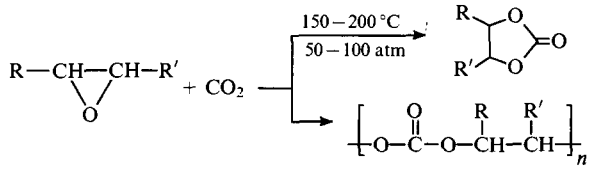


Aspirin (acetylsalicylic acid) is obtained from sallicylic acid.



In 1990, 25 000 tonnes of aspirin were produced in the USA.

A new rapidly developing field in which CO_2 is utilised involves the syntheses of organic carbonates. They are obtained by the interaction of oxiranes with CO_2 in the presence of inorganic and organic halides.

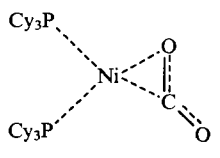


Organic carbonates are used as solvents and extractants, whilst polycarbonates are employed as constructional mateirals.

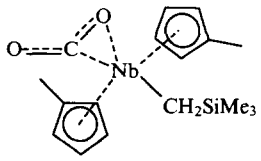
The examples quoted above virtually exhaust the applications of CO_2 in the chemical industry. On the other hand, scientific research has shown that carbon dioxide can enter into numerous reactions and can serve as the starting material for the synthesis of a series of useful chemical products. Disregarding the evident possibility of using CO_2 for the neutralisation of bases, we shall consider reactions involving the incorporation of CO_2 in transition metal complexes.

2. Carbon dioxide in transition metal complexes

Comnparatively few studies are known in which the binding of CO_2 as a ligand in transition metal complexes has been observed (see the relevant review[11]). Thus the stable nickel complex **1**[12] and the stable niobium complex **2**[13,14] have been described.



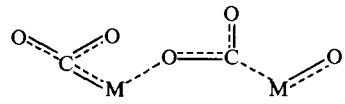
1



2

Cy = cyclo-C_6H_{11}.

Nonasssociative CO_2 complexes have also been found on the surfaces of transition metal.[15,16] For example, the study of the adsorption and desorption of CO_2 and $CO^{18}O$ on K/Ag(111) by Auger spectroscopy, electron energy loss spectroscopy (EELS), and other methods[15] made it possible to detect both associated and undissociated CO_2 complexes.



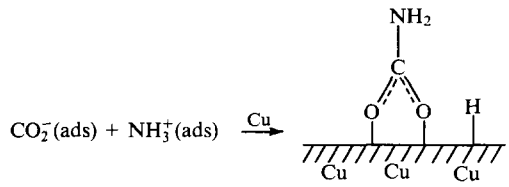
The energy of the bond between CO_2 and the metal in such complexes is low; for example, it is 34.3 kJ mol^{-1} in the complex $W(CO)_5CO_2$.[17] The study of the adsorption of CO_2 on crystalline potassium showed[18] that this entails the formation of oxalate ions $C_2O_4^{2-}$, which permeate under the potassium layer. They decompose into CO_3^{2-} and CO. Complexes similar to those indicated above have been found on potassium-promoted rhodium.[19]

It has been demonstrated by X-ray photoelectron spectroscopy (XPES) and EELS that CO_2 is not chemisorbed on the Cu(100) and Zn(0001) faces of metallic single crystals.[20] The coefficient of the adhesion of CO_2 to these faces is exceptionally low (their lifetime is $\sim 10^{-10}$ s at 20 °C). However, as a result of electron transfer, chemisorbed complexes are formed in the presence of ammonia.

$$CO_2(gas) + e \rightleftharpoons CO_2^-(ads),$$

$$NH_3(gas) \rightleftharpoons NH_3^+(ads) + e,$$

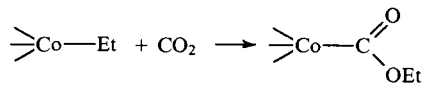
These interact with one another and give rise to adsorbed carbamate.



3

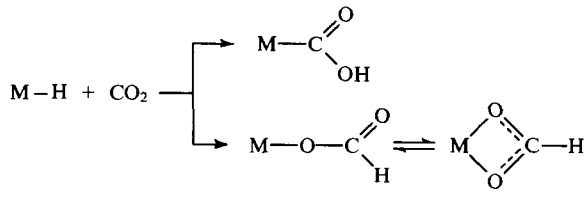
The bidentate carbamate **3** is inclined relative to the surface, so that the two O atoms are nonequivalent. It is of interest that the interaction of CO_2 with H_2O under these conditions does not lead to their joint adsorption.

There have been appreciably more studies on the incorporation of CO_2 in transition metal complexes (Co, Ni, Rh, Pd, Pt, Ir, Cu, etc.) in the M–C, M–H, M–O, and M–N bonds (where M = transition metal).[21,22] When CO_2 is inserted in the M–C bond, carboxylate complexes are formed. For example, the ethyl ester of the metalcarboxylic acid was obtained in the reaction of CO_2 with ethylcobalt.[23,24]

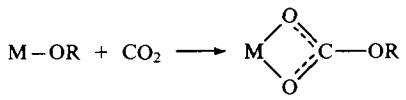


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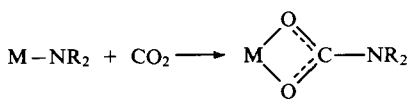
When the carboxylate complex **4** was treated with methyl iodide, ethyl acetate was obtained in a high yield. The carboxylate complexes of Cu, Zn, Ti, Zr, Mn, Fe, Co, Ni, and Rh have been synthesised similarly.[13] The insertion of CO_2 into the M–H bond leads to the formation of formate complexes and in certain cases of metalcarboxylic acids (see, for example, Kolomnikov et al.[24]).



The insertion of CO_2 into the M–O bond results in the formation of complexes with carbonic acid monoesters.



Finally, the insertion of CO_2 in the M–N bond leads to the corresponding carbamate complexes.[14,21]

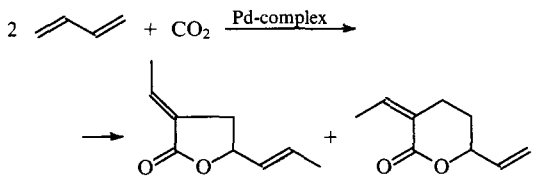


The interaction of CO_2 with organic compounds at the C–H bond constitutes the basis of the catalytic syntheses of carboxy-compounds: acids, esters, lactones, etc. For example, propionic acid and its ethyl ester have been obtained by carboxylating ethene at a high pressure and a temperature of 165 °C on a rhodium complex promoted by hydrogen halides.[25]

$$H_2C{=}CH_2 + CO_2 \xrightarrow[150-700\ atm]{\text{Rh-complex}} CH_3CH_2COOH + CH_3CH_2COOC_2H_5$$

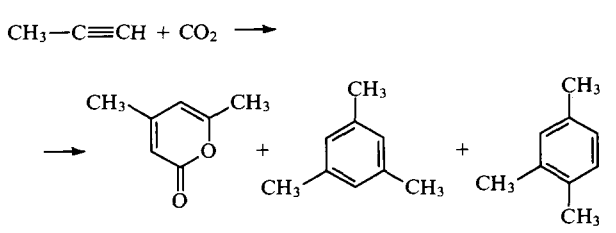
The simultaneous coordination of CO_2 and C_2H_4 to the complex $PtCl(SnCl_3)(PPh_3)_2$ deposited on SiO_2 led to the formation of methyl 3-hydroxypropionate.[26]

The carboxylation of saturated hydrocarbons constitutes an attractive reaction, which, however, is not favoured energetically. The preparation of carboxylic acids in the cracking of $C_{12}-C_{40}$ hydrocarbons in the presence of CO_2 has been described.[9] The interaction of ethyne and diene hydrocarbons with CO_2 affords cyclic compounds.[27]



Cyclic carbonates are formed readily in the interaction of CO_2 with epoxides in the presence of Zn, Ni, Sn, Mg, Al, etc. compounds.

The interaction of CO_2 with methylethyne under a 60 atm pressure on Rh_4 and Fe_xRh_y clusters deposited on SiO_2 or Al_2O_3 leads to a mixture of cyclic compounds.[28]



A surface carbonate is an intermediate.

A number of examples of the use of CO_2 as a cocatalyst for the modification of homogeneous and heterogeneous catalysts are known. For example, CO_2 has been used effectively to regulate the catalytic activity and selectivity of zeolitic catalysts.[29] Carbon dioxide can alter appreciably the activity and selectivity of many catalysts for the oxidative condensation of methane.[30] In the presence of CO_2, oxygen alters the oxidative properties of Fe and Ru complexes.[31]

The examples presented above show that recently CO_2 has been used increasingly for the modification of homogeneous and heterogeneous catalysts. All the catalytic reactions with participation of these complexes which have been investigated belong to the class of reactions in which CO_2 is inserted into C–H, C–O, and C–N bonds. We shall not consider them in detail since they have been described in the reviews mentioned above.

Thus carbon dioxide can enter into numerous reactions and can serve as the starting material for the syntheses of a number of useful chemicals, i.e. the concept of the 'inertness' of CO_2, which existed for a long time, proved to be a myth. Nevertheless, the reactions listed above do not solve the problem of not only the reduction of the emissions of CO_2 but also of its large-scale employment as a raw material. In all these cases, the involvement of CO_2 in a reaction requires large amounts of another fairly expensive and environmentally unfriendly compound (ammonia, phenol, etc.).

The oxidation–reduction reactions in which CO_2 is used as the oxidant are more promising for large scale application. In this case, cheap reductants, mainly hydrocarbons found in natural raw materials (gas, petroleum) or which can be readily obtained from them (coal), could be involved in the reaction with CO_2.

III. Interaction of carbon dioxide with hydrogen

Hydrogen might become the best reductant for carbon dioxide. The most important reactions of CO_2 with hydrogen are the Sabatier reaction [reaction (1)], the Bosch reaction [reaction (2)], the reverse conversion of water gas [reaction (3)], and the syntheses of methanol [reaction (4)], dimethyl ether [reaction (5)], and formic acid [reaction (6)].

$$CO_2 + 4H_2 \rightleftharpoons CH_4 + 2H_2O, \quad \Delta H_{298} = -164.1\ kJ\ mol^{-1}, \tag{1}$$

$$CO_2 + 2H_2 \rightleftharpoons C + 2H_2O, \quad \Delta H_{298} = -14.6\ kJ\ mol^{-1}, \tag{2}$$

$$CO_2 + H_2 \rightleftharpoons CO + H_2O, \quad \Delta H_{298} = 42.3\ kJ\ mol^{-1}, \tag{3}$$

$$CO_2 + 3H_2 \rightleftharpoons CH_3OH + H_2O, \quad \Delta H_{298} = -49.4\ kJ\ mol^{-1}, \tag{4}$$

$$2CO_2 + 6H_2 \rightleftharpoons CH_3OCH_3 + 3H_2O, \quad \Delta H_{298} = -112.2\ kJ\ mol^{-1}, \tag{5}$$

$$CO_2 + H_2 \rightleftharpoons HCOOH, \quad \Delta H_{298} = 16.7\ kJ\ mol^{-1}. \tag{6}$$

Reactions (1), (2), (4), and (5) are exothermic whilst reactions (3) and (6) are endothermic.[32] In all the reactions listed above, except reaction (6), between one and three water molecules correspond to one molecule of the target product (CH_4, C, CO, CH_3OH, CH_3OCH_3), i.e. a considerable proportion of the expensive hydrogen is consumed on the formation of the cheap and useless water.

1. Synthesis of hydrocarbons

Although the Sabatier reaction (1) leads to the formation of the cheap methane, it is nevertheless frequently used to remove CO_2 from technological gases ('methanation of CO_2').[33] This reaction proceeds at temperatures above 200 °C in the presence of various catalysts, the best of which are ruthenium or nickel on carriers. Depending on the design of the reactor, the process can take place in various regimes: from isothermal to autothermal with a large or small temperature drop across the catalyst bed.[34] Above 590 °C, the equilibrium in reaction (1) shifts to the left: the steam conversion of methane is observed.

A catalytic activity series has been obtained[35] for noble metals deposited on Al_2O_3 and used as catalysts in the reaction under consideration: Ru > Rh > Pt = Ir = Pd. Ruthenium also proved to be the most active of the metallic catalysts deposited on SiO_2: Ru > Co > Ni > Fe.[36] Ruthenium catalysts deposited on membranes are good methanation catalysts.[37] The study of nickel and cobalt catalysts deposited on carbon, Al_2O_3, and SiO_2 showed that the cobalt catalysts on carbon are the most active in

the methanation of CO_2.[38] The lanthanum–nickel alloys are also highly active.[39]

Oxide catalysts are less effective in this process. The spinels $La_{1-x}M_xCoO_3$ (M = Sr or Th) become active in the hydrogenation of CO_2 only after the formation of metallic cobalt.[40] Rhodium accelerates the hydrogenation of CO_2 in CH_4 on the Fe–Mn–O catalyst, while lanthanum slows down the process. In the presence of rhodium, CO_2 is apparently activated by the oxide component, while H_2 is activated by the metallic rhodium.[41]

A similar separation of functions is characteristic also of metals deposited on oxides. When the carrier in the Rh/CeO_2 [42,43] and Pd/CeO_2 [44] catalysts is reduced to Ce_2O_3, the latter acquires the ability to accept CO_2 as a result of the formation of vacancies in the oxide lattice. On the other hand, hydrogen dissociates on rhodium and further methanation takes place. Catalysts obtained by the 'reverse' method — the deposition of the oxides of Al, Zr, Nb, Ta, and W on rhodium foil — have been investigated.[45,46] It was found that AlO_x and FeO_x inhibit the hydrogenation of CO_2, whilst the remaining oxides accelerate it. The authors explain this acceleration by the formation of an anionic vacancy at the metal–oxide interface. The degree of reduction of the oxide in the hydrogenation of CO_2 is greater than in the hydrogenation of CO owing to the higher concentration of H on rhodium. The authors[46] observed a correlation between the acidity of the deposited oxide and the catalytic activity. This was explained by the fact that, in the adsorption of CO or CO_2 molecules on the metal–oxide interface, they are oriented with their oxygen atoms towards the acid Lewis centre. In the case of the Pt/CaO and Pt/MgO catalysts, the alkaline earth metal oxide accepts CO_2, affording CO_3^{2-}, while H_2 dissociates on Pt.[47]

When the hydrogenation of CO_2 is compared with that of CO on metallic catalysts, two interesting features are noted: (1) the rate of hydrogenation of CO_2 to methane appreciably exceeds the rate of methanation of CO; (2) whereas higher hydrocarbons are formed together with methane in the hydrogenation of CO, methane is formed with an almost 100% selectivity in the hydrogenation of CO_2.[48–55]

Only methane is obtained on an iron foil, CO_2 being hydrogenated seven times faster than CO.[52] The activation energy for the methanation of CO_2 on Ru/Al_2O_3 was appreciably lower than that for the methanation of CO.[53] The submonolayer deposition of TiO_2 on rhodium increases the rate of hydrogenation of CO_2 by a factor of 15 and that of CO only by a factor of 3.[48] The selectivity in the conversion of CO_2 into methane on a cobalt foil was 99%, while that in the conversion of CO into methane was only 80%.[54]

All these facts show that CO_2 is reduced to methane via the intermediate formation of CO.

$$CO_2 + H_2 \rightleftharpoons CO + H_2O$$

$$CO + 3\,H_2 \rightleftharpoons CH_4 + H_2O$$

The complete dissociation of CO and subsequent hydrogenation of C(ads) and O(ads) are necessary for the synthesis of methane and other hydrocarbons.[56]

According to Gupta et al.,[55] the lower temperatures of the methanation of CO_2 compared with CO on Ru/TiO_2 can be explained by the higher reactivity of the metal carbonyls formed initially, the latter being rapidly converted into reactive carbon atoms.

The rate of reduction of CO_2 on the reduced Fe/Al_2O_3 and Re/Al_2O_3 catalysts under thermoprogrammed conditions increases sharply after the addition of 1%–3% of H_2. For example, the interaction of CO_2 with 8% Fe/Al_2O_3 begins at 520 °C when 1%–3% of H_2 is added to the reaction mixture and not at 740 °C, as happens in the absence of H_2. Under these conditions, the rate of reaction increases by a factor of 20–25.

According to the data of Highfield at al.,[58] after the addition of H_2 a new path arises in the interaction of CO_2 and Fe, resembling a chain reaction and requiring a lower activation energy.

$$Fe + 0.5H_2 \rightarrow Fe(H) \quad (8)$$

$$Fe(H) + CO_2 \rightleftharpoons FeHCOO \quad (9)$$

$$FeHCOO + Fe \rightarrow FeO + Fe(H) + CO \quad (10)$$

$$CO_2 + Fe \rightarrow FeO + CO$$

Reaction (8) corresponds to the 'initiation', whilst reactions (9) and (10) correspond to the 'propagation' of the chain reaction. One hydrogen molecule can ensure the conversion of many CO_2 molecules. It is suggested that a surface formate is an intermediate. To test this hypothesis, formic acid was deposited on the surface of iron and rhenium, after which an increase in the rate of methanation was observed.

On the rhenium catalyst in the presence of hydrogen, the Boudouard reaction is also accelerated.

$$CO_2 + C \rightarrow 2CO$$

When 1%–3% of H_2 was added to the stream of CO_2, the rate of conversion of the latter increased by a factor of 20, while the coke oxidation temperature fell by 200 °C.

It is also possible to formulate a chain mechanism of the Boudouard reaction. For this purpose, stage (10) in Schemes (8)–(10) must be replaced by the stage

$$FeHCOO + FeC \rightarrow Fe + Fe(H) + 2CO. \quad (11)$$

In this case, the 'initiation' is evidently again ensured by reaction (8), whilst 'chain propagation' is effected by reactions (9) and (11). At higher H_2 concentrations, reaction (3) takes place on Fe and Re.

The complexes Ru(H)CO, RuOCO, RuCO, and RuHCOO have been detected in an IR spectroscopic study of the $CO_2 + H_2$ reaction on Ru/TiO_2 [49] and Ru/Al_2O_3.[50] However, in most cases these complexes are present on the surfaces of the Al_2O_3, SiO_2, and TiO_2 carriers. In the most detailed studies, the rate of formation of CH_4 was compared with the rate of change in the intensities of the IR bands due to the intermediate adsorption complexes. For example a correlation between the concentration of adsorbed CO and $HCOO^-$ and the rate of methanation has been observed on Ru/TiO_2.[51,52] Hence it was concluded that the reaction has a dissociative mechanism (in the scheme below the symbol 'm' denotes the metal and the symbol 'c' denotes the carrier):

$$CO_2(gas) \rightleftharpoons CO_2(m),$$

$$H_2(gas) \rightleftharpoons 2H(m),$$

$$CO_2(m) + 2H(m) \rightleftharpoons HCOOH(c),$$

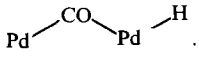
$$HCOOH(c) \rightleftharpoons H(m) + HCOO(c),$$

$$HCOOH(c) \rightleftharpoons CO(m) + H_2O,$$

$$CO(m) + 6H(m) \rightarrow CH_4 + H_2O.$$

On the Rh/Al_2O_3 catalyst, formates are intermediates in reaction (3) and the CO formed in this reaction undergoes methanation.[53] According to the data of Lahtinen et al.[54] and Gupta et al.,[55] the adsorption of H_2 on Rh/Al_2O_3 promotes the adsorption of CO_2, since this involves the formation of the formate, which may decompose into H_2O and CO on Rh or migrate on Al_2O_3, where it is more stable. On Rh/SiO_2, the formate is formed only in the presence of potassium.[56]

An increase in the degree of adsorption of CO_2 in the presence of H_2 has also been observed on deposited palladium,[57] where the complex



is formed. The formation of the formate, which occurs only in the presence of a carrier, is ensured by the spill-over of H atoms.

The formation of formate complexes has been observed by the IR spectroscopic method under the conditions of the interaction of H_2 and CO_2 on deposited ruthenium,[58,59] rhodium,[60-64] and palladium,[65] and nickel.[66]

The study of the interaction of H_2 with CO_2 on Ni(111) [67] and Cu(100) [68] single crystals and also on deposited nickel catalysts,[69,70] with the aid of various spectroscopic methods, showed that formate complexes are formed on their surfaces, their further reactions leading to the evolution of CO and H_2:

$$CO_2(ads) + H(ads) \rightleftharpoons HCOO(ads), \quad (12)$$

$$HCOO(ads) + H(ads) \rightleftharpoons H_2O + CO. \quad (13)$$

Reactions (12) and (13) apparently proceed simultaneously with the methane formation reaction, which require the complete dissociation of CO_2 and H_2 on adsorption.

The formation of higher hydrocarbons in the hydrogenation of CO_2 has been noted in comparatively few studies. For example, an increase in the heat treatment temperature of the Rh/Nb_2O_5 catalyst for the hydrogenation of carbon dioxide promotes an increase in the selectivity in the formation of C_2H_6 compared with CH_4.[71]

The carbides Mo_2C, Fe_3C, and VC proved to be active in the hydrogenation of CO_2;[72] the carbides TiC and SiC are inactive. C_1-C_3 hydrocarbons as well as CO and alcohols are formed in this process. Promotion with copper increases the selectivity in the formation of hydrocarbons.

When a mixture of iron and carbon powders is ground in a ball mill, a mixture of iron carbides is formed. The selectivity in the hydrogenation of CO_2 on this catalyst changes: instead of CO [reaction (3)], C_2-C_4 hydrocarbons and CH_4 are formed. With increase in the duration of grinding, the rate of reaction also increases and the alkanes : alkenes ratio diminishes from 0.37 to 0.16.[73]

On iron catalysts, higher hydrocarbons are formed apparently only in the presence of iron carbide.[74] On Fe-silicalite, higher hydrocarbons were not detected on hydrogenation of CO_2. This has been explained by the difficulty of reducing Fe, which hinders the formation of carbides.[75]

On polycrystalline cobalt, C_1-C_4 hydrocarbons were isolated on hydrogenation of CO, whilst methane and ethane were isolated on hydrogenation of CO_2.[54] The selectivity in the formation of CH_4 on the spinels $La_{1-x}M_xCoO_3$ (M = Sr or Th) increases with increasing degree of reduction, whilst the selectivity in the formation of C_2H_6 falls.[40]

2. The Bosch reaction

This reaction has been used in life support systems for the removal of CO_2 in the form of solid carbon.[34] It is employed also for the preparation of filamental carbon fibres.[76] Reaction (2) can be represented as the sum of reaction (1) and the catalytic cracking of methane:

$$CH_4 = C + 2H_2 \quad (14)$$

The dissociation of CH_4 on nickel proceeds rapidly even at 345 °C.

Reactions (1) and (14) can be carried out in a single reactor, where provision is made for the recirculation and isolation of water from the cycle. Depending on the nature of the catalyst (Ni, Co, Fe), pressure, and the number of times the recirculation has been carried out, the process is performed at temperatures ranging from 500 to 700 °C. There is also a possibility of another variant, where CH_4 is decomposed to C + $2H_2$ at 500 °C on Ni/SiO_2 in the first reactor, whilst in the second reactor CO_2 is methanated on the same catalyst at 300 °C, after which methane is returned to the first reactor. Filamental carbon is formed, in which Ni remains at the tip of the filament so that the activity is maintained at an unchanged level.[77]

CO_2 has also been reduced to carbon on iron, gallium, and zinc oxides and also on $LaFeO_3$.[78] The yield of carbon on WO_3 at 700 °C was 27%. Graphite was formed in the form of small isolated spots.

3. The reverse conversion of water gas

Reaction (3) proceeds on the same catalyst as the forward conversion of water gas but at a higher temperature (the equilibrium constant exceeds unity only above 530 °C).

The hydrogenation of CO_2 on oxide catalysts (in contrast to metallic catalysts) does not proceed as far as methane but only as far as CO. On oxides, the rate of hydrogenation of CO_2 is lower than the rate of hydrogenation of CO. Among the catalysts, mention should be made of the familiar iron–chromium oxide catalyst for the conversion of water gas. The selective reduction of CO_2 to CO has also been observed on Fe/MgO and Cu/ZnO [79] as well as Fe/C.[80] In addition, new active and selective catalysts for the reduction of CO_2 to CO, such as MoS_2 [81] and WS_2,[82] have been discovered.

Surface formates are produced as intermediates in reaction (3). However, there are data showing that the reaction proceeds via different surface compounds in the forward and reverse directions.[83]

In the hydrogenation of CO_2 on the chromium–manganese oxide catalyst, the only product is CO.[57] The formation of methane is observed only after the deposition of HCOOH on the surface. The mechanism of the reduction of CO_2 includes the interaction of H_2 with the carbonate structures formed initially:

$$H_2 + CO_3^{2-} \rightleftharpoons H_2O + CO + O^{2-}, \quad (15)$$

$$H_2 + O^{2-} \rightleftharpoons H_2O + [\ ], \quad (16)$$

where [ ] denotes a vacancy.

4. The synthesis of methanol and other oxygen-containing compounds

It is technologically inconvenient to synthesise methanol directly via reaction (4), since one third of hydrogen is consumed in the formation of water. The $CO + 3H_2$ mixture is therefore usually employed for the synthesis of methanol:

$$CO + 3H_2 = CH_3OH \quad (17)$$

For a long time, the zinc-chromium oxide catalyst, on which the process occurred with a high productivity at 320–400 °C and a pressure of 300 atm, was mainly used. In the 1960s–1970s new more active copper–zinc oxide catalysts, which made it possible to reduce the temperature to 250 °C and the pressure to 100 atm, were introduced into practical employment.

It was believed[84] that methanol is synthesised via the intermediate hydrogenation of CO. However, the use of the labelled $^{14}CO_2$ and ^{14}CO molecules showed[85] that in reality the species hydrogenated is not CO but the CO_2 formed from the latter. Careful elimination of CO from CO_2 and H_2O sharply reduced the rate of synthesis of methanol and only the formation of CO_2 via the water gas conversion reaction leads to the establishment of a stationary regime in the process. The rate of synthesis of methanol from CO_2 is many times higher than from CO.[86] This enabled the authors[87,88] to reach an unambiguous conclusion about the reaction paths of carbon oxides on oxide catalysts. According to their view, methanol is synthesised in two macroscopic stages. In the first stage, CO is converted by treatment with steam and this is followed by reaction (4).

It has been suggested that up to 5% of CO_2 be added to the synthesis gas in the industrial manufacture of methanol.[10]

The study of the kinetics and mechanism of the $CO_2 + H_2$ reaction on copper–zinc oxide catalysts permitted the conclusion that it proceeds via adsorption substitution stages.[89] Stable surface compounds participate in the reactions

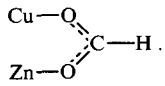
$$X \cdot H_2O + CO_2 \rightleftharpoons X \cdot CO_2 \cdot H_2O \rightleftharpoons X \cdot CO_2 + H_2O,$$

$$X \cdot CO_2 \cdot H_2O + CO \longrightarrow X \cdot CO_2 \cdot H_2 + CO_2,$$

$$X \cdot CO_2 + H_2 \longrightarrow X \cdot CO_2 \cdot H_2 \xrightarrow{2H_2} CH_3OH + X \cdot H_2O,$$

where X is a copper-containing surface centre, which is not part of the copper phase, for example a doublet of copper ions in the zinc oxide lattice.[88] The $X.H_2O.CO_2$ species may comprise the hydroxocarbonate and OH^- ions bound to a single X centre; this complex is hydrogenated to CH_3OH already at 120 °C. However, it is insufficiently stable above 200 °C and most probably does not participate in the synthesis of CH_3OH. The high-temperature chemisorption of CO_2 precedes the formation of CH_3OH and the only path leading to its formation is the adsorption substitution of H_2O.

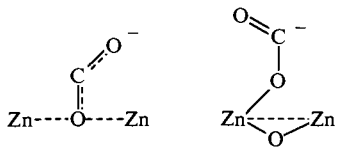
According to the results of Jackson[90] and Walker et al.,[91] the adsorption of CO_2 is dissociative under the conditions of the synthesis of methanol. IR spectroscopy in situ[92–97] made it possible to detect the surface formates, bicarbonates. and carbonates on the surfaces of the $Cu-ZnO-Al_2O_3$ and $Cu-ZnO-SiO_2$ catalysts. $HCOO^-$ complexes have been detected on ZnO and Al_2O_3. There are also data indicating the formation of the bidentate formate



at the interface.

According to Amenomiya and Tagawa,[95] the activity of the catalyst in the synthesis of methanol from CO_2 and H_2 is proportional to the $HCOO^-$ concentration on copper. On the other hand, the $HCOO^-$ concentration on aluminium remains unchanged under the conditions of the catalytic reaction.

After the adsorption of CO_2 on ZnO/SiO_2 and $Cu-ZnO/SiO_2$, two complexes were detected,[94] one of which is bound to the polar surface (**A**) and the other to the nonpolar surface (**B**).



A **B**

Complex **B** is more readily hydrogenated to the formate. Further hydrogenation results in the formation of $CH_3O.Zn$ and CH_3OH. The function of the polar surface consists in the dissociation of H_2 and the supply of H atoms for the hydrogenation of complex **B**. The addition of CO to the $CO_2 + H_2$ mixture inhibits the formation of the formate as a result of the re-reduction of the surface.

Carbonates, bicarbonates, and the CH_3O and CH_2O groups have been detected by NMR on the surfaces of the catalysts under the conditions of the synthesis of methanol from CO_2 and H_2.[98]

Apart from $Cu-ZnO/Al_2O_3$, Cu/ZrO_2 and $Cu-ZnO/ZrO_2$,[99–101] as well as Cu/Ga_2O_3, Cu/Cr_2O_3, and $Cu-ZnO/Ga_2O_3$[95,102] are also active and selective catalysts for the hydrogenation of CO_2 to methanol. It has been shown[102] that Al_2O_3 and ZrO_2 are the true carriers: they increase the surface of the catalyst but do not affect the specific activity of copper. On the other hand, Ga_2O_3 increases the specific activity of copper by 40% and that of Cr_2O_3 by 30%.

Copper is stabilised on the surface of the carrier in the Cu^0 or Cu^+ state.[103,104] It may be that the stable active centre of $Cu^+-[\,]-Zn-O$, where [ ] is an oxygen vacancy, arises at the interface between Cu and ZnO.[100] The role of the reversible absorption of hydrogen by the lattice in the course of the stabilisation of the active centres of the copper catalysts has been noted.[105]

The discussion concerning the mechanism of the reaction and the nature of the intermediates and the active centres in the synthesis of methanol from CO_2 and H_2 is continuing. The vast majority of investigators accept nowadays[87] that methanol is not formed directly from the synthesis gas but via the intermediate formation of CO_2. As regards the active centres of the Cu–ZnO catalyst, it is claimed in some studies that the reaction proceeds only on copper in the Cu^0 state,[106] while in others (see, for example, Sizgek et al.[107]) it is stated that the active centres are both copper and zinc.

It has been shown in a theoretical study[108] that CO_2 is stabilised in a linear form, bound to the surface via an O atom, on Cu^+ and Zn^{2+}, whilst on Cu^0 coordination via the C atom is preferred. In the case of 'O-coordination', methanol may be formed on the Cu^+ and Zn^{2+} centres via the pathway

$$CO_2 + M \xrightarrow{H_2} HCOO-M \xrightarrow{H_2} H_2CO-M \xrightarrow{H_2}$$

$$\longrightarrow CH_3O-M \xrightarrow{H_2} CH_3OH + M,$$

whilst on 'C-coordination' it is produced on Cu^0 and Zn^{2+} centres via the pathway

$$CO_2 + M \xrightarrow{H_2} M-COOH \xrightarrow{H_2} M-CO \xrightarrow{H_2}$$

$$\longrightarrow M-CHO \xrightarrow{H_2} M-CHOH \xrightarrow{H_2}$$

$$\longrightarrow M-CH_2OH \xrightarrow{H_2} CH_3OH + M.$$

It is as yet difficult to say which path predominates. The first intermediate complex in the first path is the formate, which has been detected spectroscopically, whilst in the second it is a metal-carboxylic acid. The existence of active centres participating in the second reaction path appears preferable.

Copper analogues, namely silver[109] and gold,[110] deposited on oxides have also been investigated as catalysts for the synthesis of methanol from CO_2 and H_2. It was found[109] that the $Ag-ZnO-Ga_2O_3/Al_2O_3$ catalyst is more selective than $Cu-ZnO-Ga_2O_3/Al_2O_3$, but the yield of methanol on it is lower.

Carbonates, formates, bridging CO groups, and CH_2O have been detected on the Cu/ZrO_2, Hg/ZrO_2, and Au/ZrO_2 catalysts under the conditions of the synthesis of methanol from CO_2 and H_2.[111] On this basis, the following reaction mechanism has been proposed:

$$CO_2 + H_2 \longrightarrow HCOO^- + H^+ \underset{OH}{\overset{-OH}{\rightleftharpoons}} CO(ads) \xrightarrow{H_2}$$

$$\longrightarrow CH_2O \xrightarrow{H_2} CH_3OH$$

The formate is apparently formed on ZrO_2, whilst H_2 comes from the metal via the spill-over mechanism.

Palladium catalysts deposited on La_2O_3, CeO_2, and TiO_2 have also been used to synthesise methanol from CO_2 and H_2.[112,113] On Pd/CeO_2 at 230 °C and 30 atm, the selectivity in the formation of CH_3OH exceeded 90% for a 3% conversion. The authors[113] noted the role of the spill-over of H atoms from Pd to CeO_2 and observed the reduction of Ce^{4+} to Ce^{3+}.

The study of palladium catalysts on various carriers showed that they are more active in the synthesis of methanol than Cu/ZnO. Pd/Ga_2O_3 is especially active: at 250 °C and a pressure of 5 MPa and for the $H_2:CO_2 = 3:1$ ratio, the turnover number of the reaction on this catalyst is ten times greater than on Cu/ZnO.[114]

The liquid-phase synthesis of methanol from CO_2 and H_2 may be used to solve the technological problem of removal of the excess heat. This process has been achieved on a $Cu-Zn/Al_2O_3$ catalyst; the yield of CH_3OH was 93%.[115]

More reduced forms of the catalyst are apparently needed for the synthesis of higher alcohols from CO_2 and H_2. Ethanol, propanol, and butanol are formed on a bimetallic $Ir-Mo/SiO_2$ catalyst.[116] On a catalyst such as 5% $Rh-Ni-Mn-O/SiO_2$ at 220 °C, a pressure of 50 atm, and for the $H_2:CO_2=3:1$ ratio, the selectivities in the transformation of CO_2 into CH_3OH and C_2H_5OH reached 5.4% and 41.1% respectively for a degree of conversion of 1.6%.[117] Nickel- and ruthenium-containing zeolites with added copper are active in the synthesis of higher alcohols. The selective formation of C_2H_5OH from CO_2 and H_2 on the copper–chromium oxide catalyst is observed when an alkali or a lanthanide is added to it. This can be explained by the need for the presence of OH groups on the catalyst surface in order to activate CO_2.[118]

According to the data of Wang et al.,[119] mainly CO and hydrocarbons are formed on the $K-Cu-Co-Cr-O$ catalyst. The selectivity in the conversion into the C_1-C_6 alcohols is only 1.8%, the fraction of ethanol among the alcohols being 44.0%. The Cu–Ni alloy proved to be an active and selective catalyst for the hydrogenation of CO_2 to a mixture of alcohols. The Ni–Mn and Ni–Co alloys are less selective.[120] The conversion of methanol into a higher homologue has been observed[121] in a mixture with CO_2 and H_2 in contact with a suspension of $Cu_3Zr_2H_{11}$ in solution in an alcohol–benzene mixture. At 210 °C and 25 atm, small amounts of propanol, butanol, and the corresponding ethers were detected in the products.

Hydrocarbons may be synthesised from a mixture of CO_2 and H_2 on Cu–Zn catalysts, methanol being formed as an intermediate. This process is a modification of the familiar 'Mobil process'.

On the Cu–Zn–Cr oxide catalyst mixed with the HY zeolite at 400 °C, carbon dioxide is converted into C_2-C_6 hydrocarbons.[122,123] The conversion of CO_2 with formation of a mixture of methanol and hydrocarbons greatly exceeds the equilibrium yield of methanol under these conditions as a consequence of the shift of the equilibrium in reaction (4) to the right.

Liquid hydrocarbons (up to C_8) have been obtained on a catalyst of the Fischer–Tropsch type containing 95% Fe and 5% Cu at 400 °C and a pressure of 50 atm.[124,125]

It has been suggested[126] that a two-stage flow reactor be employed for the synthesis of petrol from a mixture of CO_2 and H_2. In the first stage (in the first part of the reactor), methanol is synthesised (250 °C, 50 atm) on the $Cu-Zn-Cr-Al-O$ catalyst modified with Ag and Pd. In the second stage, a mixture of C_1-C_6 hydrocarbons is formed on the H–Fe silicate, the structure of which is similar to that of the HZSM-5 zeolite. The overall selectivity in the conversion of CO_2 into petrol reaches 46% and the yield is 71 g litre^{-1} h^{-1}. The authors believe[126] that the CO_2-containing effluent gases from electric power stations may be used in this process.

5. Synthesis of dimethyl ether

It has been noted[127,128] that the best way of overcoming the thermodynamic limitations associated with the synthesis of methanol is the direct synthesis of CH_3OCH_3 from CO_2 and H_2. Dimethyl ether may be formed from the synthesis gas on a mixture of the catalyst for the synthesis of methanol and an acid dehydration catalyst.[129] The conversion of $CO_2 + H_2$ into CH_3OH and $(CH_3)_2O$ was achieved[130] on a mixture of the $Cu-ZnO-Al_2O_3$ catalyst with solid acid catalysts (zeolites, WO_3/SiO_2 silicalite). The use of a type Y zeolite afforded the best result: at 240 °C, the yield was 17% for a selectivity of 55.1% with respect to $(CH_3)_2O$ and of 13% with respect to CH_3OH. On the $Cu-Zn-Cr_2O_3-Al_2O_3$ catalyst mixed with a zeolite, the yield of oxygenated products reached 18.8%.

Another reaction which makes it possible to overcome the thermodynamic limitations involves the conversion of a mixture of CO_2 and H_2 into methyl formate by the carboxylation of the intermediate methanol:

$$2CO_2 + 4\,H_2 \rightleftharpoons HCOOCH_3 + 2H_2O.$$

This reaction has been achieved on a mixture of the methanol catalyst with the K–Fe/L zeolitic catalyst.[131]

6. Synthesis of formic acid

Under standard conditions reaction (6) is thermodynamically unfavourable. For this reason, only negligible yields of HCOOH are observed. In order to increase the yield under mild conditions, alkaline and alkylating agents are used, for example ruthenium and iridium complexes. Methyl formate has been obtained with their aid from the $CO_2 + H_2 + CH_3OH + H_2O$ mixture.[22]

CO_2 has been reduced[132,133] in aqueous solution by Na, Zn, and Al amalgams. Very small amounts of HCOOH were obtained. Triethylammonium formate was formed in the hydrogenation of CO_2 on the complex $[Rh(NBD)(PMe_2Ph)_3]BF_4$, where NBD = norbornadiene, in solution in tetrahydrofuran.[134]

On the whole, the data presented in this section demonstrate that, despite the high cost of hydrogen and the large amount of energy consumed in a series of CO_2 hydrogenation processes, many of them, especially those involving the syntheses of methanol and dimethyl ether, can already be regarded as a basis for large scale industries, serving as an alternative to the CO-based processes. Highly active low-temperature catalysts are necessary for this purpose. As regards scientific theory, the greatest advance achieved in the very recent years has been the detection with the aid of physical methods of intermediate compounds on the catalyst surfaces. Spectroscopic methods have still been inadequately employed in situ.

IV. Interaction of carbon dioxide with methane

The reduction of carbon dioxide by hydrocarbons, i.e. the employment of CO_2 an oxidant, is the most promising procedure for the establishment of large scale processes involving the utilisation of carbon dioxide.

1. Metallic catalysts

The direct interaction of methane with CO_2 on metallic catalysts has been investigated by many workers, starting with Fischer and Tropsch.[135] Kurganova et al.[136] studied the catalytic reactions of an equimolar mixture of methane and carbon dioxide on platinum deposited on various carriers. Platinum deposited on the BAU activated charcoal proved to be the most active. Reaction (18), involving the preparation of the synthesis gas, and to an even greater extent reaction (19), involving the formation of carbon, and reaction (20), in which methane is converted by steam, take place on this catalyst starting at a temperature as low as 350 °C:

$$CH_4 + CO_2 = 2CO + 2H_2, \quad \Delta H = 209.3 \text{ kJ mol}^{-1}, \tag{18}$$

$$CH_4 + 2CO_2 = C + 2CO + 2H_2, \quad \Delta H = 641.1 \text{ kJ mol}^{-1}, \tag{19}$$

$$CH_4 + H_2O = CO_2 + 3H_2, \quad \Delta H = 76.6 \text{ kJ mol}^{-1}. \tag{20}$$

The following reactions are also possible:

$$CH_4 + 3CO_2 = 4CO + 2H_2O, \quad \Delta H = 330.6 \text{ kJ mol}^{-1}, \tag{21}$$

$$2CH_4 + CO_2 = C_2H_6 + CO + H_2O, \quad \Delta H = 16.7 \text{ kJ mol}^{-1}. \tag{22}$$

All five reactions (18)–(22) are endothermic and take place at high temperatures (600–900 °C). At 800 °C, ΔG for the first four reactions is negative, whilst for reaction (22) it is positive but not very large. The equilibrium yield of C_2H_6 in reaction (22) at 800 °C is 13%, which is fairly large.

In the preparation of synthesis gas by reaction (18), $\Delta G = 0$ at 630 °C. Above this temperature, the equilibrium is displaced towards the formation of synthesis gas, while below it it is

displaced towards $CH_4 + CO_2$. The possibility of regulating the direction of the reversible reaction (18), i.e. the formation of synthesis gas at a high temperature and of methane at low temperatures, has been used to devise cells in which solar energy is employed: the endothermic reaction takes place on heating with sunlight, whilst the exothermic reaction is used to give up the energy.[137] The 1% Ru/Eu_2O_3 catalyst, containing 3 nm ruthenium particles having a hexagonal structure, is most suitable for the solution of the problem.[138]

Reaction (18) can be represented as a combination of the methane steam conversion reaction (20) and the reverse conversion of water gas [reaction (3)]. The study of the kinetics of reaction (18) on a nickel catalyst at 800–900 °C showed[139] that its rate is described by the same equation as the rate of the steam conversion:

$$r = \frac{k_1 P_{CH_4}}{1 + k_2(P_{H_2O}/P_{H_2}) + k_3 P_{CO}},$$

where k_1, k_2, and k_3 are constants and P_{CH_4}, P_{H_2O}, P_{H_2} and P_{CO} are the partial pressures of methane, water, hydrogen, and carbon monoxide respectively. The authors[139] explain this by the fact that CH_4 reacts initially not with CO_2 but with H_2O. Reaction (20) is rate-limiting. The hydrogen obtained in this reaction interacts rapidly with CO_2 via reaction (3) with reformation of H_2O.

The kinetics of all three reactions (18), (20), and (3) have been investigated[140] on eight different metallic catalysts deposited on MgO or Al_2O_3. It was found that the rate of reaction (3) exceeds slightly (in some cases by an order of magnitude) the rates of reactions (18) and (20). On the other hand, the rate of reaction (18) is lower than the rate of the steam conversion of methane with the exception of those cases where the latter is carried out on the Ni/MgO and Ni/Al_2O_3 nickel catalysts, where reactions (18) and (20) proceed at similar rates.

According to Blom et al.,[141] the reduced selectivity in the formation of H_2 compared with CO on Ni/Al_2O_3 at 600–800 °C can be explained by the fact that reaction (3) is much faster than the steam conversion of methane [reaction (20)]. Similar data have been obtained also on deposited cobalt catalysts.[142]

In conformity with Eqn (19), the interaction of CH_4 with CO_2 leads to the formation of carbon, which poisons the nickel catalyst. Carbon is formed both from methane on dissociation of the latter into carbon and hydrogen and from CO via the Boudouard reaction. Carbon is formed in the form of carbon filaments, probably on the Ni(111) face.[143]

Various procedures are used for the industrial preparation of synthesis gas from a mixture of CH_4 and CO_2. The so called 'Calcor' process involving the conversion of a natural or petroleum gas in the presence of CO_2, is available.[144,145] The Haldor Topsoe Company uses the $CH_4 + CO_2 + H_2O$ mixtures to reduce the poisoning of the nickel catalyst and the blocking of the tubes with carbon.[140,146–148] The same company has developed the SPARG (9 atm, 900 °C) process, where sulfur vapour, which passivates nickel and prevents the formation of carbon, is added to the active gas. Rostrup-Nielsen[146] believes that the formation of carbon requires an *ensemble* of several nickel atoms: the *ensemble* for the carbonic acid conversion of methane contains a smaller number of nickel atoms.

Inui et al.[149] suggested that joint $CH_4 + CO_2 + H_2O + O_2$ reforming be employed. This makes it possible to solve the problems of both coke formation and energy consumption. Whereas at 350 °C, the catalytic conversion of methane takes place, i.e.

$$CH_4 + 2O_2 = CO + 2H_2O, \quad \Delta H = 803.5 \text{ kJ mol}^{-1}, \qquad (23)$$

above 500 °C the weakly exothermic reaction involving the formation of the synthesis gas takes place:

$$2CH_4 + O_2 = 2CO + 4H_2, \quad \Delta H = -49.0 \text{ kJ mol}^{-1}. \qquad (24)$$

On the very active 6.6% Ni–3.9% CeO_2–2.2% Pt–0.02% Rh/Al_2O_3 catalyst, the degree of conversion of methane in a mixture with CO_2 and H_2O at a space velocity of 73 000 h^{-1} agrees with the equilibrium value, whereas at 358 000 h^{-1} (contact time 0.01 s) it is lower than the latter. However, if O_2 is added to this mixture, it is possible to achieve a yield of hydrogen of 2877 mol litre^{-1} h^{-1}.

The Ni/SiO_2 catalyst exhibits a much higher activity than the oxides CaO and Fe_2O_3. The temperature of the 50% conversion of CO_2 is 640 °C on Ni/SiO_2 and 900–1000 °C on the oxides.[150,151] The above oxides are coated by carbon faster than is nickel. At 800 °C, the degree of conversion of the $CH_4 + CO_2$ mixture into the synthesis gas was 83.1% on Ni/Al_2O_3, 74.2% on Co/Al_2O_3, and only 3.4% on Fe/Al_2O_3. On Ni/SiO_2, the rate of reaction is approximately 1.5 times lower than on Ni/Al_2O_3.[152,153] When the nickel content is less than 13%, the catalyst is fairly resistant to the deposition of coke. In the presence of a high nickel content, carbon filaments are formed.[154]

The use of MgO or CaO–MgO as carriers for nickel[155,156] and cobalt[156] catalysts greatly increases their activity and especially their stability. On interaction with CO_2, the alkaline carrier gives rise to a carbonate, which coats the surface and prevents coke formation.

A layer having the composition $CH_{0.08}$, i.e. close to pure carbon, is formed on nickel foil under the catalytic conditions. The layer has the composition $CH_{0.06}$ on Ni/SiO_2 and CH_2 on Ni/MgO. For this reason, less coke is formed on Ni/MgO. It has been postulated[157] that MgO acts as an electron-donating carrier and retards the dissociation of CH_x. The conversion of CH_x into C_{ads} leads subsequently to the formation of inactive graphite and the deactivation of nickel. It has been observed[159] that the composition of the CH_x fragment on nickel depends on the nature of the carrier: $x = 2.7$ on MgO, 2.5 on ZnO, 2.4 on Al_2O_3, 1.9 on TiO_2, and 1.0 on SiO_2. However, according to the data of Takeyasu et al.,[159] on the nickel catalysts Ni/MgO, Ni/SiO_2, and Ni/α-Al_2O_3 the ratios C:Ni are the same and equal to the corresponding ratio for metallic nickel.

Iron, cobalt, and nickel powders mixed with an ultradisperse ceramic material in proportions of 1:10 exhibit a high activity. At 740 °C, the yield of the reaction product was 94% at a space velocity of 4500 h^{-1} and 71% at 6100 h^{-1}. The catalysts retain their activity for 70 h.[160]

Nickel catalysts deposited on the nonacid MgY and NaY zeolites also exhibit a catalytic activity at 580 °C.[161] The maximum yield was observed in the presence of a 20% nickel content.

Nickel and cobalt metallic particles are probably formed also in the carbonic acid conversion of methane into the synthesis gas on the $Ca_{0.8}Sr_{0.2}Ti_{0.8}Co_{0.2}O_{3-\delta}$ and $Ca_{0.8}Sr_{0.2}Ti_{0.8}Ni_{0.2}O_{3-\delta}$ catalysts.[162] The nickel-containing catalyst is more active: at 755 °C, the degree of conversion of CO_2 was 64.6% and that of CH_4 was 89.6% on this catalyst. Under these conditions, the yield of CO reached 69.0% and that of H_2 54.8%, while the selectivity in the formation of H_2 was 84.8%. Reaction (18) is accompanied by the simultaneous deposition of coke via reaction (19). The basic properties of the surface may promote the occurrence of the oxidation-reduction process on the latter.

Platinum group metals are active catalysts for the carbonic acid conversion of methane.[138,140,151,163–180] The reaction already proceeds at an appreciable rate at 500 °C. It has been shown by the alternate pulse method that CO is formed when the CO_2 pulse is supplied. C_2H_6 and C_2H_4 are formed in the first pulses, i.e. the oxidative condensation of methane takes place. Carbon is less soluble in noble metals than in nickel, but after a time poisoning takes place — slow at 500 °C and rapid at 600 °C.

An evident disadvantage of noble metals is their high cost, while an advantage is their higher activity than that of nickel, cobalt, and iron and a smaller susceptibility to poisoning. Among the catalysts deposited on Al_2O_3, the most active at 500–700 °C is Rh/Al_2O_3[151,162–166] (Ru/Al_2O_3[171,175,178] and Ir/Al_2O_3[174] according to other data) and is followed by Pt/Al_2O_3 and

Pd/Al_2O_3. This series corresponds to the activity series of the catalysts for the dissociation reaction

$$CO_2 \rightleftharpoons CO + O(ads).$$

The activity series $Ru/MgO > Rh/MgO > Ni/MgO > Pt/MgO > Pd/MgO$ has been obtained for metals deposited on MgO.[153] Rhodium and palladium are poisoned to the least extent, but they are the most expensive.

When the same metal is deposited on different carriers, the latter form the following activity series:[171-173,179] $Al_2O_3 > TiO_2 > SiO_2 > MgO$. According to certain data,[165] acid carriers are more active because they promote the dispersion of the deposited metals. However, the formation of carbonates on basic carriers diminishes the deposition of coke.

The high activities of all the deposited noble metals investigated have been demonstrated.[161,168] It is also significant that in almost all cases the gas mixture had the $CO:H_2 = 1$ composition, i.e. virtually no side reactions were observed. Synthesis gas was formed from the initial $CH_4:CO_2 = 1$ mixture at 780 °C with the following yields: 1% on Al_2O_3, 85% on 1% Ni/Al_2O_3, 73% on 1% Pd/Al_2O_3, 89% on 1% Ru/Al_2O_3, 87% on 1% Rh/Al_2O_3, and 89% on 1% Ir/Al_2O_3. The Ni/Al_2O_3 and Pd/Al_2O_3 catalysts were saturated with coke faster than any others. The Ir/Al_2O_3 catalyst proved to be most resistant to coke formation: it retained its activity for 260 h. The yield of H_2 was found to exceed that of CO on Ru/Al_2O_3. When the $13CH_4 + O_2 + CO_2$ mixture is used, the yield of products on Ni/Al_2O_3 may reach 91% and the reaction becomes thermoneutral. The gas obtained from the $4CH_4 + O_2 + 9CO_2$ mixture contained exactly 50% of CO and H_2 and carbon was not formed on the surface.

The iridium and ruthenium catalysts obtained from the iridate ($Ln_2Ir_2O_7$) and ruthenate ($Ln_2Ru_2O_7$) pyrochlores (Ln = Nd, Sm, Eu, Gd) had a high activity.[169,170] These oxides are activated under the reaction conditions, being converted into the corresponding metals.

Mechanisms have been proposed for the reaction under consideration presupposing the dissociation of CH_4 and CO_2. The correlation between the activity series of the catalysts in the $CH_4 + CO_2$ reactions and in the dissociation reaction $CO_2 \rightleftharpoons CO + O$ suggested[158,180] the following mechanism:

$$CH_4 + S = [CH_{x,S}] + (4 - x)H_S = C_S + 2H_2,$$

$$CO_2 + 2S = CO_S + O_S,$$

$$CO_S = CO + S$$

(The symbol S denotes the catalyst surface).

Other investigators[168,173] also postulate the stepwise dissociation of the CH_4 molecule, but the process mechanism includes the Boudouard reaction.

$$CH_4 + O(ads) = CH_3(ads) + OH(ads),$$

$$CH_3(ads) = CH_x + H(ads),$$

$$CO_2 + H(ads) = CO(ads) + OH(ads),$$

$$CH_x + O(ads) = CO + xH(ads),$$

$$2OH(ads) = H_2O + O(ads),$$

$$CO_2 + C = 2CO,$$

$$C + H_2O = CO + H_2.$$

The study of the $CH_4 + CO_2$ interaction on the $Rh/\gamma\text{-}Al_2O_3$ catalyst with the aid of a TAP reactor[181] showed that the reverse Boudouard reaction proceeds exceptionally rapidly and the mechanism involving it is extremely likely.

Above 500 °C (on Rh), carbon forms a supersaturated solution which inhibits the reaction. The reactions

$$CH_2(ads) + CO_2 = CO + H_2O + C(ads),$$

$$CH(ads) + OH(ads) = CO + H_2$$

are also possible.

The ratio $CO:H_2 > 1$, frequently observed in the products, indicates the occurrence of a number of secondary reactions: the conversion of water gas, the hydrogenation of CO, CO_2, etc.

The study of pure metals by XPS and Auger spectroscopy[182] showed that the reactions

$$CH_4 + Z \rightarrow CH_3-Z \rightarrow CH_2-Z \rightarrow CH-Z \rightarrow C-Z,$$

$$CH_x-Z + O-Z = CO + \tfrac{1}{2}xH_2 + 2Z$$

and the equilibrium reaction

$$H_2O + Z = O-Z + H_2$$

(Z is a catalyst surface centre) occur on the surface.

According to this scheme, the carbonic acid conversion of CO_2 requires that the CH_x particles, formed on interaction between methane and the metal, do not last sufficient time to be fully dehydrogenated and that they should have reacted with O_2. In this case, the reaction

$$CO_2 + Z = O-Z + CO$$

is rate-limiting and the carbonic acid conversion of CH_4 is therefore slower than the steam conversion. It is also possible that the rate of the overall process depends on the CO concentration on the surface. Carbon monoxide participates in the reactions

$$CO + Z = CO-Z$$

and

$$CO-Z \rightarrow C-Z + O-Z.$$

C–Z is probably less reactive than O–Z. The metals on which the heat of adsorption of CO is high undergo a greater reduction in their activity following the replacement of H_2O by CO_2.

However, the study of the carbonic acid conversion of methane on Rh/Al_2O_3 and Ir/Al_2O_3 showed that the dissociation of CO_2 into $CO + O_{ads}$ is not observed under the catalytic conditions (700 °C).[183] On the other hand, methane decomposes quantitatively into $C + 2H_2$. There are no CH_x particles on the surface, since all the surface carbon is hydrogenated quantitatively to methane. The authors therefore propose the following reaction mechanism:

$$CH_4 + Rh_S \rightarrow C_S-Rh_S + 2H_2,$$

$$C_S-Rh_S + CO_2 \rightarrow 2CO + Rh_S.$$

Dissociative mechanisms have also been put forward. Analysis of the IR spectra in situ indicate the formation of formate species (apparently on the carrier),[171,184] linear and bridging carbonyls,[185] and CH_x groups.[173,174]

2. Oxide catalysts

A series of oxide catalysts for the oxidative condensation of methane have been investigated.[186-199] Their behaviour in two reactions was compared: (1) $CH_4 + O_2$ (100 : 1) and (2) $CH_4 + CO_2 + O_2$ (100 : 100 : 1). It was found that, on a catalyst with a moderate basicity, an even higher yield of C_2 hydrocarbons is achieved in the $CH_4 + CO_2 + O_2$ mixture than in the $CH_4 + O_2$ mixture. For example, on 50% PbO–MgO the yield of C_2 species was 3.28% in the first reaction and 4.37% in the second; on $CaO-BaO-CeO_2$, the yields were 2.2% and 3.5% respectively. These results led to the conclusion[188] that the oxygen atoms split off from CO_2 participate in the oxidative dehydrogenation of hydrocarbons:

$$CO_2 \rightarrow CO + O(ads), \quad (25)$$

$$2CH_4 + O(ads) \rightarrow C_2H_6 + H_2O, \quad (26)$$

$$C_2H_6 + O(ads) \rightarrow C_2H_4 + H_2O. \quad (27)$$

Experiments with labelled $^{13}CO_2$ and CD_4 molecules showed that ^{13}CO and C_2D_6 are formed in the reaction.[189] This means

that the CO is obtained only from CO_2 and not as a result of the further oxidation of the hydrocarbon. In the absence of the hydrocarbon, the CO_2 on the catalyst is absolutely unreactive. A certain initial amount of ethane is necessary to initiate the reaction. The conversion of CO_2 is apparently achieved via the reversible conversion of water gas [reaction (3)] by the hydrogen formed in the gas-phase dehydrogenation of ethane with the intermediate dissociative adsorption of CO_2 [reaction (25)]. Thus, in the oxidative dehydrogenation of CH_4 and C_2H_6, the mechanism of the activation of the hydrocarbon is the same regardless of whether O_2 or CO_2 is used as the oxidant.

On pure MgO, synthesis gas is formed via reaction (18), reactions (19) and (21) take place on PbO, while the oxidative condensation reactions (22) and (27) occur preferentially on PbO.MgO. Catalysts with strong basic centres, for example Li/MgO or Ni/ZnO, are less active in the $CH_4 + CO_2$ reaction than in the $CH_4 + O_2$ reaction and are rapidly deactivated.[189]

The carbonic acid conversion of methane has been achieved on vermiculite 22 $MgO.22SiO_2.5Al_2O_3.Fe_2O_3.40H_2O$ at 900–970 °C, for the ratio $CO_2 : CH_4 = 0.5 - 1.5$, and fairly long contact times (10.5–21 s). The degree of conversion of the $CH_4 + CO_2$ mixture into synthesis gas was 99.2%–99.7%. In the empty reactor at even lower rates of supply of the starting material at the same temperature, 62% of CH_4 and 40% of CO_2 were converted, the walls of the reactor becoming coated with a layer of carbon.[190]

The influence of various oxide additives (Cu, Mn, Fe, etc.) on the activity of the nickel catalyst for the carbonic acid conversion of CH_4 has been investigated.[191] Manganese oxides proved to be most effective. The formation of carbon was reduced in their presence, while the degree of conversion of CO_2 increased with increasing manganese content in the nickel catalyst.

Further studies showed that it is possible to do without nickel altogether in carrying out reaction (18). The characteristic features of the $CH_4 + CO_2$ reaction on manganese oxide catalysts have been investigated in detail.[192–203] Under stationary conditions the 5% Ca–12% $Mn-O/Al_2O_3$ catalyst proved to be the most effective. At 870 °C and a space velocity of 900 h^{-1}, the degree of conversion of CH_4 was 83.1%, that of CO_2 was 62.7%, and the selectivity with respect to H_2 was 76.5%. An equimolecular mixture of CO and H_2 was obtained. Extensive oxidation of methane by the catalyst oxygen occurred initially and the conversion of CO_2 did not take place. As the reaction proceeded and the catalyst was reduced, the activation of CO_2 began. The CO and H_2 concentrations then increased continuously. The complete conversion of CO_2 and CH_4 was achieved on the catalyst operating under stationary conditions at 930 °C (the selectivity was 99.7% in the formation of CO and 84.6% in the formation of H_2). The activity of the catalyst was retained for a long time (> 500 h) and carbon was not formed via reaction (19).

The study of the phase composition of the working Ca–MnO/SiO_2 catalyst showed[193] that the more oxidised Mn_2O_3 and Mn_3O_4 phases are reduced during the reaction and only the reduced MnO phase is retained in the catalyst. After the stabilisation of the composition of the catalyst, the formation of the manganese carbide and metallic magnesium phases was not observed.

After the initial treatment of the catalyst with carbon dioxide and subsequent exposure of the former to methane at 850 °C, ethane and ethene are formed, i.e. the oxidative dimerisation reactions (22) and (28) take place, possibly with participation of the carbonate phase.[196]

$$2CH_4 + CO_2 = C_2H_4 + CO + H_2O, \quad \Delta H = 176 \text{ kJ mol}^{-1}, \; T_{\Delta G=0} = 750 \text{ °C}. \qquad (28)$$

The yield of C_2 hydrocarbons is 9%.

A decrease in the temperature of the treatment of the catalyst with carbon dioxide raises the yield of C_2H_6 and C_2H_4 to 13%. When the reduction of Mn_2O_3 and Mn_3O_4 has been completed, the yield of C_2 hydrocarbons falls and only synthesis gas is formed in the stationary state. An increase in the degree of conversion of CH_4 hardly affects the selectivity. This may be associated with the establishment of equilibrium in the water gas conversion reaction (3).

The La–Na–$Mn-O/SiO_2$ catalyst exhibits a high selectivity in the conversion of CH_4 into C_2 hydrocarbons under non-stationary conditions.[197] After its treatment with carbon dioxide and subsequent admisison of methane at 800 °C, C_2 hydrocarbons are formed in almost 100% yield, whereas CO is not produced. Consequently the process takes place via the interaciton of CH_4 with the carbonate fragments of the catalysts and not via a multistage oxidation-reduction mechanism:

$$CO_3^{2-} + 2CH_4 \rightarrow C_2H_6 + CO + H_2O + O^{2-},$$

$$CO_3^{2-} + C_2H_6 \rightarrow C_2H_4 + CO + H_2O + O^{2-},$$

$$CO_3^{2-} \rightleftharpoons CO_2 + O^{2-}.$$

The selectivity of another catalyst investigated in the formation of C_2 hydrocarbons, namely La–Cu–O/SiO_2 was lower.[197,199] Under alternation conditions, the reaction of CO_2 with the catalyst produced CO, whilst the subsequent reaction with methane gave rise to C_2 hydrocarbons. The oxidation–reduction mechanism is more probable in this case. Under stationary conditions, synthesis gas, and not ethane and ethene, is formed on both catalysts.

The properties of the La–$Mn-O/Al_2O_3$ catalyst proved to be similar to those of La–$Mn-O/SiO_2$.[198,199] The selectivity in the formation of C_2 hydrocarbons in separate interactions did not exceed 5%. The constancy of the rate of reoxidation of the catalyst by carbon dioxide as a function of time can be explained by the occurrence of the reverse reaction involving the reduction of the catalyst by the carbon monoxide formed on reoxidation by reaction (24).

A similar equilibrium has been observed also in the oxidative condensation of methane on the familiar Li–MgO catalyst:[198,199]

$$Li^+[\,] + Li^+O^{2-} + CO_2 \rightleftharpoons 2Li^+O^- + CO \qquad (29)$$

[ ] = lattice defect.

The rate of formation of CO in such a process is 40 times lower than in the reoxidation of the manganese systems. Reaction (29) is accompanied by the reaction involving the formation of the stable lithium carbonate Li_2CO_3, which coats the surface and does not therefore participate in the stationary reaction. The selectivity in the formation of hydrocarbons on the Li–MgO catalyst by the $CH_4 + CO_2$ reaction was only several tenths per cent.

The rates of formation of hydrogen under the conditions of the stationary catalytic reaction on $Ca-MnO/Al_2O_3$ (3×10^{-3} mol g^{-1} h^{-1}) and in the reductive reaction between CH_4 and the catalyst (1.7×10^{-3} mol g^{-1} h^{-1}) are comparable. On the other hand, the rate of the interaction of CO_2 with the reduced catalyst (reoxidation of the catalyst) exceeds the rate of the reduction. Thus, in contrast to the metallic catalysts,[139,167] the rate-limiting stage on the magnesium oxide catalysts is apparently the cracking of methane with formation of surface carbon deposits, which are then rapidly oxidised. The presence of manganese oxide in the catalyst increases the rate of oxidation of carbon on the surface. Carbon dioxide interacts with MnO giving rise to a surface carbonate, which reacts with carbon.[191,196]

Scheme 1

$$CH_4 + MnO \xrightarrow{a} MnO...C + 2H_2,$$

$$CO_2 + MnO \overset{b}{\rightleftharpoons} MnCO_3,$$

$$MnCO_3 + MnO...C \xrightarrow{c} 2MnO + 2CO,$$

$$MnCO_3 + H_2 \xrightarrow{d} MnO + CO + H_2O,$$

$$MnO...C + H_2O \xrightarrow{e} MnO + CO + H_2.$$

According to X-ray diffraction data, the MnO and $MnCO_3$ phases are stationary under the catalytic conditions: appreciable oxidation and reduction is not observed and the catalysis does not take place via the mechanism involving the alternate oxidation and reduction of the catalyst. Nevertheless, one may postulate

that intermediate oxidised forms are produced in stage *c* after the decomposition of the carbonate:[199]

$$3MnCO_3 + H_2O \rightleftharpoons Mn_3O_4 + 2CO_2 + CO. \quad (30)$$

The possibility that the carbonates perform transport functions in relation to oxygen has been noted in a study[204] where the oxidative dimerisation of methane with the use of O_2 on $La_2O_3-BaCO_3$ was investigated. The following equation for the rate of reaction arises from Scheme 1:

$$r = \frac{k_1 P_{CH_4}}{1 + (1/k_2k_3)(P_{CO}^2/P_{CO_2}) + k_2 P_{CO_2}},$$

where P_{CH_4}, P_{CO} and P_{CO_2} are the partial pressures of CH_4, CO, and CO_2 respectively and k_1, k_2, and k_3 are the reaction rate constants (Scheme 1). This equation has been confirmed by experimental data.

The introduction of potassium and chromium into the catalyst alters the nature of the process and reaction (21) becomes dominant. On $K-Cr-Mn-O/SiO_2$, the reaction apparently proceeds via the oxidation-reduction mechanism. The second transition metal oxide (Cr_2O_3) participates in the reoxidation. It apparently forms an interface, which facilitates the oxidation-reduction process. When CO_2 is employed, the oxygenating capacity in the oxidative process on $K-Cr-Mn-O/SiO_2$ is much smaller (by a factor of 8) than in the case where O_2 is used.

The $CH_4 + CO_2$ reaction may serve as the first stage in the synthesis of higher hydrocarbons. A two-stage process has been proposed,[202] according to which in the first reactor at 950–970 °C methane undergoes the carbonic acid conversion on manganese silicate modified with 21.8%–2.4% of K_2O with complete conversion of the starting material. In the second reactor, the synthesis gas is converted into C_2-C_3 alkenes with a selectivity of 20%–26% on a catalyst containing 8.1%–9.4% of Fe and 2.2%–6.9% of K on Al_2O_3 at 415–425 °C.

The reverse reaction (18) may be employed in devices utilising solar energy the forward reaction proceeds under the influence of solar energy, whilst the reverse reaction takes place at a low temperature. Owing to the lower selectivity of the reverse reaction, the process efficiency is 54%.[205]

The results presented in this section show that recently there has been a considerable growth of interest by investigators in the interaction of methane with carbon dioxide. Both reaction components are cheap and one may hope to be able to devise large scale processes on their basis. In particular, this applies to the preparation of synthesis gas. As regards the final carbonic acid condensation of methane, the prospects for its industrial application are so far not quite so evident.

Nickel catalysts are most often employed to obtain synthesis gas, but they are poisoned by carbon. Iridium and ruthenium catalysts are active and are not poisoned by carbon, but they are expensive. Finally, the oxide catalysts based on MnO and the rare earths are not poisoned, but they operate at a high temperature and their productivity is inadequate. The mechanisms of the action of the metallic and oxide catalysts are apparently different. Methane is readily dissociated on the former, but the activation of CO_2 is difficult whilst the opposite situation obtains on the latter.

V. Interaction of carbon dioxide with other paraffins

1. Interaction with ethane

When CO_2 interacts with ethane, both the oxidative dehydrogenation of the latter to ethene [reaction (28)] and the formation of synthesis gas [reaction (31)] and carbon [reaction (32)] may take place.2).

$$C_2H_6 + 2CO_2 \rightarrow 4CO + 3H_2, \quad (31)$$
$$\Delta H_{298} = 247.9 \text{ kJ mol}^{-1},$$

$$C_2H_6 + 2CO_2 \rightarrow CO + 3H_2O + 3C. \quad (32)$$

The study of the oxidative dehydrogenation of ethane with the aid of CO_2 showed that manganese oxides serve as a base for the most active and stable systems for the activation of CO_2 and hydrocarbons.[191–193, 195, 196, 202, 204, 206–210] With increase in the manganese concentration in the $Mn-O/SiO_2$ system from 8% to 17%, the degree of conversion of C_2H_6 at 800 °C, a space velocity of 3600 h^{-1}, and for the ratio $CO_2 : C_2H_6 = 1.5$ increases from 65.1% to 73.1%, the degree of conversion of CO_2 rises from 42% to 46.2%, the selectivity with respect to C_2H_4 increases from 52.5% to 61.0%, while the yield of C_2H_4 increases from 34.3% to 44.5%. On the 17% MnO/Al_2O_3 catalyst, the degrees of conversion of C_2H_6 and CO_2 were approximately the same, but the selectivity in the formation of C_2H_4 was somewhat smaller (46.6%). Under the same conditions, reactions (31) and (32) occurred on the nickel catalyst, which was rapidly poisoned as a consequence of coke formation.

A number of oxides (of antimony, zinc, vanadium, and iron), used in the hydrocarbon dehydrogenation reactions, were tested as additives to manganese oxide. The degree of conversion of CO_2 on the $Mn-Sb-O$ and $Mn-Zn-O$ systems was low. A 58% conversion was observed on $MnO-V_2O_5$, but the selectivity in the formation of C_2H_4 was low. The $Mn-Fe-O/SiO_2$ system proved more active, but a high level of selectivity (67%) is attained on this catalyst only during the initial period of its operation (up to 3 h), after which the selectivity falls.

Comparison of data on the catalytic activity of the $Mn-Fe-O/SiO_2$ system and its phase composition under stationary conditions in situ and also under reduction and reoxidation conditions showed that manganese oxides are reduced to MnO during the reaction, while iron oxides are reduced to α-Fe and the carbide. This is apparently the cause of the decrease in selectivity with respect to C_2H_4, the increase in the degree of conversion in reactions (31) and (32), and the saturation of the surface by carbon. Hence it was concluded that the modifying additive to the base oxide should be sought among variable-valence metal oxides exhibiting a catalytic activity in the dehydrogenation reactions and not reduced to the metal under the reaction conditions. Chromium oxides possess such properties. On the 5% Cr–17% $Mn-O/SiO_2$ catalyst, the selectivity with respect to C_2H_4 reaches 70% at 800 °C. A further increase in selectivity is observed when the catalyst is modified by alkali and alkaline earth metal oxides. After the introduction of 1.5% of K into this catalyst, the reaction selectivity at 830 °C increased from 65.4% to 76.8% for ethane and CO_2 conversions of 82.6% and 52.3% respectively. The yield of C_2H_4 was 55.7% for $C_2H_4 : CO \approx 1$. Under these conditions, the degrees of conversion of C_2H_6 and CO_2 on the $Cr-O/SiO_2$ catalyst, which contains no manganese, are low.

The study of the degrees of conversion of C_2H_6 and CO_2 showed that the selectivity with respect to C_2H_4 initially increases with increase in the $CO_2 : C_2H_6$ ratio and then attains a plateau (for $CO_2 : C_2H_6 > 2.5$). This effect is probably associated with the increasing degree of oxidation of the surface and with decrease in the contribution of the extensive cracking of ethane. Such variation of the selectivity differs significantly from that observed in the oxidative dehydrogenation of C_2H_6 in the presence of oxygen, where the selectivity with respect to the alkene fell with increase in P_{O_2}.

Reaction (18) can be carried out also under conditions with separate oxidation and reduction steps. In this regime, C_2H_6 is converted into C_2H_4 on reduction of the catalyst, whilst the reoxidation of the later results in the reduction of CO_2 to CO.

Bearing in mind the data showing that the dehydrogenation and extensive conversion of ethane occur on different centres, one may put forward the following mechanism for the reactions of methane in a general form:

$$\begin{array}{l} C_2H_6 \xrightarrow{I} RO \longrightarrow C_2H_4, \\ \quad\quad\quad\quad\ \downarrow \\ C_2H_6 \xrightarrow{II} R \longrightarrow \text{extensive conversion products} \end{array} \qquad (33)$$

The mode of conversion of ethane is determined by the ratio of the oxidised and reduced centres (RO : R), an increase which results in an increase in selectivity with respect to ethene. As the degree of conversion of ethane increases and CO accumulates in the reaction medium, the catalyst surface is reduced by carbon monoxide and process II predominates. The rates of the parallel processes specified in reaction (33) may be described by the equations

$$r_I = k_1 P_{C_2H_6}[RO],$$

$$r_{II} = k_2 P_{C_2H_6}[R].$$

The RO and R centres are linked by the equilibrium reaction $R \leftrightharpoons RO$.

From the stationary condition [R] + [RO] = 1 and the equations for r_I and r_{II}, we obtain the expressions

$$r_I = \frac{k_1 k_3 P_{C_2H_6} P_{CO_2}}{k_3 P_{CO_2} + k_{-3} P_{CO}},$$

$$r_{II} = \frac{k_2 k_{-3} P_{C_2H_6} P_{CO}}{k_3 P_{CO_2} + k_{-3} P_{CO}}.$$

The following equation can be formulated for the process selectivity:

$$S = \frac{r_I - r_{II}}{r_I} = 1 - \frac{k_2 k_{-3} P_{CO}}{k_1 k_3 P_{CO_2}}.$$

It explains the decrease in selectivity with increasing degree of conversion. The concave form of the curve relating the rate of reaction to the degree of conversion in the temperature range 700–830 °C can be accounted for by the inhibition of the reaction by the CO formed.

The equations for r_I and r_{II} differ from the corresponding equation for the oxidation-reduction process involving the oxidation of alkanes by oxygen. In the latter case, the denominator represents the sum $k_{Ox}P_{CO_2} + k_{Red}P_{C_nH_m}$.[207] The inhibition by ethane is not observed in this case.

The rate of reoxidation of the catalyst by carbon dioxide (0.7×10^{-3} mol g^{-1} h^{-1}) is comparable to the rate of its reduction by ethane (0.6×10^{-3} mol g^{-1} h^{-1}). However, the activation energy for the reoxidation reaction (109 kJ mol^{-1}) is significantly lower than the activation energy for the reduction reaction (176 kJ mol^{-1}).

The study of the phase composition of the K–Cr–Mn–O/SiO_2 catalyst in situ showed[206] that the Mn_3O_4 phase, observed initially, is gradually reduced and is converted into the new phase MnO. The degree of dispersion of the manganese-containing phase increases as the reaction proceeds.

The following mechanism of the dehydrogenation of ethane in the presence of CO_2 on K–Cr–Mn–O/SiO_2 was proposed on the basis of all the results obtained:[168]

Scheme 2

$$C_2H_6 \xrightarrow{a} C_2H_4 + H_2 \text{ (thermal process)},$$

$$C_2H_6 + Cr^{3+}O^{2-} \xrightarrow{b} C_2H_5 + Cr^{2+}OH^-,$$

$$C_2H_5 + Cr^{3+}O^{2-} \xrightarrow{c} C_2H_4 + Cr^{2+}OH^-,$$

$$C_2H_6 + MnCO_3 \xrightarrow{d} C_2H_4 + MnO + CO + H_2O,$$

$$2Cr^{2+}OH^- \xrightarrow{e} Cr^{2+}O{-}Cr^{2+} + H_2O,$$

$$Cr^{2+}O{-}Cr^{2+} + MnCO_3 \xrightarrow{f} 2Cr^{3+}O^{2-} + MnO + CO,$$

$$MnO + CO_2 \xrightleftharpoons{g} MnCO_3.$$

In addition, one should include here the cracking reaction, which reduces the selectivity.

$$C_2H_6 + Cr^{2+} \xrightarrow{h} Cr^{2+}...CH_x + \tfrac{1}{2}(6-x)H_2.$$

$$Cr^{2+}...CH_x + Cr^{3+}O^{2-} \xrightarrow{i} 2\,Cr^{2+} + CO + \tfrac{1}{2}xH_2.$$

The Boudouard reaction

$$CO_2 + C \longrightarrow 2CO \qquad (34)$$

also takes place with an activation energy of 201 kJ mol^{-1}, but its contribution under stationary conditions is low.

Scheme 2 makes it possible to explain why the yield of CO greatly exceeds that of hydrogen: at 700 °C, the ratio $CO : H_2$ is between 5 and 8, whilst at 830 °C it is between 1.5 and 2. This means that the contribution of the thermal pyrolysis of methane (reaction *a* in Scheme 2) is relatively small.

The activation of the manganese catalyst by chromium and the distinctly observed synergism are probably due to the fact that, being mobile, the manganese containing phase (MnO) participates during reoxidation in transferring oxygen from CO_2.

$$\begin{array}{l} MnO...[\ ]_L Cr^{2+}O^{2-}Cr^{2+}O_L^{2-} + CO_2 \longrightarrow \\ \longrightarrow MnCO_3...[\ ]_L Cr^{2+}O^{2-}Cr^{2+}O_L^{2-} + CO_2 \longrightarrow \\ \longrightarrow MnO + CO + O_L^{2-}Cr^{3+}O^{2-}Cr^{3+}O^{2-} \end{array} \qquad (35)$$

The oxidation-reduction mechanism of the decomposition of manganese carbonate plays an important role under these conditions. The reduction of Cr^{3+} to Cr^{2+} during the reaction is indicated by the decrease in the magnetic susceptibility of chromium.

The above mechanism is supported by data on the thermal desorption of CO_2.[209] During the thermoprogrammed heating of the Mn–O/SiO_2 catalyst, pretreated with CO_2, the evolution of CO_2 is observed at three temperatures — 335, 425, and 750 °C — owing to the nonuniformity of the adsorption centres. The activation energies for desorption are 93 ± 8, 226 ± 8, and 293 ± 8 kJ mol^{-1} under these conditions. During the thermal desorption of CO_2 from a surface treated with hydrogen before adsorption (500 °C, 4 h), three types of centres are also observed, their capacity with respect to CO_2 being somewhat lower probably as a result of the removal of some of the oxygen centres during the reduction of the catalyst by hydrogen. The activation energies for desorption do not change under these conditions. The activation energies for the thermal desorption of CO_2 are close to those for the thermal desorption of oxygen under the same conditions. This may indicate the similarity of the nature of the centres for the activation of CO_2 and O_2 and identical principles governing the manganese catalysts in the carbonic acid and oxygen conversions.

On the other hand, in the thermal desorption of CO_2 from the Cr–Mn–O/SiO_2 catalyst, only one high-temperature peak is observed (the activation energy for desorption is 233 ± 8 kJ mol^{-1}). Such a change in the thermoprogramming diagram (TPD) on passing from Mn–O to Cr–Mn–O is evidently associated with the reoxidation of Cr^{2+} by the intermediate CO_2-accepting manganese-containing phase. The decrease in the degree of adsorption of CO_2 during the preliminary reduction of the catalyst by hydrogen indicates that the carbon dioxide adsorption centres are regular O^{2-} lattice ions on the basic surface. The strong CO_2-accepting centres in the high-temperature region are probably less reactive in the reoxidation of Cr^{2+}. Consequently the strength of the basic centres determines the stability of the carbonate structure and hence the degree of reoxidation of the oxidation-reduction centres. Centres with a moderate basicity are needed for the acceptance of CO_2 and the reoxidation of Cr^{2+}, which is in fact observed when the system

contains the weakly basic oxide MnO. The presence of an interface between MnO and CrO under these conditions probably facilitates the reoxidation of CrO.

The capacity with respect to oxygen of the catalytic system $Cr-O/SiO_2$, which contains no manganese oxide, is significantly lower after its reoxidation by CO_2 than the similar capacity of the $Cr-Mn-O/SiO_2$ system. From this standpoint, the $Cr-Mn-O$ composition can be regarded as bifunctional: on the one hand, it activates CO_2 on the basic centres and, on the other, it converts the hydrocarbon on the oxidation-reduction centres.

The oxygen capacity and the rate of oxidation of the catalyst can be altered by adding oxygen to the $C_2H_6 + CO_2$ mixture. For a particular $CO_2:O_2$ ratio, it is posisble to attain the optimum degree of oxidation of the surface, which ensures a high selectivity in the conversion of C_2H_6 into C_2H_4.[195] The reoxidation activation energy is significantly higher than the activation energy for the decomposition of the carbonate fragments. This is probably one of the reasons for the lower oxygen capacity of the catalysts reoxidised by carbon dioxide compared with their capacity when they are reoxidised by O_2.

The activation energies for the reoxidation of $Cr-Mn$ catalysts of different composition are the same (this also applies to the $V-Mn-O$ catalyst), although their oxygen capacities are different. This means that, although CO_2 is initially bound to Mn, the second element (Cr, V) determines the rate of reoxidation.

The centres on which oxygen is bound and the oxygen ions formed promote also the transition of CO_2 to the activated state. The mobile oxygen species pass from the manganese carbonate phase via spill-over to the chromium oxidation-reduction centres.

Another example of oxides with a moderate basicity having oxidation-reduction centres is provided by lanthanide oxides. Thus the oxidative dehydrogenation of ethane has been achieved on La_2O_3.[211] Under these conditions, La_2O_3 is converted into the hexagonal carbonate $La_2O_2CO_3$, which is in fact the active phase. Other lanthanide oxides do not form monocarbonates and are much less active than La_2O_3.

2. Interaction with propane

In the heterogeneous-catalytic conversion of propane by reaction with CO_2 on different catalytic systems, three reactions take place to different extents: oxidative dehydrogenation of propane to propene [reaction (36)], its degradative cleavage to C_2H_4 [reaction (37)], and its extensive conversion with formation of CO and H_2 [reaction (38)].

$$C_3H_8 + CO_2 \rightarrow C_3H_6 + CO + H_2O, \quad \Delta H_{298} = 165.3 \text{ kJ mol}^{-1}, \tag{36}$$

$$2C_3H_8 + 2CO_2 = 3C_2H_4 + 2CO + 2H_2O, \tag{37}$$

$$C_3H_8 + 3CO_2 = 6CO + 4H_2. \tag{38}$$

Like the interaction of ethane with CO_2 [reaction (31)], reaction (38) is of interest as a method of preparation of a synthesis gas with an increased CO content. According to the data of Mamedov et al.,[192] the degree of conversion of CO_2 in an equimolar mixture with propane is 80%–85% on a nickel catalyst at 750 °C. However, the process is accompanied by extensive coke deposition.

The $CO_2 + C_3H_8$ reaction has been investigated on the Ni/SiO_2, Rh/SiO_2, and Pd/SiO_2 catalysts at 600 °C. The Ni/SiO_2 catalyst proved to be the most active and selective: the degree of conversion reached 92% and the selectivity in the formation of $CO + H_2$ reached 70%–80%. According to the authors,[212] the rate-limiting stage is the dissociation of propane:

$$C_3H_8 + 2Ni \rightarrow 2NiCH_2 + CH_4.$$

This is followed by the reactions

$$CH_4 + Ni \rightleftharpoons NiCH_2 + H_2,$$

$$NiCH_2 + CO_2 \rightleftharpoons Ni + 2CO + H_2,$$

$$NiCH_2 + 2CO_2 \rightleftharpoons Ni + 3CO + H_2O,$$

$$Ni + CO_2 \rightleftharpoons NiO + CO,$$

$$NiCH_2 + NiO \rightleftharpoons 2Ni + CO + H_2,$$

$$NiO + H_2 \rightleftharpoons Ni + H_2O.$$

The manganese oxide systems proved to be active and stable catalysts for the oxidative-reductive dehydrogenation of propane via reactions (36) and (37) with formation of propene and ethene.[192, 196, 204, 213]

In the presence of $Mn-O/SiO_2$, the conversion of propane into C_2-C_3 alkenes proceeds more selectively than on the nickel catalyst. At 800 °C, the yield of C_2-C_3 alkenes is 47% relative to the propane passed through the system. With increase in temperature, their yield diminishes, but the yield of CO and H_2 increases. Preliminary treatment of the catalyst with carbon dioxide increases the selectivity for the formation of the C_2-C_3 compounds. After preliminary treatment with hydrogen, the overall degree of conversion of propane and CO_2 increases, but the selectivity for the formation of alkenes falls. Evidently the selective degradation of propane to ethene and methane and the oxidative dehydrogenation to propene take place on the oxidised surface, whereas on the reduced surface propane undergoes cracking with formation of carbon fragments, which are oxidised by carbon dioxide to CO. Thus the overall characteristics of the conversion of propane are similar to those of the conversion of ethane.

The best catalyst for the selective conversion of propane by CO_2 is, for ethane, the 1.5% K–5.5% Cr–17% $Mn-O/SiO_2$ system. At 830 °C, a space velocity of 3600 h^{-1}, and for $CO_2:C_3H_8 = 1.5$, a degree of conversion of C_3H_8 of 96.0%, a degree of conversion of CO_2 of 52.0%, a selectivity in the formation of the C_2H_4 and C_3H_6 hydrocarbons of 75% (80% in the case of C_2H_4), a yield of C_2-C_3 alkenes of 72%, and the $CO:(C_2H_4 + C_3H_6)$ ratio = 1.4 were attained on this catalyst. At 890 °C, the ratio $CO:(C_2H_4 + C_3H_6)$ increases to 4. The amount of hydrogen present in the reaction product is smaller by a factor of 5–8 than that of CO. With increase in the degree of conversion, there is a considerable fall in the selectivity in the formation of alkenes. This behaviour can probably be accounted for by the higher degrees of conversion of the hydrocarbon and the formation of a reaction mixture with more effective reducing properties than in the case of ethane.[196]

After the reduction of the catalyst by propane, the rate of formation of C_2-C_3 alkenes diminishes: the rate of formation of C_2H_4 on the oxidised surface is 2–3 times greater than on the reduced surface. It must be emphasised that, in the interaction of propane with a catalyst pretreated with air, the extensive oxidation products (CO and CO_2) are formed preferentially. This can apparently be explained by the fact that, when the catalyst is treated with air, chromium passes to a higher oxidation state (up to Cr^{6+}) than in Cr_2O_3. On the other hand, the intermediate state of chromium (Cr^{3+}) is responsible for the formation of C_2-C_3 alkenes. Manganese oxides are reduced in the stationary state to MnO (according to X-ray diffraction data obtained in situ). This phase participates in the oxygen transport and maintains chromium in the Cr^{3+} oxidation state [see reaction (35)].

The $Cr-O/SiO_2$ catalyst is less active and selective. Evidently without MnO it is impossible to maintain chromium in the oxidised state.

Under stationary conditions with $C_3H_8:CO_2 = 1-1.2$, the amount of coke formed does not exceed 3.6% relative to the weight of the catalyst. Electron microscopy shows that, after the treatment of the catalyst under nonstationary conditions, coke is present on the surface in two forms: as filamental carbon and in the form of flat scales Under stationary conditions, filamental carbon is not formed. This is associated either with the absence of metallic inclusions in the catalyst (Cr^0) or with the rapid interaction of the nuclei of the carbon phase with CO_2 in

accordance with the Boudouard reaction. Coke is removed from the $Mn-Cr-O/SiO_2$ catalyst at a much lower temperature (610 °C) than from $Mn-O/SiO_2$ (870 °C).

A scheme for the oxidative pyrolysis of propane in the presence of CO_2 (Scheme 3) has been proposed.[168] It is similar to the scheme for the $CO_2 + C_2H_6$ interaction on the $K-Cr-Mn-O/SiO_2$ catalyst (Scheme 2). According to Scheme 3, C_2H_4 is formed mainly on the Cr^{3+} centres, while CH_4, CO, and H_2 are formed on the Cr^{2+} centres; MnO ensures the activation of CO_2. The gas-phase reactions of the radicals are not included in the scheme.

Scheme 3

$$C_3H_8 + Cr^{3+}O^{2-} \xrightarrow{a} C_3H_7^{\cdot} + Cr^{2+}OH^-,$$

$$C_3H_7^{\cdot} + Cr^{3+}O^{2-} \xrightarrow{b} C_2H_4 + CH_3O^-...Cr^{2+},$$

$$CH_3O^-...Cr^{3+} \xrightarrow{c} Cr^{3+}O^{2-} + CH_3^{\cdot},$$

$$CH_3O^-...Cr^{2+} \xrightarrow{d} Cr^{2+}[\ ] + \text{extensive oxidation products}$$

$$C_3H_8 + 2[\ ]Cr^{2+} \xrightarrow{e} C_2H_4...Cr^{3+} + C...Cr^{2+} + 2H_2,$$

$$C_2H_4...Cr^{2+} \xrightarrow{f} CH_4 + C...Cr^{2+},$$

$$C_2H_4...Cr^{2+} + [\ ]Cr^{2+} \xrightarrow{g} 2C...Cr^{2+} + 2H_2,$$

$$2Cr^{2+}OH^- \xrightarrow{h} Cr^{2+}[\ ] + Cr^{2+}O^{2-} + H_2O,$$

$$Cr^{2+}[\ ] + Cr^{2+}O^{2-} + MnCO_3 \xrightleftharpoons{i} \rightleftharpoons 2Cr^{3+}O^{2-} + MnO + CO,$$

$$C...Cr^{2+} + Cr^{3+}O^{2-} \xrightarrow{j} 2Cr^{2+}[\ ] + CO,$$

$$MnO + CO_2 \xrightleftharpoons{k} MnCO_3.$$

The first two stages in Scheme 3 may be combined into one, i.e. the Scheme may be formulated also without the participation of free radicals, although their formation in the high-temperature interaction of alkanes with oxides is extremely probable. If it is postulated that, in the case where the process proceeds via a parallel reaction mechanism, the catalyst may be reduced both by the initial hydrocarbon and by CO, the rate of the selective formation of ethene from propane may be expressed by the equation

$$r_{C_2H_4} = \frac{k_1 P_{C_3H_8} k_2 P_{CO_2}}{k_1 P_{C_3H_8} + k_2 P_{CO_2} + k_3 P_{CO}}.$$

However, under real conditions the catalyst is reduced by the hydrocarbons 17 times more slowly than by carbon monoxide (the rate of oxidation of CO is 17 times higher than the rate of the extensive oxidation of propene). We then have $k_3 P_{CO} \gg k_1 P_{C_3H_8}$ and the rate equation is transformed into

$$r_{C_2H_4} = \frac{k_1 P_{C_3H_8} k_2 P_{CO_2}}{k_2 P_{CO_2} + k_3 P_{CO}}.$$

The activation energy for the formation of ethene from propane is 151 kJ mol^{-1}, which is close to the value obtained in the case of ethane (167 kJ mol^{-1}), confirming the similarity of the mechanisms of the primary activation of these hydrocarbons on the $K-Cr-Mn-O/SiO_2$ catalyst. The kinetic equations for the conversion of ethane and propane are also similar and differ from the corresponding equations describing the oxidation of alkanes by oxygen.

The chemistry of the interaction of propane with CO_2 on metals (Ni) and oxides (MnO_x) is different. On the former, synthesis gas is formed selectively, whilst on the latter C_2-C_3 alkenes are formed preferentially. On metals, propane dissociates into C(ads) or CH_x, whereas on oxides hydrogen is split off from propane or oxidative cracking takes place. On metals, CO_2 reacts with carbon via the reverse Boudouard reaction, whilst on oxides it interacts with hydrogen (the reverse water gas conversion).

On zeolitic catalysts, the oxidative dehydrogenation of propane in the presence of CO_2 takes place at lower temperatures and is directed towards aromatisation.

$$2C_3H_8 + 2CO_2 = C_6H_6 + 2H_2O + 3H_2 + 2CO$$

The interaction of propane with CO_2 on the Zn-HZSM-5 catalyst (10% of H atoms replaced by Zn) has been investigated.[214,215] It was observed that CO_2 greatly increases the conversion of C_3H_8, suppressing the formation of coke. The yield of CO exceeds the conversion of CO_2, which indicates the partial formation of CO from propane via coke. At 550 °C, the maximum degree of conversion of C_3H_8 was 68.4%, whilst that of CO_2 was 13.1%. A mixture of C_1 and C_4 hydrocarbons as well as aromatic hydrocarbons is also formed with a selectivity in the formation of the aromatic hydrocarbons of 50.8%. The first reaction stage is the dehydrogenation of propane, which is initially faster in the absence of CO_2, but the deactivation in the presenc e of CO_2 is very slow. This indicates a considerable role for the Boudouard reaction.

Among the zeolites investigated, the highest activity in the oxidative aromatisation of propane in the presence of CO_2 was shown by Zn-ZSM-5. On H-ZSM-5 and Na-ZSM-5, the yield of aromatic hydrocarbons from C_3H_8 in the presence of CO_2 was somewhat higher than in its absence, whilst on Pt-ZSM-5 it was lower. This can be explained by the higher cracking capacity of platinum in relation to propane. In the reaction involving the formation of synthesis gas, the zeolitic catalysts can be arranged in the following activity series: Pt > Zn > Ga > H-ZSM-5.[216]

We have already mentioned studies in which the influence of CO_2 on the reactions of hydrocarbons on zeolites was investigated. it may be that in these studies too the positive effects of CO_2 can be accounted for by its oxidising properties, for example by its interaction with the coke formed.

3. Interaction with n-butane

The conversion of n-butane by reaction with CO_2 also proceeds on manganese-containing oxide catalysts.[204,209] At 630-650 °C and for the ratio $n\text{-}C_4H_{10}:CO_2 = 1-1.2$ on the $Cr-Mn-La-V-O/SiO_2$ catalyst, the degree of conversion of n-butane reached 81%-84%, whilst the selectivity for the formation of C_2-C_4 alkenes reached 76%-78%. Oxidative cracking predominates over oxidative dehydrogenation: more C_2H_4 is formed than C_3H_6 and the amount of the latter is greater than that of C_4H_8. The selectivity with respect to synthesis gas reached 22%-24%, CO and H_2 being obtained in approximately equal amounts, in contrast to the reaction of CO_2 with ethane and propane.

Consequently, the simple catalytic or noncatalytic dehydrogenation

$$C_4H_{10} = C_4H_8 + H_2$$

and the oxidative dehydrogenation

$$C_4H_{10} + CO_2 = C_4H_8 + CO + H_2O$$

take place to only a limited extent. The principal reaction path is oxidative cracking with formation of alkenes and synthesis gas:

$$C_4H_{10} + CO_2 = 2C_2H_4 + CO + H_2O,$$

$$C_4H_{10} + CO_2 = C_3H_6 + 2CO + 2H_2,$$

$$C_4H_{10} + CO_2 = C_2H_4 + CH_4 + 2CO + H_2.$$

Direct cracking

$$C_4H_{10} \rightarrow C_3H_6 + CH_4,$$

apparently also makes a considerable contribution, which is indicated by the high CO_2 content in the final gas. However, it is not clear why this process proceeds to a very limited extent in the absence of CO_2.

It is of interest that the MnO/SiO_2 catalyst, which contains no vanadium and has more basic properties, exhibits a higher selectivity in relation to dehydrogenation. It may be that, as in the case of C_2-C_3 hydrocarbons (see above), oxidative dehydrogenation of n-butane with the aid of CO_2 proceeds via the formation of intermediate carbonates, while oxidative cracking (or simply cracking) takes place with participation of more reduced centres.

4. Interaction with isobutane

The dehydrogenation of isobutane with participation of carbon dioxide can be described by the equation

$$\text{iso-}C_4H_{10} + CO_2 = \text{iso-}C_4H_8 + CO + H_2O, \quad \Delta H = 195.4 \text{ kJ mol}^{-1}. \tag{39}$$

In the absence of the catalyst, the degree of conversion of isobutane in a mixture with CO_2 (or N_2) to isobutene at 665 °C is 19%; under these conditions, CO_2 does not react. In the presence of the $K-Cr-Mn-O/SiO_2$ catalyst at 670 °C, the degree of conversion of iso-C_4H_{10} is 35%–36%, whilst that of CO_2 is 5.8%; on the $K-Cr-Mn-O/Al_2O_3$ catalyst, the degree of conversion of iso-C_4H_{10} increases to 50% and that of CO_2 increases to 9%–10%; on $Cr-Mn-O/Al_2O_3$ (in the absence of potassium), the degree of conversion of iso-C_4H_{10} reaches 61%–66% and that of CO_2 reaches 20%–29.5%.[204, 209, 217] The selectivity with respect to the main product (iso-C_4H_8) on the last catalyst is 78%–81%. CO and H_2 are also formed in equal amounts. This distinguishes this process from those involving ethane and propane, where $CO : H_2 = 7$.

Preliminary treatment of the catalyst with hydrogen does not lead in this case, in contrast to the reactions of ethane and propane, to a decrease in the yield of the alkene, whilst preliminary treatment with CO_2 reduces both the yield and the selectivity. The selectivity in the cleavage of isobutane into propene and methane increases under these conditions. As the reaction proceeds, the selectivity and activity of the catalyst increase similarly: this also distinguishes the above process from reactions involving ethane and propane, where the selectivity with respect to the alkene increases as the surface is oxidised.

The reaction of CO_2 with isobutane has also been investigated under the conditions of their separate interaction with the catalyst. When isobutane came into contact with the surface at 670 °C in the absence of CO_2, iso-C_4H_8, CO, H_2, C_3H_6, and CH_4 were obtained. The rate of formation of CO in such interaction of iso-C_4H_{10} with the surface is significantly lower (by a factor of 12–30) than the rate of its formation under stationary conditions. Calculations showed that under stationary conditions only 3%–4% of CO is the result of the regeneration of the coke-saturated catalyst by the reaction

$$C + CO_2 \rightarrow 2\ CO.$$

However, this reaction ensures the activity of the catalyst for a long time.

The study of the oxidation of hydrogen by carbon dioxide on this catalyst showed that the rate of formation of CO under these conditions is comparable to the rate of its formation under stationary conditions. Consequently, the main path leading to the formation of CO under stationary conditions is reaction (3).

The rate of formation of CO in the interaction of CO_2 with the reduced catalyst is also appreciably lower (by a factor of 10 in the case of the $Cr-Mn-O/SiO_2$ catalyst) than the rate of formation of CO under stationary conditions at 670 °C [reaction (39)]. It is observed preferentially at temperatures above 700 °C.

Consequently, at 600–700 °C the interaction of isobutane with CO_2 represents mainly the sum of two consecutive reactions:

$$\text{iso-}C_4H_{10} \rightarrow \text{iso-}C_4H_8 + H_2, \qquad H_2 + CO_2 \rightarrow CO + H_2O. \tag{40}$$

The overall mechanism of the reactions of iso-C_4H_{10} on the Mn–Cr catalyst can be represented by Scheme 4.

Scheme 4

$$\text{iso-}C_4H_{10} + Cr^{3+}O^{2-} \xrightarrow{a} \text{iso-}C_4H_9 + Cr^{2+}OH^-,$$

$$\text{iso-}C_4H_9 + Cr^{3+}O^{2-} \xrightarrow{b} \text{iso-}C_4H_8 + Cr^{2+}OH^-,$$

$$2Cr^{2+}OH^- \xrightarrow{c} Cr^{2+}[\ ] + Cr^{2+}O^{2-} + H_2O,$$

$$MnO + CO_2 \overset{d}{\rightleftharpoons} MnCO_3,$$

$$H_2 + MnCO_3 \xrightarrow{e} H_2O + CO + MnO,$$

$$H_2 + Cr^{3+}O^{2-} \xrightarrow{f} H_2O + Cr^{2+}[\ ],$$

$$Cr^{2+}[\ ] + CO_2 \xrightarrow{g} Cr^{3+}O^{2-} + CO.$$

Dehydrogenation (in addition to the thermal dehydrogenation) takes place with participation of the reduced centres, probably chromium ions. The presence of hydrogen in the gas phase shows that oxidative dehydrogenation does not predominate over direct dehydrogenation. H_2 interacts with CO_2 apparently via the $MnCO_3$ carbonate fragments (reactions *d* and *e* in Scheme 4).

The kinetic equation for the process differs from the equation describing the interaction of ethane and propane with CO_2 and has the form of the Mars–Van Krevelen equation:

$$r_{\text{iso-}C_4H_8} = \frac{k_1 P_{\text{iso-}C_4H_{10}} k_2 P_{CO_2}}{k_1 P_{\text{iso-}C_4H_{10}} + k_2 P_{CO_2}}.$$

This shows that the role of the reduction of the catalyst by the carbon monoxide formed during the reaction is small. The change in the reaction kinetics on passing from C_2H_6 and C_3H_8 to iso-C_4H_{10} is probably caused by the lower energy of the C–H bonds in isobutane, which ensures their cleavage with participation of less oxidised or carbonate centres. In this case, hydrogen should be present in the reaction mixture.

At a high temperature (750–900 °C), the reaction does not proceed via carbonates but via the dissociative adsorption of CO_2 and subsequent oxidative dehydrogenation.

$$\text{iso-}C_4H_{10} + [O] \rightarrow \text{iso-}C_4H_8 + H_2O,$$

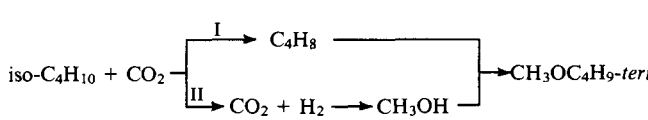
$$CO + H_2O \rightleftharpoons CO_2 + H_2.$$

In both cases, the last reaction is the equilibrium conversion of water gas, leading to an equilibrium mixture of H_2, CO, H_2O, and CO_2.

The hydrogen formed in the dehydrogenation of isobutane is not fully oxidised [only half of its participates in the subsequent reduction of CO_2 in accordance with the equilibrium reaction (3)]. This results in the formation of a mixture containing iso-C_4H_8, CO, and H_2 as the main products. The selectivity for the formation of the side products (C_3H_8 and CH_4) is about 10%.

The addition of n-butane to the reaction mixture does not alter the characteristics of the dehydrogenation of isobutane by carbon dioxide.[217]

The simultaneous formation of isobutene and synthesis gas in the reaction of isobutane with CO_2 makes it possible to propose a new process for the preparation of *tert*-butyl methyl ether — the high-octane component of nonethylated petrol.



Reaction I is endothermic (155 kJ mol^{-1}), whilst reaction II is exothermic (92 kJ mol^{-1}). The combination of these reactions makes it posisble to diminish by a factor of 2 the energy consumption in reaction I.

5. Interaction with n-heptane

Studies have shown[194,218] that, on interaction with CO_2 on manganese oxide catalysts, heavy alkanes undergo mainly oxidative cracking. Under stationary conditions, it proceeds without the accumulation of coke fragments and a high degree of conversion of the hydrocarbon is attained. By altering the nature of the hydrocarbon employed and the catalyst, it is possible to direct the process towards the formation of light alkenes, alkanes, and also isomeric paraffinic hydrocarbons.

On $K-Mn-O/Al_2O_3$, $La-Mn-O/Al_2O_3$, and La–Mn/NaY, the reaction takes place at 540–670 °C. Oxidative cracking with formation of H_2, CO, CH_4, C_2H_4, C_3H_6, and C_4H_8 is observed. The La–Mn/NaY catalyst is more active in cracking than $La-Mn-O/Al_2O_3$ and $K-Mn-O/Al_2O_3$. The degree of conversion of n-heptane on this catalyst at 670 °C reaches 100% for a low degree of conversion of CO_2 (4.2%). On $La-Mn-O/Al_2O_3$, the overall degree of conversion of n-heptane is lower (86.4% at 670 °C), but that of CO_2 is higher (30.2%). In addition, a low yield of H_2 ($CO:H_2 = 10$) was observed on La–Mn/NaY, whilst on $La-Mn-O/Al_2O_3$ and $K-Mn-O/Al_2O_3$ carbon monoxide and H_2 were formed in equal amounts. It follows from the foregoing that $La-Mn-O/Al_2O_3$ and $K-Mn-O/Al_2O_3$ are more active in the activation of CO_2.

The reduction of CO_2 with the formation of CO probably proceeds via several paths: as a result of the oxidation of H_2 (a cracking product) by carbon dioxide and via the gasification of the surface carbon fragments.

Experiments have been carried out on the reoxidation of the $La-Mn-O/Al_2O_3$ catalyst by treating it with CO_2 after the stationary oxidative cracking process. The rate of reoxidation at 620–670 °C is constant in time, i.e. the saturation of the surface is not observed. The interaction of H_2 with CO_2 has also been investigated. The rate of formation of CO in this reaction was somewhat lower than in the conversion of heptane by reaction with CO_2.

The rate of formation of CO under stationary conditions at 670 °C is 14 times higher than in the reoxidation of the catalyst. This shows tht the oxidation of the catalyst

$$MnO + CO \rightleftharpoons MnCO_3,$$

$$3MnCO_3 \rightleftharpoons Mn_3O_4 + CO + CO_2$$

is not the main path leading to the formation of CO under stationary conditions. Reaction (3) does not proceed via the direct alternate oxidation-reduction

$$H_2 + [O] \rightarrow [\ ] + H_2O,$$

$$[\ ] + CO_2 \rightarrow CO + [O],$$

but via the 'associative' interaction of H_2 with the surface carbonates:

$$H_2 + MnCO_3 \rightarrow CO + H_2O + MnO.$$

In the stationary state, an intermediate carbonate structure participates in the process.

Another source of CO is reaction (40), i.e. the interaction of CO_2 with carbon deposits. This ensures the selective oxidative (carbonic acid) cracking and a stable activity of the $La-Mn-O/Al_2O_3$ and $K-Mn-O/Al_2O_3$ catalysts without the accumulation of coke fragments on the surfaces.

The low rate of formation of CO on the La–Mn/NaY catalyst is apparently associated with the formation of stable carbonates. Presumably decationated zeolites modified with manganese should serve as a base for an effective catalyst for the cracking process in the presence of CO_2.

Thus the oxidative cracking of n-heptane with the aid of CO_2 may be described by the following equations:

$$C_7H_{16} \rightarrow C_4H_8 + C_3H_6 + H_2,$$

$$C_7H_{16} \rightarrow 3C_2H_4 + C^* + 2H_2,$$

$$H_2 + CO_2 \rightleftharpoons CO + H_2O,$$

$$C^* + CO_2 \rightleftharpoons 2CO.$$

Summarising the results of the study of the oxidative interaction of C_4-C_7 alkanes with CO_2, we may note that experiments have demonstrated the possibility of the simultaneous formation of alkenes and synthesis gas. In contrast to the familiar cracking and dehydrogenation processes, this path makes it possible to employ CO_2 as the starting material.

Nickel-containing compounds are known to be deposited from petroleum during catalytic cracking on zeolitic catalysts and to poison the latter as a consequence of the increased coke formation. CO_2 has been used to passivate this process.[219] The $C_7H_{16} + CO_2$ reaction has been investigated on the $Ni-La-8\%\ MnO/Al_2O_3$ catalysts containing between 0.5 mass% and 2.5 mass% of lanthanum and nickel. With increase in the nickel content, the degrees of conversion of C_7H_{16} and CO_2 at 670 °C increase. It is especially important that the presence of CO_2 in the mixture ensures the maintenance of the stable activity of the catalyst, whereas in the traditional catalytic cracking an increase in the CO_2 content entails an increase in coke formation and a decrease in the catalyst activity. If CO_2 is replaced in the reaction mixture by N_2, the overall activity falls and the yield of C_4 hydrocarbons diminishes, but that of C_2 hydrocarbons increases, i.e. the undesired extensive cracking takes place. In the absence of manganese, nickel is reduced to the metallic state even in the presence of CO_2, which also leads to deactivation. Evidently manganese promotes the binding and activation of CO_2 in accordance with the scheme

$$MnO + CO_2 \rightleftharpoons MnCO_3,$$

$$MnCO_3 + Ni \rightarrow MnO + NiO + CO.$$

In conclusion of this section about the reactions of hydrocarbons in the presence of CO_2, we may note certain general features. The mechanisms of the activating effect of CO_2 on the reactions of C_1-C_3 and C_4-C_7 hydrocarbons are different. In the case of the lower alkanes, CO_2 enters into an oxidation–reduction interaction with the catalyst, after which the surface O^{2-} ions oxidise the hydrocarbon. The reaction takes place at a high temperature (750–850 °C). The decrease in temperature to 550–650 °C in the oxidative aromatisation of propane on zeolitic catalysts can be accounted for by the greater role of the reverse Boudouard reaction [reaction (40)] in this process.

In the conversion of C_4 hydrocarbons (at 650–700 °C), the first stage is their direct dehydrogenation, after which hydrogen is oxidised by reaction with CO_3^{2-}. (We examined the accelerating effect of hydrogen on the reactions with participation of CO_2 in Section III).

The principal path in the interaction of higher hydrocarbons with CO_2 (at 650–750 °C) is oxidative cracking, the reverse Boudouard reaction [reaction (40)], i.e. the interaction of C* with CO_2, playing a major role in the reaction mechanism. The activation of carbon dioxide and not of the hydrocarbons is rate-limiting. The hydrogen evolved accelerates the Boudouard reaction.

Manganese-containing catalysts can be used to convert both groups of hydrocarbons. This can be explained, firstly, by the fact that manganese oxides gives rise to moderately stable carbonates, which are capable of decomposing under reaction conditions. Secondly, manganese affords oxides capable of being readily oxidised and reduced under the reaction conditions.

When alkaline (Na, K) oxides are added, the stability of these carbonates increases, while the addition of acid oxides (Mo, V) diminishes the stability. Alkaline oxides shift the process towards oxidative dehydrogenation, whilst acid ones shift it towards oxidative cracking. The surface carbonates participate in the oxidation-reduction reactions with the hydrocarbon or hydrogen.

VI. Oxidation reactions of carbon dioxide with other compounds

Transition metal and lanthanide oxides also catalyse the oxidative reaction of CO_2 with other organic compounds.

1. Interaction of carbon dioxide with the carbon fragments in cracking catalysts

The regeneration of the coke-saturated cracking catalyst is known to involve combustion processes entailing the development of high temperatures, which reduce the process efficiency. The use of CO_2 instead of O_2 for the regeneration makes it possible, in principle, to increase the process efficiency.[220-222]

In the interaction of the coke-saturated zeolite-containing KNTsU-B catalyst with CO_2 at 680 °C and a space velocity of the supply of CO_2 of 900 h^{-1}, the degree of conversion of CO_2 does not exceed 1%. The rate of regeneration of the catalyst modified by manganese acetate (5% Mn) after saturation with coke exceeds by a factor of 15 the rate of regeneration of the unmodified catalyst under similar conditions. Apart from CO, methane is also formed, the rate of its formation being greater by a factor of 1.3 than the rate of formation of CO. Hydrogen is detected only in trace amounts.

When the coke-saturated catalyst is modified with chromium, an increase in the rate of formation of CO is also observed. In this case, $CO:CH_4 = 4-5$. On regeneration of the coke-saturated catalyst modified by lanthanum carbonate with CO_2, the formation of CO has already begun at 400 °C.

The modifying additives can be introduced into the catalyst during its preparation, before its employment in cracking and its regeneration. When 5% of lanthanum is introduced into the zeolite-containing catalyst Tseokar-2, the regeneration with the aid of CO_2 begins at 400 °C. Under programmed heating conditions, the thermogram showed two maxima corresponding to the formation of CO ($E = 138$ and 226 kJ mol^{-1}) and a maximum corresponding to the evolution of CH_4 ($E =$ 201 kJ mol^{-1}). H_2 is also evolved during the heating process.

The stoichiometric equations for the formation of CO, H_2, and CH_4 can be expressed in the form

$$CH_x + CO_2 \rightarrow 2\ CO + \tfrac{1}{2}xH_2,$$

$$2CH_x \rightarrow CH_4 + C + (x - 2)H_2.$$

For $x = 2$, the overall equation assumes the following form:

$$2CH_2 + CO_2 \rightarrow CH_4 + 2CO,$$

whence it follows that methanation and the Boudouard reaction take place in the oxidation of CH_x fragments by CO_2.

Thus the effective acceptance of CO_2 by manganese or lanthanum oxides ensures a high rate of oxidation of the surface CH_x fragments.

The processing of heavy petroleums is greatly hindered by the presence of heavy metals (Ni and V) in them, mainly in the form of porphyrins, which are deposited on the surfaces of the catalyst. These metals greatly increase the poisoning and coke formation. In this case too, the addition of manganese proved useful. In the presence of manganese, nickel appreciably accelerates the regeneration of the catalyst by CO_2.[219] On the other hand, the oxidation of vanadium by carbon dioxide is retarded in the presence of MnO_x or La_2O. The positive effect of CO_2 reduces in this case to the stabilisation of the surface as a result of its being blocked by the lanthanum and manganese carbonate fragments, which prevents the deactivation of the catalyst by vanadium.[223]

It is well known that the gasification of coal by CO_2 or H_2O is accelerated by alkaline additives. Tunnels are formed in the layer of carbon beneath the alkalies (K, Na, Li, Ba, and Ca oxides) deposited on it. Evidently here too the carbon formed interacts with the carbonate ions.[224]

2. Interaction with other hydrocarbons

In the absence of a catalyst, ethene does not interact with CO_2 at temperatures below 750 °C. A low degree of conversion of C_2H_4 (up to 12%) is observed at 750-820 °C with formation of CH_4, C_4H_6, C_3H_6, and traces of C_2H_4. Mainly synthesis gas is obtained on the nickel catalyst under these conditions.

$$C_2H_4 + 2CO_2 = 4CO + 2H_2 \qquad (41)$$

Up to 2%-3% of butadiene is also evolved. The degree of conversion of ethene at 750 °C is 65%.

On Ru/Al_2O_3 and $Ru-Co/Al_2O_3$, carbon dioxide interacts with hex-1-ene at a low temperature (100 °C) and a pressure of 10-35 atm.[225] Alkenes, ethers, aldehydes, and ketones have been detected in the products; the degree of conversion has not been reported.

The use of the $Mn-O/SiO_2$ oxide catalyst (see Refs 200, 204, 226, and 227) in the reaction of ethene with CO_2 led to the formation of butadiene and propene. On the 17% $Mn-O/SiO_2$ catalyst at 820 °C, a degree of conversion of C_2H_4 of 22.3% was attained, that of CO_2 was 11.6%, and the selectivity was 25.0% with respect to C_4H_6 and 18.0% with respect to C_3H_6. We may note that the reaction involving oxidative dimerisation with the aid of CO_2, i.e.

$$2C_2H_4 + CO_2 \rightarrow C_4H_6 + CO + H_2O, \quad \Delta H = 243\ kJ\ mol^{-1} \qquad (42)$$

is highly endothermic and thermodynamically unfavourable ($\Delta G > 0$). However, CO, H_2, CH_4, C_3H_6, and C_4H_8 are also formed under the catalytic conditions, so that it is difficult to carry out an exact thermodynamic calculation for these conditions. Treatment of the $Mn-O/SiO_2$ catalyst with carbon dioxide reduces the selectivity with respect to C_4H_6 and C_3H_6, whilst treatment with hydrogen increases it. A different behaviour has been observed with alkanes. The process proceeds on the reduced catalyst.

On Cr_2O_3/SiO_2, the degree of conversion of C_2H_4 at 820 °C was 27.3%, that of CO_2 was 14.8%, and the selectivity was 39.0% with respect to C_4H_6 and 24.2% with respect to C_3H_6.[226] Surface carbonate fragments participate in the process. At low temperatures (400-600 °C), the oxidation of the CH_x fragments by CO_2 takes place in accordance with the scheme

$$CH_x + CO_3^{2-} \rightarrow CH_xO + CO + O^{2-},$$

$$CH_xO \rightarrow CO + \tfrac{1}{2}xH_2.$$

At high temperatures (600-750 °C), carbon monoxide is formed mainly from carbon:

$$CO_3^{2-} + C \rightarrow 2CO + O^{2-}.$$

We may note that the characteristics of the interaction of CO_2 with ethene are not the same as those of its interaction with alkanes. Thus, in the $C_2H_4 + CO_2$ reaction, the addition of the acid oxide WO_3, instead of a basic one, to Mn/SiO_2 increased the degree of conversion of C_2H_4 and the selectivity in the formation of C_3H_6 and C_4H_6.

On the 2% W-17% $Mn-O/SiO_3$ catalyst at 820 °C, a space velocity of 2700 h^{-1}, and for $C_2H_4:CO_2 = 1$, the degree of conversion of C_2H_4 was 30.1%, that of CO_2 was 12.4%, and the selectivity was 33.4% with respect to C_4H_6 and 20% with respect to C_3H_6.

On the 2% W-5.5% $Cr-O/SiO_2$ catalyst, the best parameters for the conversion of C_2H_4 and for the selectivity in the

formation of butadiene were attained; the catalyst was not saturated with coke under the reaction conditions. At 820 °C, the degree of conversion of C_2H_4 was 30.5%, that of CO_2 was 13.7%, and the selectivity was 50.2% with respect to C_4H_6 and 30.6% with respect to C_3H_6; CO, CH_4, C_3H_6, and C_4H_8 were also formed. The degree of conversion of CO_2 was 2–3 times smaller than that of ethene. This is apparently associated with the fact that CO_2 is consumed in the interaction with the coke deposits and the contribution of this reaction is small compared with the target reaction.

During the operation of the 2% W – 5.5% Cr – O/SiO_2 oxide catalyst, the WO_3 and Cr_2O_3 phases are detected in its composition. After the attainment of the stationary state, the WO_3 phase ceases to be detected, while a large proportion of Cr_2O_3 is reduced, which is indicated by the decrease in the intensity of the corresponding band in the spectrum by a factor of 15–20.

The study of the kinetics of the $C_2H_4 + CO_2$ reaction on the Cr – W – O/SiO_2 catalyst showed that the rate of formation of C_4H_6 and C_3H_6 increases with increase in the degree of conversion to 25%, after which it begins to fall. The activating effect of the reaction products, especially CO, is apparently due to the reduction of the surface, which promotes the activation of ethene. Extensive oxidation of the target product is not observed. When no account is taken of the homogeneous pyrolysis of ethene, the rate of accumulation of butadiene is expressed by the following equation according to Mirzabekova and Mamedov:[226]

$$r_{C_4H_6} = \frac{kP^2_{C_2H_4}k_{-r}P_{CO}}{k_rP_{CO_2} + k_{-r}P_{CO}},$$

where k is the reaction rate constant and k_r and k_{-r} are the rate constants for the reoxidation and reduction of the catalysts.

The rate of the overall catalytic conversion of ethene in the mixture with CO_2 into butadiene at 820 °C is greater by a factor of 5–6 than the rate of the thermal pyrolysis.

The rate equation for the accumulation of butadiene differs significantly from the rate equations for the carbonic acid converiso of alkanes (see above). This difference is caused by the nature of the tungsten – chromium catalyst. In contrast to the catalysts for the conversion of alkanes, it exhibits a high Lewis acidity, as a result of which its accepting capacity in relation to CO_2 is reduced and the CO formed during the reaction does not affect quite so much the state of the surface.

The study of the interaction of propene with CO_2 on the Mo – Mn – O/SiO_2 catalyst made it possible to observe the occurrence at 640 °C of partial oxidation with formation of formaldehyde (8% selectivity) and acrolein (32% selectivity) for degrees of conversion of C_3H_6 and CO_2 of 25.0% and 12.0% respectively.[227] Degradative decomposition with formation of products of the radical reactions (C_2H_4 and CH_4) predominates at higher temperatures.

On the K – Cr – Mn – O/SiO_2 catalyst, the process proceeds in the direction of the formation of the synthesis gas in accordance with Eqn (41). This is probably associated with the fact that the intermediates are oxidised to CO on the oxidised catalyst surface.

The possibility of the conversion of ethene into butadiene suggests a new scheme for its preparation from natural gas:

$$CH_4 \rightarrow C_2H_4 \rightarrow C_4H_6.$$

The interaction of toluene with CO_2 on a Pd/γ-Al_2O_3 catalyst promoted by Ce, Y, Sm, and La oxides has been investigated.[228]

$$C_6H_5CH_3 + CO_2 \rightarrow C_6H_6 + 2CO + 2H_2, \quad \Delta H = 209.7 \text{ kJ mol}^{-1}.$$

At 400 °C, the ratio C_6H_6 : CO was 0.41 on Pd(Ce)/γ-Al_2O_3 and 0.83 on Pd/γ-Al_2O_3. Lanthanide oxides retard the activation of the catalyst. When CO_2 is admitted, the catalyst is oxidised.

$$Pd + CO_2 \rightarrow PdO + CO.$$

When toluene is brought into contact with this catalyst, stoichiometric amounts of C_6H_6, CO_2, CH_4, CO, and H_2 with a small content of xylene are formed. The subsequent introduction of CO_2 leads to the appearance of slightly higher amounts of CO, evidently due to the coke formed from toluene. The overall process mechanism is

$$C_6H_5CH_3 \xrightarrow{Pd} [C_6H_5CH:] + H_2 \xrightarrow[CO_2]{PdO} C_6H_6 + CO + Pd(0).$$

The CeO_2 phase in contact with palladium gives rise to the Pd^{2+}/Pd^0 and Ce^{4+}/Ce^{3+} couples, facilitating thereby the oxidation of palladium.

3. Interaction with alcohols

The attempt to combine the dehydrogenation of methanol to formaldehyde with the reduction of carbon dioxide to CO is of considerable interest.

$$CH_3OH + CO_2 \rightarrow CH_2O + CO + H_2O, \quad \Delta H = 204.2 \text{ kJ mol}^{-1}. \tag{43}$$

This makes it possible to employ CO together with the unreacted methanol in the reaction involving carbonylation to methyl formate and the process can be carried out in accordance with a scheme balanced with respect to carbon.

The oxide compositions Mn – O, Mo – Mn – O, Fe – Mn – O, Cr – Mn – O, Cu – Mn – O, and Mo – Cr – Mn – O deposited on SiO_2 have been investigated in the reactions considered.[229] The catalysts without manganese were relatively inactive. The 10% Mn – 5.5% Cr – 5% Mo – O/SiO_2 catalyst showed the highest activity and selectivity at 560–750 °C (space velocity 900–7200 h^{-1}, $CH_3OH : C_2 = 1$). Under stationary conditions, reaction (43) was accompanied also by others:

$$CH_3OH + 2CO_2 \rightarrow 3CO + 2H_2O, \tag{44}$$

$$CH_3OH \rightarrow CH_2O + H_2, \tag{45}$$

$$H_2 + CO_2 \rightarrow CO + H_2O,$$
$$CH_3OH \rightarrow CO + 3H_2. \tag{46}$$

At 650 °C, the degree of conversion of CH_3OH was 30.2%, that of CO_2 was 14.6%, the selectivity with respect to CH_2O was 91%, and the yield of formaldehyde was 27.5%.

Under nonstationary conditions, the reduction of the catalyst by methanol or H_2 lowers the selectivity in the formation of CH_2O. The reoxidation of the catalyst by oxygen increases the selectivity. The reoxidation of the reduced Mn – O/SiO_2 catalyst by carbon dioxide takes place above 700 °C and is accompanied by the formation of CO. Consequently the low activity of the catalyst under stationary conditions is associated with the low rate of its reoxidation. It increases markedly in the case of the binary Cr – Mn, Mo – Mn, and Cu – Mn catalysts At the beginning of operation of the fresh catalyst, a high selectivity with respect to formaldehyde is observed, but, as the reaction proceeds, it falls, probably owing to the reduction of the catalysts by the reaction mixture.

Formaldehyde does not have an inhibiting effect on the conversion of methanol. Under the reaction conditions, it is converted into CO and CO_2 with a low degree of conversion. The rate of reaction is proportional to the CH_3OH pressure and, up to a certain surface coverage, the CO pressure. Subsequently it attains a constant value. The rate of formation of formaldehyde may be expressed by the kinetic equation

$$r_{CH_2O} = r'_{CH_2O} - r''_{CH_2O}$$

$$= \frac{k'P_{CH_3OH}P_{CO_2}}{k_rP_{CO_2} + k_rP_{CO}} - \frac{k''P_{CH_2O}P_{CO_2}}{k_rP_{CO_2} + k_{-r}P_{CO}},$$

where r'_{CH_2O} and r''_{CH_2O} are the rates of formation and decomposition of CH_2O.

The principal stages in the reaction on the Mn–Cr–Mo–O catalyst are presented in Scheme 5 below.[229]

Scheme 5

$$CH_3OH + Cr^{3+}O^{2-} \xrightarrow{a} CH_2O + Cr^{2+} + H_2O,$$

$$MnO + CO_2 \overset{b}{\rightleftharpoons} MnCO_3,$$

$$MnCO_3 + Cr^{2+} \overset{c}{\rightleftharpoons} Cr^{3+}O + MnO + CO,$$

$$CH_2O + Cr^{3+}O \xrightarrow{d} CHOCr^{2+}H,$$

$$CHOCr^{2+}H + Cr^{3+} \xrightarrow{e} CO + 2Cr^{2+}H,$$

$$2Cr^{2+}H \xrightarrow{f} 2Cr^{2+} + H_2.$$

The $Cr^{3+}O$ centres correspond to the Cr_2O_3 phase. The Mo_8O_{23} phase has also proved useful. Both phases have been detected by X-ray diffraction. Thus methanol is dehydrogenated with participation of the oxidised chromium and molybdenum phases, whilst the reduced manganese oxide phase participates in the activation of CO_2.

We may note that the Cr–Mo–Mn–O/SiO_2 catalyst has more acid properties than Cr–Mn–O/SiO_2. The presence of acid centres has been confirmed in a study of the desorption of ammonia. The acid centres apparently activate methanol, whilst the basic centres (MnO) activate CO_2. The reduction of the catalyst increases the rate of the extensive cleavage of CH_2O.

The data on the conversion of methanol in the absence of CO_2 show that a significant amount of formaldehyde is formed via the direct dehydrogenation [reaction (45)], but is obtained mainly via reaction (43). In the absence of the catalyst, the rate of conversion of methanol is insignificant.

The oxidation of methanol to formaldehyde by CO_2 or the $CO_2 + O_2$ mixture may prove convenient compared with the direct dehydrogenation or oxidation with O_2, since it makes it possible to carry out the process via a thermally neutral mechanism.

The interaction of ethanol with CO_2 on manganese oxide catalysts has been investigated. Mainly the same products as in the Lebedev reaction are obtained: thus butadiene is obtained from the alcohol.[230]

$$2\ C_2H_5OH = C_4H_6 + 2\ H_2O + H_2 \qquad (47)$$

For reasons which have not so far been explained, reaction (47) stops after the attainment of a certain limiting yield, which is appreciably lower than the yield allowed by thermodynamics. The use of CO_2 makes it possible to increase the yield of C_4H_6. The reaction was carried out at 500–600 °C and a space velocity of 1000–3600 h^{-1} in the presence of the Cu–Mn–O/Al_2O_3 catalyst. C_4H_6 and C_4H_8 predominate in the ethanol conversion products. C_2H_4, CH_4, and H_2 have also been obtained. When a $C_2H_5OH + N_2$ mixture is used at 550 °C, the selectivity in the formation of C_4H_6 is 43% for a degree of conversion of C_2H_5OH of 52%. The replacement of nitrogen by CO_2 increases the degree of conversion of C_2H_5OH to 63% and the selectivity with respect to C_4H_6 to 60%, the degree of conversion of CO_2 amounting to 16% under these conditions. The ratio $CO : H_2$ in the contact gas is close to unity, while the concentration of butadiene exceeds by a factor of 2–3 the concentrations of CO and H_2.

The overall stoichiometric equation can be expressed in the form

$$4\,C_2H_5OH + CO_2 \rightarrow 2\,C_4H_6 + CO + H_2 + 5\,H_2O. \qquad (48)$$

Bearing in mind that the generally accepted mechanism[230] of the Lebedev reaction [reaction (41)] presupposes the combination of the dehydrogenation, hydrogenation, condensation, and hydration stages, CO_2 probably prevents the extensive hydrogenation of the aldol condensation products by reacting with the hydrogen formed as an intermediate, increasing thereby the selectivity in the formation of C_4H_6.

The effectiveness of CO_2 as an oxidant in the presence of manganese oxide catalysts both in the conversion of methane[194] and in the condensation of ethanol to C_4H_6 may be important for the alternative synthesis of C_4H_6 from natural gas and CO_2 in accordance with the scheme

$$C_4H_6 + CO_2 \longrightarrow CO + H_2 \longrightarrow C_2H_5OH$$
$$\uparrow \qquad\qquad\qquad\qquad \downarrow$$
$$\longleftarrow C_4H_6 + CO + H_2$$

It follows from the foregoing that carbon dioxide may be used as an oxidant not only for alkanes but also for other organic substances, including alkenes and alcohols. Some of these reactions are of potential practical importance, but the number of investigations of this kind is so far small.

VII. Conclusion

The data presented show, contrary to widespread ideas, that carbon dioxide is capable of entering into a wide variety of reactions with other compounds. The most important classes of reactions involving CO_2 are as follows: (1) the incorporation of CO_2 in the C–C, C–H, and C–N bonds with formation of carboxy- and carbonyl compounds; (2) the oxidation of other compounds by CO_2. The reactions of the first class occur at low temperatures and are catalysed by homogeneous transition metal complexes, while those of the second class are as a rule carried out at a high temperature and are accelerated by metals or transition metal oxides.

Despite the numerous studies carried out, high yields of useful products and appreciable reaction rates have so far been achieved in only a few of them. This is associated with various thermodynamic and kinetic difficulties. One of the main causes of this for reactions of the first class is that the energy of the bond between CO_2 and the transition metal atom in the complex is low (20–60 kJ mol^{-1}) and there is insufficient time for the CO_2 molecule in the coordination sphere to react with another molecule: its lifetime is insufficient. The CO_2 molecule has a filled electron shell and its reactivity is therefore low. Hence it is necessary to increase its reactivity by using another, more effective catalyst or by introducing another ligand. Incidentally, this problem is outside the scope of the present review.

As regards reactions of the second class, in most cases thermodynamic limitations prohibit their occurrence at a low temperature, whilst at a high temperature not every catalyst is able to operate: problems of mechanical strength, resistance to sintering, etc. arise. The most important task is therefore to seek new reactions which do not occur at quite such high temperatures but are promising as regards their economic and environmental aspects and also to seek new catalysts. This requires in its turn the elucidation of the rules governing the selection of the catalysts and the kinetics and mechanisms of the reactions, in particular the paths in the surface reactions, with the aid of physical methods in situ. The application of the latter is difficult at high temepratures, although isolated examples exist, as shown above.

Numerous catalytic and noncatalytic reactions of the first class are known, in which carboxylic acids, esters, carbamates, etc. are formed. However, at present one can only speak of two processes achieved on a large scale — the syntheses of urea and salicylic acid. This does not of course mean that such processes will not develop extensivley in the future.

However, nowadays reactions of the second class — the employment of carbon dioxide as an oxidant — are more promising both from the standpoint of the use of CO_2 as the starting material and from the standpoint of the solution of the environmental problem of the utilisation of CO_2 from gaseous waste. The largest scale process in which CO_2 is used as an

oxidant is the synthesis of methanol. It has been discovered recently that the compound reacting with hydrogen is not CO, as thought previously, but the CO_2 obtained from CO. It would be attractive to synthesise CH_3OH directly by the $CO_2 + H_2$ reaction, although from the thermodynamic standpoint it is preferable to obtain dimethyl ether rather than methanol.[112,113] The synthesis of higher alcohols from CO_2 and H_2 also has apparently a number of advantages compared with the synthesis from CO and H_2.[85,231]

For so long as cheap methods for the preparation of hydrogen have not been found, the reactions of CO_2 with a cheap starting material — hydrocarbons and other organic compounds — are preferable. Such reactions can lead to large scale syntheses of C_2H_4, C_3H_6, C_4H_6, and CH_2O and also would make it possible to devise an alternative method of preparation of the $CO + H_2$ synthesis gas.

The catalytic reactions involving the reduction of C_1-C_7 hydrocarbons and C_1-C_2 alcohols in their interaction with CO_2 were examined above. A disadvantage of the highly active metallic catalysts (Ni, Co, and Fe) is their rapid poisoning by coke. Among the catalysts investigated, the manganese oxide systems proved to be the most effective. There are still many obscure questions concerning both the mechanism of the action of manganese and the kinetics of the above processes.

An essential condition for the correct selection of the catalyst is the selection of systems capable of accepting and activating CO_2. The acid nature of CO_2 necessitate the employment of a catalytic system with basic properties. However, alkali and alkaline earth metals, which form stable carbonates, are ineffective. Moderately strong bases forming carbonates with reduction of CO_2 are needed. Such requriements are met by manganese oxide and apparently certain lanthanide oxides. Their acid and oxidation-reduction properties may be altered by adding other oxides.

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The structure and vibrational spectra of proton solvates in solution

G V Yukhnevich, E G Tarakanova, V D Maiorov, N B Librovich

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Abstract. The experimental and theoretical studies on the structure and properties of the simple stable proton hydrate are surveyed. It is shown that the hydrate is the ion $(H_2O\cdots H\cdots OH_2)^+$. The mechanism of the generation of the continuous absorption observed in the IR spectra of solutions of acids and strong bases is examined. It has been found that a common feature of the structures of all stable proton solvates — the ions $(A\cdots H\cdots A)^{\pm}$ — is the presence in the latter of a symmetrical hydrogen bridge, the properties of which hardly depend on the nature of the ligand A. The constancy of the parameters of the hydrogen bridge provided a basis for the creation of a unique quantitative theory of the catalytic action of acids and bases. The bibliography includes 103 references.

I. Introduction

The physicochemical and catalytic properties of solutions of acids are determined mainly by the presence in the latter of protons, which appear on dissociation of the acid. In solution the protons form stable solvates, the structure and principal properties of which do not change on further solvation.[1] The simplest stable proton solvates actually participate in the majority of the processes occurring in solutions of acids. Special mention should be made of the fact that they play a primary role in homogeneous acid catalysis. In the chemical reactions of organic and inorganic compounds, stable proton solvates act as reactants and ionising agents, forming various intermediate complexes. Thus they participate in the equilibrium and nonequilibrium stages of the acid-catalytic process.

The simplest stable proton solvate is the stable chemical species formed on interaction of the dissociated proton with a specific number of solvent molecules. The properties and structure of the 'excess' solvent molecules solvating it hardly differ from those of the molecules of the pure solvent (the 'free' molecules). The desolvation of the simplest stable proton solvate leads to a rearrangement of its structure and of the system of its chemical bonds, which is manifested by a marked alteration of its properties.

II. The origin of the hypothesis that the H_3O^+ ion is the simplest stable proton hydrate

The problem of the determination of the stoichiometric compositions and structures of the simplest stable proton solvates in solutions arose long before the appearance of the physical methods which make it possible to achieve this. As long ago as the past century it was known that, when salts and especially acids are dissolved in water, heat is evolved, indicating strong binding of the solute to water. In 1886, Arrhenius and van't Hoff showed that many salts and acids decompose into ions in an aqueous medium.[1,2] Hence it was possible to conclude that the high heats of solution of acids in water are due to the formation of stable proton hydrates.

On the basis of the above considerations and also data on the kinetics of esterification in aqueous alcoholic systems, Hantzch and Caldwell[3] and Goldschmidt and Ulby[4] postulated as early as 1907 that the dissociation of an acid in water results in the formation of the hydroxonium ion H_3O^+. The firm establishment of this view was in many respects promoted by the proton theory of acids established independently by Brønsted[5] and Lowry.[6] According to this theory, the interaction of an acid and water takes place as follows:

$$HA + H_2O \rightleftharpoons H_3O^+ + A^- .$$

G V Yukhnevich, E G Tarakanova Division of Vibrational Spectroscopy of Solutions, Kurnakov Institute of General and Inorganic Chemistry, Russian Academy of Sciences, Leninskii prosp. 31, 117907 Moscow, Russian Federation.
Fax (7-095) 954 12 79. Tel. (7-095) 952 20 84 (G V Yukhenevich)
V D Maiorov, N B Librovich Laboratory for Acid – Base Processes, Semenov Institute of Chemical Physics, Russian Academy of Sciences, ul. Kosygina 4, 117334 Moscow, Russian Federation.
Fax (7-095) 938 21 56. Tel. (7-095) 939 71 64 (N B Librovich)

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At that time, there were no data whatsoever indicating the simultaneous addition of several molecules to the proton. This was also the reason why the vast majority of investigators had no doubt that the simplest proton hydrate was always the hydroxonium ion.

The concept of the H_3O^+ ion, which existed for decades, became generally accepted and the appearance in the literature of alternative hypotheses was entirely ignored. An extremely instructive situation arose as a result of this. In the 1950s, it was already possible to identify proton hydrates with the aid of physical methods and to estimate their geometrical parameters. Nevertheless, the efforts of all investigators were directed not to the establishment of the composition and structure of the simplest stable proton hydrate but to the search for H_3O^+ in the solid and liquid phases. Experimenters therefore made a special selection of the conditions under which only the hydroxonium ion could be formed (naturally the appearance of any other proton hydrates was impossible under these circumstances). Such conditions are fulfilled when there is not more than one water molecule for each dissociated proton.

III. The hydroxonium ion in the solid phase

The above approach was used in studies designed to detect and identify the H_3O^+ ion in the solid phase with the aid of resonance and diffraction methods. This made it possible to obtain data on its structure and properties. The first hypothesis of the existence of an ion with three equivalent O–H bonds was put forward in 1924 on the basis of the results of crystallographic studies on perchloric acid monohydrate and ammonium perchlorate, which demonstrated that these substances are fully isomorphous.[7] The structure of the hydroxonium ion in the solid phase (in crystalline strong acid hydrates) was established a quarter of a century later, after the NMR method had become available. It was shown that[8,9] the H_3O^+ ion in the crystalline monohydrates of perchloric, nitric, and sulfuric acids is a pyramid with three O–H bonds 0.98–1.02 Å long and apical angles of ~115° (Fig. 1*a*).

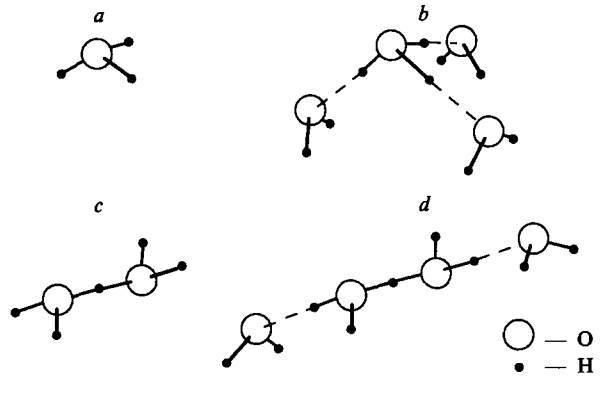


Figure 1. The structures of proton hydrates: (*a*) the hydroxonium ion H_3O^+; (*b*) the hydroxonium ion trihydrate $H_9O_4^+$; (*c*) the proton dihydrate $H_5O_2^+$; (*d*) the proton tetrahydrate $H_9O_4^+$.

The vibrational frequencies of the H_3O^+ ion in the crystalline monohydrates of hydrogen halides and also of nitric, perchloric, and sulfuric acids were measured by IR spectroscopy.[10–12] The frequencies for different crystals, assigned to the vibrations of the hydroxonium ion, differ significantly. The scatter of the deformation and stretching vibrational frequencies can reach several tens or hundreds of reciprocal centimetres respectively. Such a considerable difference between the frequencies does not conflict with the theory of vibrations because the influence on the H_3O^+ ion of the surrounding anions is different in different systems.[13] In individual cases, the influence of the anion is so strong that the hydroxonium ion loses its initial C_{3v} symmetry.

Evidently the distortion of the geometry of the H_3O^+ ion under the influence of the surrounding anions is smaller the lower the charge density on the latter, i.e. the larger their ionic radii. The frequencies observed in the $H_3O^+ \cdot ClO_4^-$ crystal (3220, 2820, 1670, and 1020 cm^{-1}), in which the charge density on the ClO_4^- anion and hence the distortion of the structure of the hydroxonium ion should be smallest, can therefore be most legitimately adopted as the vibrational frequencies of the H_3O^+ ion unperturbed by anions.[14] By analogy with the isoelectronic ammonia molecule and other molecules of the type XH_3, these vibrations were interpreted as follows:[10] $\nu_1 = 2820\ cm^{-1}$, $\nu_2 = 1020\ cm^{-1}$, $\nu_3 = 3220\ cm^{-1}$, and $\nu_4 = 1670\ cm^{-1}$.

Among the numerous studies on the Raman spectra of the hydroxonium ion in the solid state, mention should be made of the communications[15,16] in which the Raman spectra of the $H_3O^+ \cdot SbCl_4^-$, $H_3O^+ \cdot Cl^-$, and $H_3O^+ \cdot Br^-$ were published. The frequencies of the fundamental vibrations of the H_3O^+ ions in these crystals had the following values respectively: 3509, 3463, 1604, and 1095 cm^{-1}; 2900, 2700, 2570, 1605, and 970 cm^{-1}; 2895, 2630, 2525, 1650, 1615, and 970 cm^{-1}.

Since the $SbCl_4^-$ anion has the largest radius, the spectrum of the H_3O^+ ion in the $H_3O^+ \cdot SbCl_4^-$ crystal is closest to that of the unperturbed symmetrical hydroxonium ion. With decrease in the radius of the anion, the splitting of the second (2700 and 2570 cm^{-1}) and then also the third (1650 and 1615 cm^{-1}) vibrational frequencies of the H_3O^+ ion, associated with the loss of the C_{3v} symmetry by the latter, is observed. The occurrence of such splitting indicates unambiguously that, in frequency terms, the second and third vibrations of the unperturbed H_3O^+ ion (3463 and 1604 cm^{-1} for the $H_3O^+ \cdot SbCl_4^-$ crystal) are degenerate stretching (ν_3) and deformation (ν_4) vibrations respectively. This assignment agrees fully with results of measurements of the degree of depolarisation of the lines considered.[15,16]

Thus the interpretation of the vibrations of the H_3O^+ ion based on the Raman spectra is better founded that the assignment based solely on the isoelectronic nature of the H_3O^+ ion and the NH_3 molecule. In contrast to the free ammonia molecule,[17] the highest-frequency vibration of the hydroxonium ion proved to be the symmetrical stretching vibration (ν_1) and not the degenerate stretching vibration (ν_3). From the standpoint of the theory of vibrations, such inversion of the frequencies is possible. The ratio of the ν_1 and ν_3 frequencies depends on the angle between the X–H bonds and on the force constant for their interaction.[18]

Analysis of the literature data shows that towards the 1980s the structures and spectra of proton hydrates had been investigated in detail only in those cases where not more than one water molecule corresponded to each acid proton, i.e. when only the H_3O^+ ion could be formed in the system. The question of the composition and structure of the simplest stable proton hydrate in systems with a stoichiometric water : proton ratio greater than 1 : 1 was not considered at all. Investigators assumed that the simplest stable proton hydrate is always the hydroxonium ion even in the presence of an excess of water.

IV. The hydroxonium ion in the liquid phase

It is impossible to obtain quite such detailed data on the structure of the H_3O^+ ion in solution as in the solid phase. In the study of the structures of the molecular formations in a liquid, the X-ray and neutron diffraction methods as well as the NMR method yield little information (owing to the thermal motion of the molecules and ions). The conclusions reached concerning the structure of the simplest proton hydrate in aqueous solutions of acids were therefore based solely on the study of their IR spectra.

Three absorption bands with maxima near 2900, 1750, and 1205 cm^{-1} (2170, 1400, and 960 cm^{-1} in the case of the deuterio-analogues) have been recorded in the IR spectra of aqueous solutions of HCl, HBr, HNO_3, $HClO_4$, and H_2SO_4.[19–21] The observed bands were located near those of the H_3O^+ ion in the

solid phase. They were therefore assigned to the vibrations of the hydroxonium ion without additional studies. Here no account was taken of the fact that the vibrations of this ion, which according to the theory should be active simultaneously in the IR and Raman spectra,[18] were detected only in absorption spectra. All attempts to record hydroxonium lines in the Raman spectra of the above aqueous solutions were unsuccessful.[12,22]

However, on passing to liquid systems in which only the hydroxonium ion may be formed (with the ratio water : acid = 1 : 1) the picture changes sharply. Thus the Raman spectrum of a solution of the equimolar $H_2O-HSbCl_4$ mixture in dichloroethene exhibits all four lines of the H_3O^+ ion: 3560 (ν_1), 3510 (ν_3), 1600 (ν_4), and 1095 cm^{-1} (ν_2).[23] The reliability of the assignment of the observed lines to the corresponding vibrations of the H_3O^+ ion has been confirmed, as in the spectra of the crystalline monohydrates (see above), by the splitting of the degenerate vibrational frequencies (3510 and 1600 cm^{-1}) following the replacement of the $SbCl_4^-$ anion by smaller anions (Cl^- and Br^-).

Summarising the foregoing, it must be emphasised that the H_3O^+ ion has been detected only in those solid and liquid systems where only one water molecule corresponded to each acid proton. On the other hand, the conclusion that this ion is present in dilute aqueous solutions of acids clearly conflicted with the theory of vibrational spectra. Nevertheless, the concept of the H_3O^+ ion as the simplest stable proton hydrate in aqueous solutions of acids was not questioned.

Together with the experimental data listed above, the theoretical results conflicting with this idea also remained disregarded. Since the 1930s, the study by Hückel, who showed that the addition of a water molecule to the proton results in the formation of an ion with three equivalent O–H bonds the enthalpy of formation of which is ~170 kcal mol^{-1},[24] has been frequently quoted in the literature. On the other hand, nobody discussed the theoretical study by Huggins,[25] which was carried out at approximately the same time. On the basis of quantum-chemical estimates, the hypothesis was put forward in the latter study that in aqueous solutions of acids the dissociated proton can be strongly hydrated by two water molecules. This results in the formation of the symmetrical ion $H_5O_2^+$, in which the hydrogen bond is significantly shorter (2.55 Å) than in liquid water (Fig. 1*b*). According to Huggins' view, this ion is in fact the principal form of the hydrated proton.

V. The proton dihydrate $H_5O_2^+$

The first experimental results indicating that the simplest stable proton hydrate in aqueous solutions is not the hydroxonium ion were obtained by Eigen.[26,27] He estimated the kinetic diameter of the proton hydrate from measurements of the rate of recombination of the H^+ and OH^- ions in water and found it to be ~9 Å. This is very close to the size of the hydroxonium ion trihydrate $H_9O_4^+$, which has the C_{3v} symmetry like the H_3O^+ ion (Fig. 1*b*). The hypothesis that the simplest stable proton hydrate is the $H_9O_4^+$ ion, put forward on the basis of the above agreement, was confirmed also by certain indirect data. However, more careful measurements of the rate constants for the recombination of the H^+ and OH^- ions showed[28] that in reality they are almost twice as high as the values obtained by Eigen.[27] It followed from these data that the diameter of the proton hydrate should be ~5 Å and not 9 Å.[29] This value of the diameter of the simplest proton hydrate in aqueous solutions does not agree with the size of not only the H_3O^+ ion but also the $H_9O_4^+$ ion. Nevertheless the concept of the $H_9O_4^+$ ion, which was very popular in the 1950s and 1960s, can still be encountered in isolated communications even at the present time.

Since the beginning of the 1960s, experimental data began to appear in the literature from which it followed that in aqueous acid solutions the proton is bound firmly to two water molecules. The formation of the stable proton dihydrate was first established as a result of an analysis of the changes in the IR spectrum of a polymeric film of poly(styrenesulfonic acid) occurring when it is moistened.[30] In aqueous solutions of strong acids, such dihydrates were detected in a study of the kinetics and mechanisms of the hydrolytic reactions of organic compounds.[31] Later their presence in solutions was confirmed by IR spectroscopy.[32] The above data demonstrated incontrovertibly that the simplest stable proton hydrate in aqueous solutions has the composition $[H\cdot 2H_2O]^+$. However, there was no information about its molecular structure in solution, stability, and energetic stability.

Studies on the proton dihydrate in the crystalline phase proved more informative. Thus it followed from crystallographic data that, when a water molecule adds to the H_3O^+ ion, the structure of the entire hydrate undergoes a major rearrangement. This results in the formation of the $H_5O_2^+$ ion with a shortened symmetrical (or quasi-symmetrical) O···H···O bond. On further hydration of this ion, its structure hardly changes and the length of the hydrogen bridge always remains 2.4–2.5 Å.[26]

The IR and Raman spectra of the $H_5O_2^+$ ion in the solid phase have been investigated thoroughly.[33,34] The results obtained by Picotin et al.[33] are presented in Figs 2 and 3. Crystals of $H_5O_2^+\cdot SbCl_6^-$, $H_5O_2^+\cdot GaCl_4^-$, and $H_5O_2^+\cdot GaBr_4^-$, as well as their deuterio-derivatives were chosen as the objects of study. The selection of crystals with large anions ensured the least distortion of the geometry of the $H_5O_2^+$ ion, so that its spectra are fairly close to those of the free ion (Figs 2 and 3). Analysis of the vibrational frequencies of the initial and deuteriated crystals showed that only the vibrations of the proton dihydrates are manifested in the region above 500 cm^{-1}. We may note that the

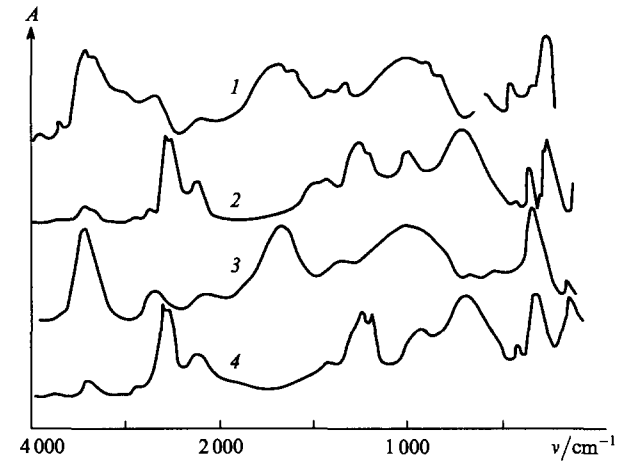


Figure 2. IR spectra of the crystals of $H_5O_2^+\cdot SbCl_6^-$ (curve *1*), $D_5O_2^+\cdot SbCl_6^-$ (curve *2*), $H_5O_2^+\cdot GaBr_4^-$ (curve *3*), and $D_5O_2^+\cdot GaBr_4^-$ (curve *4*) according to the data of Picotin et al.[33]

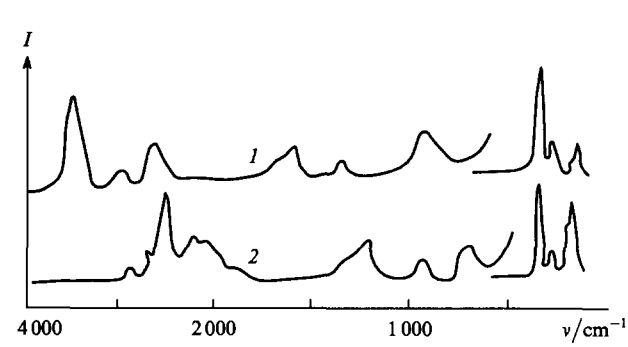


Figure 3. Raman spectra of the crystals of $H_5O_2^+\cdot SbCl_6^-$ (curve *1*) and $D_5O_2^+\cdot SbCl_6^-$ (curve *2*) according to the data of Picotin et al.[33]

IR spectrum of the $H_5O_2^+$ ion (Fig. 2) contains significantly more components than the Raman spectrum (Fig. 3). However, the marked overlap of the bands precludes the determination of not only their positions but also their total number.

The spectrum of the $H_5O_2^+$ ion has a much more elaborate structure and is better resolved when it is recorded by the inelastic neutron scattering method. Such a spectrum (Fig. 4) has in fact been obtained[35] for the ionic crystal of $(H_5O_2^+)_3(PW_{12}O_{40}^{3-})$. In the frequency range 350 – 1800 cm^{-1}, it is possible to note in this spectrum 28 vibrational bands in the form of inflections or distinct peaks. The selection rules for the absorption, Raman, and incoherent inelastic neutron scattering spectra are different, so that comparison of these spectra is legitimate only as regards the frequencies of their bands.

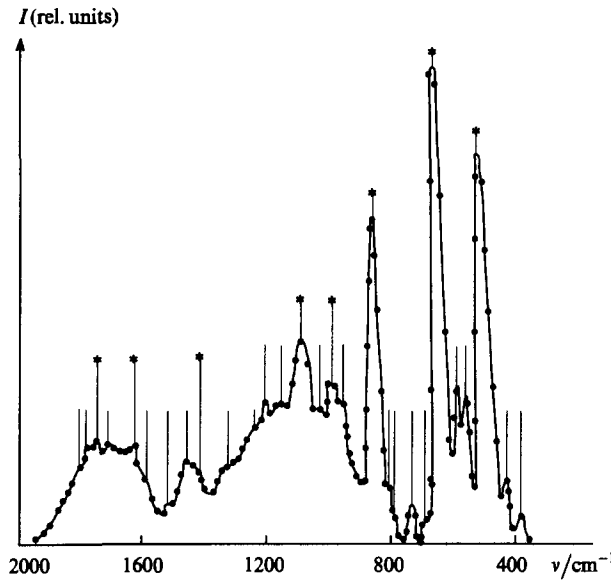


Figure 4. The spectrum of the incoherent inelastic neutron scattering by a crystal of $(H_5O_2^+)_3(PW_{12}O_4^{3-})$ according to the data of Kearley et al.[35]

Interesting results have been obtained in the study of proton hydration in the gas phase. Kebarle and coworkers performed a series of novel investigations[36,37] of gas-phase reactions of the type

$$H^+(H_2O)_{n+1} + H_2O \rightleftharpoons H^+(H_2O)_n .$$

It was shown that the heat of addition of a water molecule to the hydroxonium ion in the gas phase is 31.6 kcal mol^{-1}.[37] This greatly exceeds the energies of the strongest hydrogen bonds, indicating the stability of the $H_5O_2^+$ ion formed. The energy of the addition of the third and subsequent water molecules to the proton is significantly smaller, decreasing monotonically with increase in their number (Fig. 5).

The above investigations[36,37] stimulated a whole series of theoretical studies of the structure and the shape of the potential energy surface of the hydrated proton $H^+(H_2O)_n$. As a result, it was established that the energy of the addition of a H_2O molecule to the H_3O^+ ion is 32 kcal mol^{-1}.[38] This value agrees well with experimental data.[37] It has also been shown that a linear symmetrical hydrogen bond with an equilibrium O···O distance of 2.39 Å corresponds to the energy minimum of the $H_5O_2^+$ ion.[38] The potential energy curve for the central proton has a very flat minimum — when the proton is displaced by 0.3 Å, the potential energy hardly changes. For fixed O···O distances, significantly exceeding the equilibrium value, the cross-section through the potential energy surface along the O···H coordinate has two minima. The calculations of Kraemer and Diercksen[38] have been confirmed in other studies (see, for example, Kollman and Allen[39] and Yukhnevich et al.[40]).

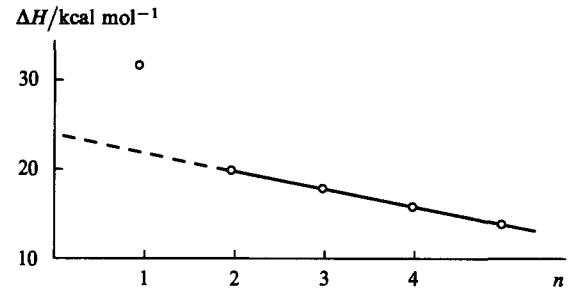


Figure 5. Variation of the heat of addition of a water molecule (ΔH) to the proton hydrate $H^+(H_2O)_n$ with the composition of the latter (n), according to the data of Kebarle et al.[36]

Nonempirical calculations for the hydrates $H_3O^+ \cdot (H_2O)_n$ with $n = 0-4$ showed[41] that the $H_9O_4^+$ ion has a stable chain structure with a central symmetrical hydrogen bond (Fig. 1*d*). The O···O distance (2.36 Å) then proves to be the same as in the $H_5O_2^+$ ion. This result was unexpected to Newton and Ehrenson,[41] who believed that the simplest stable proton hydrate is the hydroxonium ion and that $H_9O_4^+$ represents H_3O^+ hydrated by three water molecules, i.e. has the C_{3v} symmetry (Fig. 1*b*). Thus the results of quantum-chemical calculations led to the same conclusions as the results of the experimental studies examined above: first, the existence of the stable ion $(H_2O\cdots H\cdots OH_2)^+$ with a strong symmetrical hydrogen bond is energetically favoured and, second, the structure and properties of this ion are almost independent of the surrounding molecules.

VI. The $H_5O_2^+$ ion in solutions

The claim that the simplest stable proton hydrate in aqueous solutions is the symmetrical ion $(H_2O\cdots H\cdots OH_2)^+$ was first made on the basis of the analysis of the IR spectra of such solutions.[42] It was shown[42] that, despite the fact that the vibrational frequencies of the H_3O^+ and $H_5O_2^+$ ions are fairly similar (Table 1), these ions may be identified by comparing the IR and Raman spectra of the system investigated.

Table 1. The vibrational frequencies (cm^{-1}) of proton hydrates in IR (IRS) and Raman (RS) spectra.

H_3O^+ (C_{3v})		$H_5O_2^+$ (C_s)	
IRS	RS	IRS	RS
			460
1100	1100	1170	–
–	–	1370	–
1600	1600	1710	1710
2900	2900	2900	2900
3500	3500	3500	3500

The concept formulated by Librovich et al.[42] permitted an approach from a single standpoint, to the consideration of various physicochemical properties of aqueous solutions of acids. By employing it, it has been possible to account for the experimental hydration numbers of protons in aqueous solutions,[32] the kinetics and mechanisms of acid-catalytic hydrolytic reactions,[31,43] and a number of other features. It also made it possible to establish the ionic-molecular composition of the sulfuric acid – water system.[44]

The results of diffraction measurements on aqueous HCl solutions have been published,[45] showing that the O···O distance is shortened and equal to 2.52 Å. The authors attributed it to the complex $H_2O \cdot H_3O^+$. However, taking into account the data

considered above, one must recognise that such a short distance is more likely to be characteristic of the $H_5O_2^+$ ion.

The $H_5O_2^+$ ion has also been detected in the liquid phase by high-resolution NMR.[46] When an equimolar amount of water was added to a solution of octanesulfonic acid in a mixture of deuteriohalomethanes (Fig. 6, spectrum *1*), the bands of the H_3O^+ ion were recorded (Fig. 6, spectrum *2*). The addition of an excess of water to the solution led to a sharp weakening of these bands and the appearance of two new narrow lines with a 1:4 intensity ratio (Fig. 6, spectrum *3*). These lines are due to the central and terminal protons of the symmetrical ion $(H_2O\cdots H\cdots OH_2)^+$.

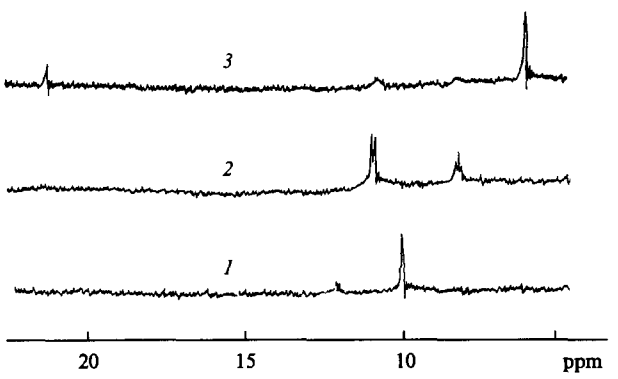


Figure 6. NMR spectra of dilute solutions of $H_2O-HSO_4C_8H_{17}$ mixtures in deuteriohalomethanes according to Golubev's data[46] for different $H_2O:HSO_4C_8H_{17}$ ratios: (*1*) 0:1; (*2*) 1:1; (*3*) 2:1.

Solutions of the $CF_3SO_3H-H_2O$ and $HI-H_2O$ mixtures in an inert solvent (CCl_4) diluted to 10^{-2} M have been investigated by IR spectroscopy.[47] For the acid : water = 1:1 ratio, the bands of the hydroxonium ion were observed in the spectrum of the solution (Fig. 7, spectrum *1*). Following an increase in the water concentration to give the ratio 1:2, the spectrum changed sharply (Fig. 7, spectrum *2*). Further addition of water to the system did not affect the IR absorption curve.

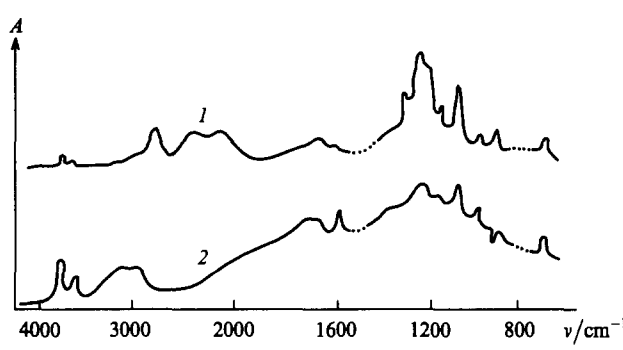


Figure 7. IR spectra of the $H_2O-HSO_3CF_3-CCl_4$ ternary system according to data of Dogonadze et al.[47] for different molar component ratios: (*1*) 1:1:50; (*2*) 2:1:50.

Artificially created systems, fairly remote from aqueous acid solutions, have been studied.[46,47] Nevertheless, the results obtained demonstrated unambiguously the following most important features of the interactions of the proton with water molecules in solution.

1. The hydroxonium ion exists in the liquid phase only when there is not more than one water molecule per acid molecule.

2. With increase in the water content in the system, a chemical reaction between H_3O^+ and H_2O and not simple hydration of the H_3O^+ ion takes place in the system. It is accompanied by a rearrangement of the bonds and the formation of the symmetrical ion $H_5O_2^+$.

3. The hydration of the $H_5O_2^+$ ion (to give a water : acid ratio in excess of 2:1) does not alter its structure.

VII. The continuous absorption in the IR spectra of solutions of acids. Initial interpretation

The determination of the molecular structure of the simple proton solvate in solutions is indissolubly linked to the study and interpretation of its vibrational spectra. Until recently, such interpretation involved considerable difficulties. The point is that the IR spectra of all systems in which proton dihydrates (as well as other proton disolvates formed via a strong symmetrical hydrogen bond) are present exhibit an intense continuous absorption (CA) in the range from ~3500 to 800 cm^{-1}. The positions and intensities of individual, usually indistinct, maxima on the contour of this continuum depend on the composition of the test solution. A significant factor proves to be not only which species, other than the proton disolvate $(A\cdots H\cdots A)^{\pm}$, are present in solution but also what molecules A solvate the proton.[48]

The continuous absorption in the spectra of solutions of acids and strong bases was first recorded in the near infrared (4300–6700 cm^{-1}) and it was immediately established that its optical density is proportional to the acid or alkali concentration in solution.[49,50] Much later a similar spectroscopic phenomenon was observed also in the region of the fundamental vibrational frequencies of the molecules.[51,52] Ackermann,[52] who was the first to detect a continuous absorption in this region, assumed that it is due to the delocalisation of the positive or negative charge in the solvate complex. Subsequently, the continuous absorption observed in the spectra of numerous aqueous and nonaqueous solutions was vigorously studied by various investigators.[53–57]

A large series of studies on the continuous absorption has been carried out by Zundel and coworkers.[30,57–60] Some of their results are extremely interesting. Thus it has been shown[30] with the aid of a novel experiment that the appearance of the continuous absorption requires that the solution contains a dissociated proton bound to two water molecules. On the other hand, it must be said that in his studies Zundel's aim was not to obtain the spectrum of the ion 'in a pure form'. He confined himself to the analysis of the spectra of mixtures in terms of the transmittance scale (see, for example, Fig. 8). This made it impossible for him to draw inferences about the details of the spectral absorption curve for the ion under consideration and hence about its molecular structure. We may also note that Zundel based his concept concerning the mechanism of proton hydration both on incontrovertible experimental data and on the results of studies[27,51,52] which proved subsequently to be erroneous. For this reason, the explanation which he proposed for the causes of the appearance of the continuous absorption[58] appears unconvincing. As a result of Zundel's many publications,

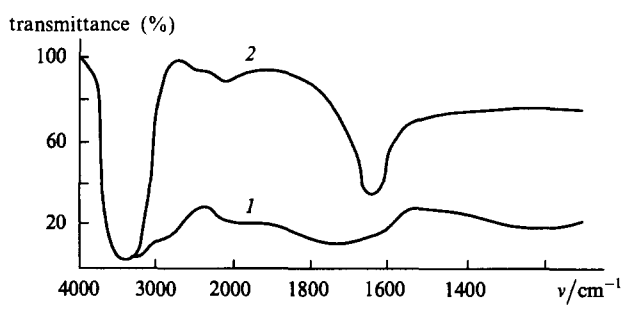


Figure 8. IR spectra of a 10 M HCl solution in H_2O (curve *1*) and of water (curve *2*) according to the data of Schioberg and Zundel.[57]

his view became well known and we shall therefore consider it in detail.

Zundel based his interpretation of the continuous absorption on the following assumptions:[58]

1. The spectra of aqueous solutions of acids and strong bases contain the same vibrational bands.

2. The lifetime of the H_3O^+ ion (which is the simplest proton hydrate in Zundel's view) is so short that its vibrations cannot be recorded by IR spectroscopy.

3. The most stable ion-molecule formation, the vibrations of which are manifested in the IR spectrum of the solution, is the $H_9O_4^+$ ion (Fig. 9).

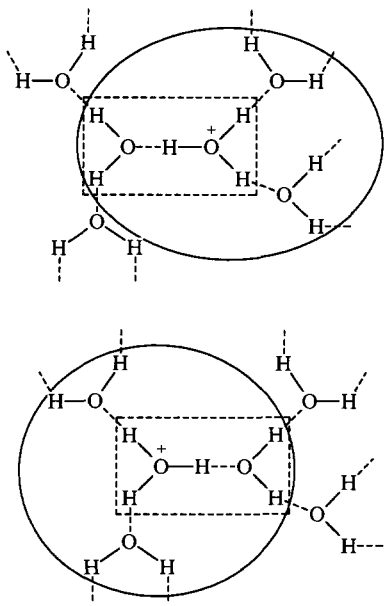


Figure 9. The molecular structure of the proton hydrate according to Zundel's data.[58] The $H_9O_4^+$ ion is shown within the circumscribed region.

On the basis of the assumptions listed,† Zundel proposed a model of the proton hydration in solution, the essential features of which reduce to the following. The $H_5O_2^+$ group (not the simplest stable ion but an unstable group which is incapable of entering into chemical reactions as an integral whole) exists in aqueous solutions of acids. The proton in this group is rapidly exchanged between the two water molecules, occupying one of the boundary positions:

$$(H_2OH^+\cdots OH_2) \rightleftharpoons (H_2O\cdots H^+OH_2).$$

The transfer of the proton, which is located in a potential well with two minima, takes place as a result of the fluctuations of the electric field generated by the environment of the $H_5O_2^+$ group. The ultrahigh polarisability of the hydrogen bond (this property of the O···H···O bond is simply postulated) plays a special role in this process. According to this model (which has not undergone significant changes since that time[59,60]), the continuous absorption arises by virtue of the appearance of additional transitions during the tunnelling of the proton through the central potential barrier.

Together with the explanation of the origin of the continuous absorption examined above, other treatments of this spectroscopic phenomenon have been proposed.[61-65] Like Zundel's hypothesis, they are all based on the hypothesis of a strong interaction between the bridging proton and the medium. For example, it has been shown[65] that the experimentally observed broad absorption region may arise as a result of the interaction of the vibrations of the central proton in the $H_5O_2^+$ ion with the low-frequency vibrations of the surrounding ligands (the proton–phonon theory). This approach made it possible to describe the isotope effects and to account for the presence of the continuous absorption in the IR spectra of solutions of strong bases. The simplest stable solvated ion in such solutions has the structure $(HO\cdots H\cdots OH)^-$.

However, in the studies by Golubev, Denisov,[47] and Pankov and coworkers[66] published at the beginning of the 1980s, it was shown that the initial postulate, on which all the proposed theories were based, conflicts with experiment. In these investigations, studies were made of the IR spectra of the ion $(H_2O\cdots O\cdots OH_2)^+$ in a water–acid–carbon tetrachloride ternary system[47] and of the complex $(RO_H\cdots H\cdots O_HR)^+$ in a alcohol–acid–aprotic solvent (CCl_4 and CH_2Cl_2) system.[66] It was established that, even when the solvation effects are reduced to a minimum, the shape of the contour and the intensity of the continuous absorption in the spectrum of the ion $(A\cdots H\cdots A)^{\pm}$ remain the same as in polar solvents. In other words, the continuous absorption is not caused by the influence of the medium but is due to the intrinsic internal properties of the ions with a symmetrical hydrogen bond.

The data obtained in the above studies[47,66] made a most important contribution to understanding the phenomenon under consideration, on the one hand, and posed a new major problem before investigators, on the other. It was now necessary to explain all the characteristics of the continuous absorption in the vibrational spectra of solutions of acids and strong bases listed above on the basis of the properties of a molecular system consisting of a small number of atoms (only five in the case of the $H_3O_2^-$ ion). The successful solution of this problem, i.e. the establishment of a quantitative relation between the properties of the individual structural elements of the proton disolvate and its vibrational spectrum, would make it possible not only to understand the mechanism of the appearance of the continuous absorption but also to determine the structure of the ion $(A\cdots H\cdots A)^{\pm}$.

Evidently, the solution of the problem formulated requires more accurate information about the nature of the vibrations of the proton disolvate, i.e. on the experimental side it was necessary to effect a transition from the spectra of mixtures to the individual spectra of ions, and on the theoretical side the consideration of the monocoordinate O···H···O bridge had to be replaced by allowance for all the degrees of freedom of the vibrational system investigated. A formulation of this kind was achieved by a number of investigators.[40,48,67-71]

VIII. Differentiation of the spectra of proton disolvates from the spectra of solutions

In practice, the structure of the simplest proton hydrate in solution may be established only by investigating its IR spectrum. It is therefore necessary to measure this spectrum as thoroughly as possible. Thus, in the case of strongly absorbing liquids, to which aqueous solutions also belong, the IR spectra must be measured not by the transmittance technique but by the multiple distorted total internal reflection (MDTIR) technique.[72] The high accuracy of the measurement of the spectrum is especially important in cases such as the resolution of the spectrum into components or the differentiation of the spectrum of a particular molecule from the spectrum of a mixture.

From the standpoint of the correctness of the primary spectroscopic measurements, mention may be made of the studies of Yukhnevich et al.[48] and Maiorov and Librovich.[71] Using the MDTIR method, these investigators obtained, with a highly satisfactory accuracy, the absolute spectroscopic absorption coefficients of aqueous and methanol solutions of hydrogen

† These postulates conflict with experimental data in Refs 11, 15, 19, 46, and 48, in Refs 15, 19, and 23, and in Refs 28, 29, and 42 respectively.

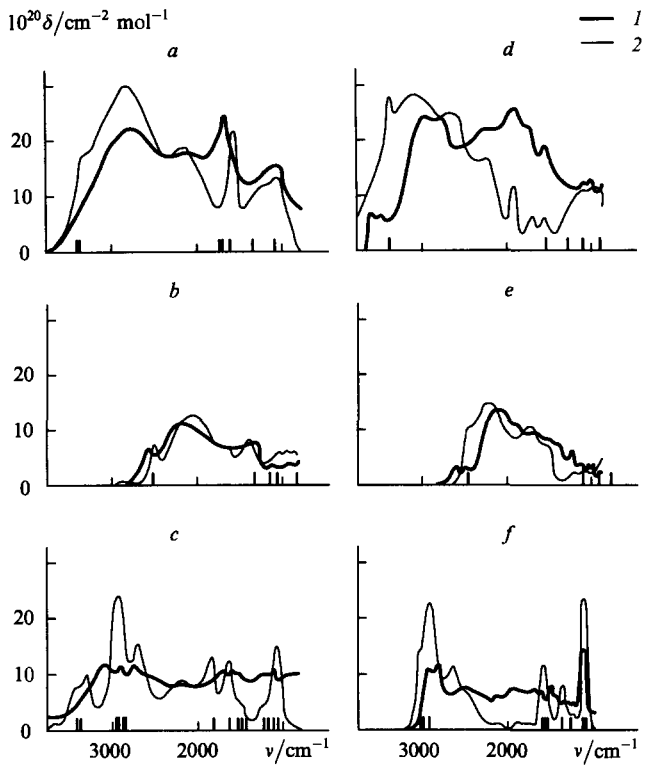


Figure 10. The measured (curves *1*) and calculated (curves *2*) IR spectra of proton disolvates according to the data of Yukhnevich et al.[48]: (*a*) $H_5O_2^+$, (*b*) $D_5O_2^+$; (*c*) $(CH_3OH)_2H^+$; (*d*) $H_3O_2^-$; (*e*) $D_3O_2^-$; (*f*) $(CH_3O)_2H^-$.

chloride and potassium hydroxide. This made it possible to differentiate for the first time the spectra of the ions $H_5O_2^+$, $D_5O_2^+$, $(CH_3OH)_2H^+$, $H_3O_2^-$, $D_3O_2^-$, and $(CH_3O)_2H^-$ 'in a pure form' by measuring the spectra of a series of auxiliary systems (Fig. 10).

In the differentiation of the spectra of positively charged ions, acid–solvent systems with known ion-molecular compositions and known molar absorption coefficients of the system were selected. The spectra of the ions $(A\cdots H\cdots A)^+$ were found directly by subtracting from the IR spectrum of the solution the absorptions due to the solvent molecules and the acid anions. The differentiation of the vibrational spectra of the negatively charged ions involved much greater difficulties. The point is that the spectrum of the solvent molecules (water and methanol respectively), which strongly solvate the $H_3O_2^-$ and $(CH_3O)_2H^-$ ions present in the solution, differs appreciably from the spectrum of the pure solvent.[73,74] Therefore, in determining the spectra, estimates were made of the position, width, and intensity of the ν_{OH} band of the H_2O and CH_3OH molecules solvating the ions $(A\cdots H\cdots A)^-$. As a result, the accuracy of the absorption cross-sections obtained for ions with a negative charge (~30%) proved to be significantly lower than for the positively charged ions (~15%).

IX. Calculation of the IR spectra of proton disolvates

Interpretation of the IR spectra of proton disolvates requires allowance for their highest-order vibrations.[47,66] In other words, the mechanism of the appearance of the continuous absorption must be analysed in terms of the anharmonic approximation of the theory of the vibrations of polyatomic molecules. This approach has been used in the calculation and analysis of the IR spectra of the ions $(A\cdots H\cdots A)^{\pm}$ in a number of studies.[40,48,67–70] Proton disolvates differing significantly in composition—$H_5O_2^+$, $D_5O_2^+$, $(CH_3OH)_2H^+$, $H_3O_2^-$, $D_3O_2^-$, and $(CH_3O)_2H^-$—were chosen as the objects of study. This made it possible to determine the influence of the ionic charge, of the nature of the ligand, and of deuteriation on the shape of the continuous absorption contour.

For the calculation of the spectra of the systems listed above, it was also necessary to know, together with the properties of the ligand molecules, also the geometrical, energetic, and electro-optical parameters of the O···H···O bridges. The authors of the studies under consideration based the determination of the above parameters on the data concerning the ions $(A\cdots H\cdots A)^{\pm}$ already available at the time. In view of the importance of the characteristic properties of these ions for the understanding of the nature of the continuous absorption, we shall consider them in detail.

The study of the kinetics of the gas-phase chemical reactions leading to the formation of the ions $(A\cdots H\cdots A)^{\pm}$ showed that the energy of the addition of the second solvating molecule to the proton is virtually unchanged (31 ± 2 kcal mol^{-1}) for several tens of compounds investigated, in which the molecule A is water, an alcohol, acid, ester, ketone, or aldehyde.[34,75–78] The invariance of the bond energy of the symmetrical hydrogen bridge in all the systems containing it was confirmed by the results of numerous quantum-chemical calculations.[76,79–82] All the available experimental data[83–88] as well as the results of calculations by various methods[79–82,89,90] showed that the length of the O···H···O bridge (2.4–2.55 Å) also depends little on the structure of the molecules solvating the proton. The results of quantum-chemical calculations[48,68] demonstrated that the force constants, the atomic charges, and the dipole moments of the bonds in the O···H···O fragment are independent of the nature of the ligand (Table 2). The last two of the characteristics indicated are determined by the ionic charge.

Table 2. Parameters of the symmetrical hydrogen bridge O···H···O (data of Yukhnevich et al.[48]).

Parameter	$H_3O_2^-$	$H_5O_2^+$	$(CH_3O)_2H^+$	$(CH_3OH)_2H^+$
$R_{O\cdots H}$/Å	1.207	1.197	1.212	1.203
$F_{O\cdots H}$/ mdyn Å^{-1}	2.35	2.0	2.62	2.48
$F_{O\cdots H,\ O\cdots H}$/ mdyn Å^{-1}	1.76	1.50	1.99	1.79
$F_{O\cdots H\cdots O}$/ mdyn Å^{-1}	0.16	0.13	0.16	0.10
Q_O/electric charge units	−0.84	−0.42	−0.67	−0.42
Q_H/electric charge units	0.36	0.41	0.36	0.40
$\mu_{O\cdots H}/\mu_{OH(H_2O)}$	1.33	0.63	1.30	0.75

There have been few experimental studies devoted to the nature of the potential energy surface of proton disolvates.[87,88] However, in the case of the ion $[(C_2H_5O)_2O\cdots H\cdots O(C_2H_5)_2]^+$, investigated for this purpose, as well as the ion $H_5O_2^+$,[38–40] the central proton is located in a symmetrical potential well with one minimum. This conclusion was reached on the basis of the results of studies of a single crystal of the etherate $(C_2H_5)_2O\cdot HZnCl_3$ by X-ray diffraction and ^1H NMR.[87,88]

The IR spectra of the ions $H_5O_2^+$, $D_5O_2^+$, $(CH_3OH)_2H^+$, $H_3O_2^-$, $D_3O_2^-$, and $(CH_3O)_2H^-$ have been calculated, taking into account the kinematic, dynamic, and electrooptical anharmonicities of the vibrations, by a variational method[91] in accordance with a general algorithm. No adjustment of the calculated frequencies and intensities of the absorption bands to achieve agreement with experimental spectra of specific ions was carried out. All the parameters of the O···H···O bridges needed to calculate the spectra of the test systems were found with the aid of

a semiempirical model for the description of the dynamic and electrooptical properties of the hydrogen bond[92] or by means of quantum-chemical calculations.[48,68]

The absorption spectra of the proton disolvates calculated in this way are presented in Fig. 10. The positions of the fundamental vibrational bands are designated by vertical lines. The complete set of the calculated frequencies of the $H_5O_2^+$ ion in the range 200–1800 cm^{-1} is presented in Table 3. The table shows that the average deviation of the calculated fundamental vibrational frequencies from the frequencies of the most intense lines in the inelastic neutron scattering spectrum[35] is ± 18 cm^{-1} (which corresponds to the accuracy achieved by a modern theory of the vibrations of polyatomic molecules[18]).

Table 3. Experimental[35] and calculated[48] vibrational frequencies (cm^{-1}) of the $H_5O_2^+$ ion in the range 0–2000 cm^{-1}.

No.	Experiment	Calculation	No.	Experiment	Calculation
1	1800		14	1080[a]	1093[a]
2	1775	1770[a]	15	1030	1026
3	1730[a]	1742[a]	16	982[a]	1021
		1721	17	955	1015
4	1710	1711	18	836[a]	833[a]
		1672			
		1644	19	805	
5	1610[a]	1622[a]	20	785	
		1603			
		1602			
6	1580	1577	21	730	724[a]
7	1515	1509	22	685	
		1503			
		1502	23	616[a]	673[a]
8	1450	1446	24	590	
9	1425[a]	1415	25	560	
		1403	26	494[a]	498[a]
		1363			497[a]
10	1325	1350	27	430	
11	1240	1256	28	380	
12	1205	1246			
13	1150				

[a] The fundamental vibrational frequency.

Analysis of the calculated IR spectra of the ions investigated established two characteristic features. Firstly, the majority of the vibrations of the proton disolvates and primarily the vibrations of the hydrogen bridge are not localised in one coordinate. Their modes, determined by the structure of the ion, are individual.[48,69] Secondly, in the region where the continuous absorption is observed experimentally the spectra of all the ions considered contain tens (40–300) compound vibrational bands and overtones, the intensities of many of which (30%–60%) are comparable to those of the fundamental vibrational bands.[67–70]

Detailed study of the influence of various anharmonic parameters on the nature of the calculated spectra of the ions $(A\cdots H\cdots A)^{\pm}$ showed that the presence in the latter of a large number of intense combination bands is a consequence of the electrooptical anharmonicity of the vibrations of the O···H···O fragment. Furthermore, it has been possible to establish unambiguously that only two nonequivalent electrooptical parameters make a decisive contribution (~85%) to the overall intensity of the higher-order vibrational bands in the spectra of proton disolvates.[70] The causes of the appearance of intense overtone vibrational bands in the spectra of the ions $(A\cdots H\cdots A)^{\pm}$ were analysed by considering the modes and intensities of the vibrations of the hydrogen bridge O···H···O. Such analysis made it possible to establish that the vibrations of the O···H···O fragment, in which the central proton shifts simultaneously along and across the direction of the hydrogen bond, are anomalously intense and to understand why precisely these vibrations are so intense.[69]

Analysis of the coefficients in the expansion of the anharmonic eigenfunctions of the vibrational energy levels in terms of the harmonic basis functions made it possible to explain why the intense combination bands in the spectra of proton disolvates are so numerous. It was found that the strong kinematic interaction of the coordinates of the hydrogen bridge with other coordinates of the ions $(A\cdots H\cdots A)^{\pm}$ causes the displacement of the proton along or across the hydrogen bond to occur in more than half of their fundamental vibrations, while the simultaneous shift in both directions indicated occurs in virtually every third overtone vibration. These composite vibrations and overtones are in fact active in the absorption spectrum.[48,69]

Thus it follows from the calculations that the continuous absorption in the spectra of proton disolvates may be due to the presence in the range 800–3700 cm^{-1} of a large number of overlapping intense higher-order vibrational bands. The appearance of such bands is caused by the intrinsic properties of the ions $(A\cdots H\cdots A)^{\pm}$ and in the first place by the electrooptical anharmonicity of the O···H···O fragment and the strong interaction of the coordinates of the hydrogen bridge with the internal coordinates of the ligand.

X. Interpretation of the continuous absorption in the IR spectra of solutions of acids and strong bases

The results of the comparison of the calculated and measured absorption cross-sections of the ions $H_5O_2^+$, $D_5O_2^+$, $(CH_3OH)_2H^+$, $H_3O_2^-$, $D_3O_2^-$, and $(CH_3O)_2H^-$ (Fig. 10, Table 4) demonstrated the validity of the explanation of the nature of the continuous absorption proposed by Yukhnevich et al.[48] It is seen from the spectra presented in Fig. 10 and the data in Table 4 that the calculation made it possible to reproduce on the whole correctly the overall form of the spectral curves and the integral absorption of all the ions in the frequency range considered and also to reproduce correctly the changes in the spectra of the $H_5O_2^+$ and $H_3O_2^-$ ions occurring on isotopic substitution.

Table 4. The absolute absorption intensities of the proton disolvates (I) and their isotopic ratios (I_H/I_D) according to the data of Yukhnevich et al.[48]

Ion	Calculation		Experiment		Frequency range/cm^{-1}
	I/D^2 Å^{-1}	I_H/I_D	I/D^2 Å^{-1}	I_H/I_D	
$H_3O_2^-$	87	2.8	62 ± 13	2.6 ± 0.8	3700–900
$D_3O_2^-$	31		24 ± 5		2700–900
$H_5O_2^+$	96	2.5	130 ± 14	3.1 ± 0.5	3700–900
$D_5O_2^+$	38		42 ± 5		2700–800
$(CH_3O)_2H^-$	66		82 ± 17		3700–900
$(CH_3OH)_2H^+$	84		131 ± 14		3700–900

Yet another confirmation of the concept concerning the origin of the continuous absorption under discussion is the fact that, when the $H_5O_2^+$ and $H_3O_2^-$ ions are deuteriated, their integral absorption (the average for both ions) diminishes by a factor of 2.85 ± 0.5 (Table 4). This value agrees well with the calculated value 2.65 (Table 4). However, it can correspond neither to the isotopic ratio of the fundamental vibrational intensities of the O–H bond nor to the ratio of the intensities of the first overtone vibrations. According to the theory of vibrations,[18] in the former case the isotopic ratio should be 1.84, while in the latter it should be 3.39. The experimental

isotopic intensity ratio (2.85) can be explained by averaging the values (1.84 and 3.39) for several fundamental and first overtone vibrations.

Thus the published data show that the continuous absorption in the spectra of acids and strong bases is caused by the intrinsic vibrations of the simplest stable proton solvates. The solvates themselves are stable charged species with a symmetrical hydrogen bridge O···H···O, the properties of which are almost independent of the nature of the ligand.

XI. The structure of the solvated proton and the catalytic properties of acids

The equilibrium stage involving the protonation of the organic compound which subsequently undergoes chemical reaction plays an important role in homogeneous acid catalysis. The degree of protonation of the organic compound depends on the catalytic activity of the acid solution and primarily on the acidity function of the solution. It was assumed for a long time that the protonation of the organic molecule B involves the transfer to the latter of a proton from the acid medium and the formation of the protonated form BH^+. It was postulated that BH^+ is the simplest stable proton solvate, the addition to which of a second and subsequent solvent molecules does not alter its structure. However, as early as 1980 it was already established[93] that in many cases the protonation of the molecule of compound B is a reaction involving the substitution of a water molecule in the $H_5O_2^+$ ion by a molecule of B:

$$(H_2O\cdots H\cdots OH_2)^+ + B \rightleftharpoons (H_2O\cdots H\cdots B)^+ + H_2O. \qquad (1)$$

The radical revision of the ideas concerning the mechanism of the catalytic action of acids was caused by the finding that the protonated form of the organic molecule in solutions is usually not the BH^+ ion but the $(H_2O\cdots H\cdots B)^+$ ion.[94] The new concept, elucidating the characteristic features of this mechanism, was based on the constancy of the enthalpy of formation of proton disolvates[34,75-78] and the independence of the parameters of the symmetrical hydrogen bridge on the nature of the molecules solvating the proton.[48,68,79-90] Understanding the fact that the properties of the central ···H··· fragment, which is common to a wide range of compounds, determine not only the nature of their vibrational spectra but also their behaviour and chemical reactions made it possible to solve the following fundamental problem in homogeneous acid catalysis.

1. The physical significance of the Hammett acidity function H_0 was discovered and the limits of its applicability were established. Previously, the use of this function was based on the postulate that the mechanisms of the protonation in acid solutions of stable compounds (indicators) and of the reacting organic molecule are the same.[95] This postulate had no physical justification, since no common properties embracing indicators and organic compounds with different structures and chemical compositions were known.

It has been shown[93] that Hammett's postulate holds only in those cases where the molecules of compound B are protonated via reaction (1). In other words, an obligatory condition for its validity is the presence in the proton solvate of a symmetrical hydrogen bridge with invariant parameters. A number of conditions must be fulfilled for the protonation of the molecule of compound B to occur in accordance with the scheme indicated.[96] Firstly, the acid–base interaction in the solution must go to completion, i.e. positively charged proton solvates must be formed in it. Secondly, the molecules solvating the proton must have lone pairs ensuring the formation of a symmetrical hydrogen bond. Thirdly, it is necessary that the heat of addition of a proton to a molecule of compound B (the proton affinity) should be greater than the proton affinity of the water molecule (i.e. >170 kcal mol^{-1}) but less than 197 kcal mol^{-1}.[96] For heats of addition of a proton to a molecule of compound B exceeding 197 kcal mol^{-1}, the preconditions for the fulfilment of Hammett's postulate vanish and protonation leads to the formation of the BH^+ ion.

2. Quantitative relations between the acidity functions of acid solutions and the thermodynamic activities of water have been obtained. It has been shown[94] that, when equilibrium (1) obtains in the solution of an acid, then the Hammett acidity function H_0 should be formulated as follows:

$$H_0 = -\lg\left(a_{H^+}\, a_{H_2O}\frac{f_B}{f_{BHOH_2^+}}\right), \qquad (2)$$

where a represents the thermodynamic activities of the corresponding species and f represents the activity coefficients.

The fundamental difference between Eqn (2) and the formulation adopted earlier for H_0 is the presence in the former of the activity of water. This made it possible to account for the long established fact[95,97] that the quantity $H_0 + \lg a_{H_2O}$ is independent of the activity of the anion in solution, while the ratio of the activity coefficients is the same for organic compounds having different structures, provided that Hammett's hypothesis holds. It has also been shown[94] that, in those cases where equilibrium (1) obtains, the degrees of protonation and the basicity constants $K_{BHOH_2^+}$ should be calculated in virtually the same way as for the previous ideas concerning the structure of the protonated form:

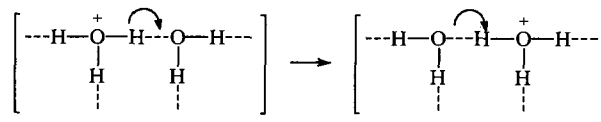
$$H_0 = pK_{BHOH_2^+} + \lg\left(\frac{c_B}{c_{BHOH_2^+}}\right),$$

$$K_{BHOH_2^+} = \frac{a_B a_{H_5O_2^+}}{a_{BHOH_2^+}\, a_{H_2O}}.$$

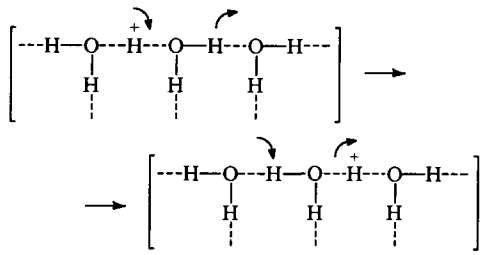
3. An explanation has been proposed for the difference between the gas-phase and liquid-phase acidities observed for many compounds. A large number of organic compounds, forming the $BHOH_2^+$ ion both in the gas and liquid phases, fall within the range of the energies for the addition of a proton to a molecule of compound B indicated above.[98] However, the mech-anisms of the protonation of a series of compounds in the gas and liquid phases are different (a substitution reaction with formation of the $BHOH_2^+$ ion takes place in the gas phase, while the BH^+ ion is formed in the liquid phase).[96] A difference between the gas-phase and liquid-phase acidities is observed in precisely such cases. Hence the above difference is caused not by the influence of the medium on the activity coefficients of the forms B and BH^+ but by the different mechanisms for the protonation of the organic molecule in the liquid and gas phases.[96]

4. The mechanism of the hydrolytic reactions of organic compounds was established. It has been shown[43] that ions with symmetrical hydrogen bonds may participate as the reactants in the rate-limiting stages of acid-catalytic processes. However, only the stoichiometric composition of the intermediate complexes could be inferred from the kinetic data. In order to establish the mechanism of the rate-limiting stage of the reaction, it was also necessary to know the structures of the reacting species. The information obtained about the structures of the simplest stable proton hydrates in aqueous solutions of strong acids made it possible to establish the structure of the intermediate complex in the hydrolytic reactions. This permitted the understanding of the detailed mechanism of the rate-limiting stage in these reactions.[99]

5. The mechanism of the proton conduction in aqueous solutions of acids was revised. On the basis of the concept of the H_3O^+ ion, it had been assumed previously that the anomalously high mobility of the proton in such cases can be explained by the Grotthus relay mechanism.[26,95]



However, in reality the simplest stable proton hydrate in aqueous solutions of acids is the $H_5O_2^+$ ion. In this case, charge transfer without disturbing the structure of the solution is possible only for a synchronous transfer of two protons in accordance with the mechanism:[100,101]



Such a transfer is equivalent to the migration of a proton from one potential well to another, overcoming a barrier of $\sim$2.4 kcal mol^{-1}.[102]

An analogous mechanism of the transfer of a negative charge (a proton defect) can be put forward for aqueous solutions or bases, where the simplest stable hydrate of the hydroxide ion is $(HO\cdots H\cdots OH)^-$.[65]

XII. Conclusion

The history of the development of ideas concerning the structure of the simplest stable proton hydrate shows how important is the correct understanding of the relation between the molecular structures of the test objects and their properties recorded experimentally.

The main outcome of studies carried out over many years, the different stages of which have been examined consecutively in the present review, is the establishment of the structures and properties of the simplest stable proton solvates in solutions of acids and strong bases. Such solvates are the ions $(A\cdots H\cdots A)^{\pm}$ with a symmetrical hydrogen bridge, the properties of which are almost independent of the nature of the ligand A. The broad region of continuous absorption observed in the IR spectra of proton disolvates is due to the electrooptical anharmonicity and the noncharacteristic nature of their vibrations.

The elucidation of the characteristic features of the mechanism of the vibrations of systems containing strong symmetrical hydrogen bonds led to a deeper understanding of the process involving the establishment of their IR spectra. Together with the interpretation of the continuous absorption, which has been confirmed experimentally, it also made it possible to achieve a simple explanation, having a clear physical significance, of the 'anomalous' dependence of the vibrational frequencies of such systems on the isotopic composition.[103]

The level of knowledge concerning the structures and properties of the simplest stable proton solvates achieved at the present time has made it possible to abandon the purely empirical relations in the determination of the mechanisms of acid–base catalytic reactions and to construct a unique quantitative theory of the catalytic action of acids and bases. The satisfactory foundations and the clear-cut definition of the limits of the applicability of this theory have made it possible to employ it successfully in order to account for the known experimental facts and to predict the conditions for the occurrence of various physicochemical processes in solutions.

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The physical chemistry of the compounds $M^IP(As)UO_6$ (M^I = H, Li, Na, K, Rb, Cs) and their crystalline hydrates

N G Chernorukov, N V Karyakin

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Abstract. Problems concerning the structures of compounds of the series $M^IP(As)UO_6 \cdot nH_2O$ (M^I = H, Li, Na, K, Rb, Cs; n = 4 for M^I = H, Li and n = 3 for M^I = Na, K, Rb, Cs) are examined. The results of X-ray powder diffraction, thermographic, and IR spectroscopic studies on the above compounds are analysed. The experimental standard enthalpies of formation ($\Delta_f H^\circ$) of the compounds $M^IP(As)UO_6$ and their crystalline hydrates are discussed. The characteristic features of the variation of $\Delta_f H^\circ$ as a function of the structural characteristics of the compounds and of the physical properties of the Group I elements in the series of phosphorus and arsenic compounds are described. The enthalpies of dehydration and ion exchange involving the compounds investigated are presented. The bibliography includes 103 references.

I. Introduction

The compounds $M^IM^VUO_6 \cdot nH_2O$, where M^I = hydrogen or an alkali metal and M^V = phosphorus or arsenic, are of interest by virtue of a whole series of factors. The compounds include well-known, and fairly widely distributed in nature, uranium minerals with M^I = H, Na, or K, the rubidium compounds which have been much less investigated and are not encountered in nature, as well as the caesium compounds and natural uranium compounds with the same formula containing vanadium as the pentavalent element, which have not been investigated at all.

It is known that the compounds $HPUO_6 \cdot 4H_2O$ and $HAsUO_6 \cdot 4H_2O$ have a high proton conductivity and may be used in autonomous energy sources. The alkali metal derivatives are interesting from the standpoint of their electrophysical characteristics: for example, a high ionic conductivity is characteristic of these substances. Finally, the natural compounds $M^IP(As)UO_6 \cdot nH_2O$ are widely distributed objects of study in the geochemistry of uranium, in the development of processes for its extraction from natural raw material, and in the processing of uranium-containing waste.

N G Chernorukov, N V Karyakin Lobachevskii Nizhnii Novgorod State University, prosp. Gagarina 23, 603600 Nizhnii Novgorod, Russian Federation. Fax (7-831) 235 64 80. Tel. (7-831) 265 76 06 (N G Chernorukov)

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For the successful practical utilisation of the compounds $M^IP(As)UO_6 \cdot nH_2O$, it is necessary to have scientific information about the characteristics of their structure, their properties which depend on their physical state, and the energy characteristics of the chemical reactions and processes involving them. The foregoing suggests that a combined physicochemical study of the compounds $M^IP(As)UO_6 \cdot nH_2O$ is of current interest and desirable.

II. Discovery of the compounds $M^IP(As)UO_6 \cdot nH_2O$

The main element determining the nature of the structure of the compounds $M^IP(As)UO_6 \cdot nH_2O$ is uranium(VI). The crystal structures of compounds of uranium(VI) are on the whole determined by its pronounced tendency to form the O⩲U⩲O structural motif with two extremely strong and axially disposed uranium–oxygen bonds with increased [substantial? (Ed. of Translation)] multiplicity. This structural element is referred to as the uranyl group. The presence of the uranyl group in a compound usually gives rise to a layered structure.[1,2] The other elements — phosphorus, arsenic, and the alkali metal — have less influence on the overall structure. They perform a subsidiary function, 'building up' the structure of the compound and making it electrically neutral. The complex compounds containing uranium(VI) have therefore come to be referred to as the uranium compounds.

Information about the compounds $M^IPUO_6 \cdot nH_2O$ first appeared in the literature at the beginning of the XIXth century. The first studies have been reviewed in two publications.[3,4] These and other investigations (for example, those of Linau[5] and Rimbach[6]), carried out in France and Germany towards the beginning of the XXth century, were descriptive in character and contained no data about any kind of physicochemical measurements.

Scientific interest in the compound $M^IP(As)UO_6 \cdot nH_2O$ was not renewed until the 1930s–1940s in connection with the development of nuclear power. The enormous interest in uranium as a strategic raw material led to a vigorous search during these years for uranium deposits throughout the world. The study of uranium minerals showed that among them there are more than 20 varieties of the so-called phosphate and arsenate mica-like materials having the composition $M^m_{1/m}P(As)UO_6 \cdot nH_2O$, where $M^m_{1/m}$ are univalent or divalent elements.[2,7–14] $HPUO_6 \cdot 4H_2O$ (hydroautunite), $HAsUO_6 \cdot 4H_2O$

(hydrouranospinite), $NaPUO_6 \cdot 3H_2O$ (sodium autunite), $NaAsUO_6 \cdot 3H_2O$ (elvailerite), $KPUO_6 \cdot 3H_2O$ (metaankoleite), and $KAsUO_6 \cdot 3H_2O$ (abernathyite) have been found among the uranium mica-like materials. The corresponding rubidium and caesium compounds have not been found in nature. Naturally, the crude mineral material does not contain the pure individual phases but solid solutions, isomorphously substituted mixtures, and mechanical mixtures with other minerals, i.e. compositions with defective structures.

In order to determine the structure and to investigate the physicochemical characteristics, the compounds $M^IP(As)UO_6 \cdot nH_2O$ with M^I = H, Na, K, or NH_4 have been synthesised. The methods of synthesis, the conditions for isolation from solution, the solubilities, the dehydration conditions, and other properties of the compounds of the elements listed above have been discussed.[3,4,13,15-27] The studies published in the 1950s–1960s are extremely contradictory and approximate and refer solely to uranium(VI) phosphate derivatives.

The next period in the study of the properties of the compounds $M^IP(As)UO_6 \cdot nH_2O$ began in the 1970s and has continued to this day. It is difficult to establish who was the first to note the high proton conductivity of $HPUO_6 \cdot nH_2O$. Most probably this was done simultaneously by different investigators.[26,28,29] The conductivity of $HPUO_6 \cdot nH_2O$, which is 0.2 Ω^{-1} cm^{-1} at 90 °C, proved to be much higher than in the solid proton-containing materials known at the time.[26,29-31] The low solubility, corrosion stability, the ease of mechanical treatment, and the fairly high thermal stability, which are characteristic of crystalline $HPUO_6 \cdot 4H_2O$, make it an extremely promising electrolyte in autonomous electrochemical energy sources. These studies initiated more detailed structural investigations employing different physical methods and aroused interest in the arsenate derivatives of uranium(VI) and alkali metals having similar compositions and structures. In the 1980s, the number of studies devoted to the proton conductivity of $HP(As)UO_6 \cdot 4H_2O$ increased in an avalanche-like fashion. However, because this aspect is outside the scope of the problem with which we are concerned we shall confine ourselves here merely to presenting a brief bibliography[32-44] of the descriptions of the electrophysical properties of the compounds $M^IP(As)UO_6 \cdot nH_2O$. We shall note only that, together with the use in electrochemical energy sources,[44] reports have appeared on the employment of $HP(As)UO_6 \cdot 4H_2O$ as a sensor for the detection of protons,[38] in a solid-state electrochromic display,[40] and in luminescent materials.[45]

Towards the beginning of the 1990s, reports concerning the application of the compounds $M^IM^VUO_6 \cdot nH_2O$, where M^V = vanadium, niobium, tantalum, or antimony, for the fixation of ecologically dangerous radionuclides in order to immobilise them in the human habitat, began to appear.[35,36,46-50]

At the same time, studies were published[52,53] in which it was shown that neptunium(VI), plutonium(VI), and americium(VI) can replace uranium(VI),[51] whilst the lanthanides(III) and the actinides(III) can replace M^I in the compounds $M^IP(As)UO_6 \cdot nH_2O$. Natural and synthetic compounds having the composition $M^{II}_{0.5}P(As)UO_6 \cdot nH_2O$, where M^{II} = an alkaline earth metal or other divalent element, are also known.[54-57]

Comparison of the structural characteristics of the compounds $M^m_{1/m}P(As)UO_6 \cdot nH_2O$, where M^m represents univalent, divalent, or trivalent elements, on the one hand, and the compounds $M^n_{1/n}M^VM^{VI}O_6W \cdot nH_2O$, where M^V = vanadium, niobium, tantalum, or antimony and M^{VI} = neptunium, plutonium, or americium, on the other, showed that all the compounds have a layer structure and probably tend to form mixed crystals. This indicates the possibility of their employment for the retention of a wide range of radionuclides in different valence states in the form of a single thermally and chemically stable crystalline matrix.[52-57]

III. The structure of the compounds $M^IP(As)UO_6 \cdot nH_2O$

Numerous studies have been devoted to problems of the structure of the compounds $M^IP(As)UO_6 \cdot nH_2O$.[2,13,30,51,58-67] However, the functional composition of the compounds is treated in different ways by different investigators. In most reports, the phosphates and arsenates of uranium(VI) and univalent elements are regarded as double salts — disubstituted uranyl phosphates and arsenates having the compositions $UO_2M^IPO_4 \cdot nH_2O$ and $UO_2M^IAsO_4 \cdot nH_2O$. Such representation of the formula unit presupposes the existence of an anionic sublattice, made up of phosphate or arsenate tetrahedra, and a cationic sublattice, the sites of which contain the uranyl groups and the cations of the univalent element. However, such representation of the compounds is more a result of the tradition established by mineralogists in relation to uranium(VI) minerals[2] rather than reflecting the true situation corresponding to the experimental facts.

According to X-ray diffraction data, the uranium in the compound $UO_2HPO_4 \cdot 4H_2O$ [30] is in an octahedral environment comprising oxygen atoms, two of which actually form shortened O⋯U⋯O linkages with an increased multiplicity along one of the fourfold axes and these have in fact been interpreted as isolated uranyl groups UO_2^{2+}. However, the remaining four uranium–oxygen bonds in the octahedron are also distinguished by an appreciable strength and do not permit the isolation of the uranyl group without the disruption of the structure as a whole.

From our point of view, which is shared also by other investigators (see, for example, Weigel and Hoffman[51]), the compounds under consideration should be regarded as salts of phosphouranic and arsenouranic acids $M^IP(As)UO_6 \cdot nH_2O$. In these compounds, phosphorus and uranium or arsenic and uranium form a common anionic framework in the form of two-dimensional layers of the type $[P(As)UO_6]^{n-}_{2\infty}$ distinguished by an increased stability. The cations binding the layers play an appreciably smaller role in the formation of the crystal structure as a whole. They merely promote the imposition of a certain order in the interlayer space, ordering the disposition of the H_2O molecules and regulating their number.

The compounds $M^IP(As)UO_6 \cdot nH_2O$ can hardly be regarded as complex uranium(VI) oxides, because according to current ideas,[68] the cationic and anionic sublattices can be fairly readily isolated in their structures. Such separation is usually difficult in the structure of a complex oxide. Thus the most correct representation of the formula unit in the compounds under consideration is $M^IP(As)UO_6 \cdot nH_2O$, since it reflects most satisfactorily their functional properties and structural characteristics.

Direct structural studies on the compounds $M^IP(As)UO_6 \cdot nH_2O$ by X-ray diffraction and neutron diffractometric methods have been carried out in relation to the $HPUO_6 \cdot 4H_2O$,[30] $HAsUO_6 \cdot 4H_2O$,[60] $LiAsUO_6 \cdot 4H_2O$,[62] $KPUO_6 \cdot 3H_2O$,[61] and $KAsUO_6 \cdot 3H_2O$ [13] single crystals. Analysis of these data showed that the phosphouranic and arsenouranic acids are full structural analogues. As an illustration, Fig. 1 presents the crystal structure of $HPUO_6 \cdot 4H_2O$ in projection onto the 100 and 001 crystallographic planes.[30] According to these data, the structure is of the typical layered type. The uranium(VI) ions are located in an octahedral environment comprising oxygen atoms, two of which form shortened O⋯U⋯O linkages along an axis perpendicular to the $[P(As)UO_6]^{n-}_{2\infty}$ layer. The remaining four oxygen atoms belong to four different tetrahedral phosphate or arsenate groups. Water molecules, linked to one another by hydrogen bonds to form squares, the planes of which are parallel to the plane of the layer, are located between the layers. The centres of the squares are located on axes passing through the 'uranyl' groups. The protons compensating for the negative charge of the layer are located between two nearest water molecules belonging to neighbouring squares. Thus only two water molecules are linked

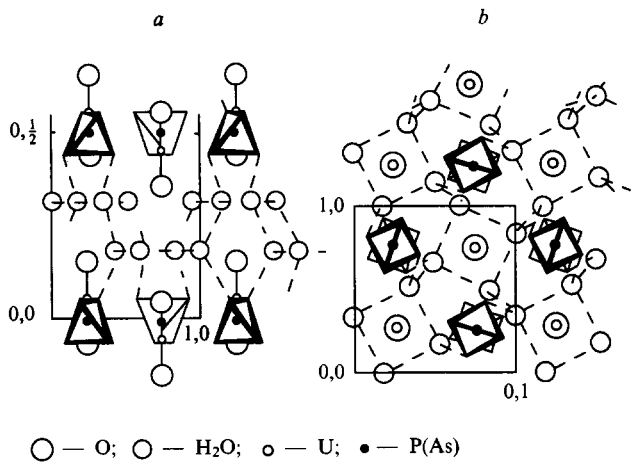


Figure 1. The crystal structure of the compound $HPUO_6 \cdot 4H_2O$ in projection onto the 100 (*a*) and 001 (*b*) planes.

to protons, forming the hydroxonium ions $H_5O_2^+$. Comparison of the crystal structures of the acids $HPUO_6 \cdot 4H_2O$ and $HAsUO_6 \cdot 4H_2O$ as well as the salts $LiAsUO_6 \cdot 4H_2O$, $KPUO_6 \cdot 3H_2O$, and $KAsUO_6 \cdot 3H_2O$ shows that both the hydrogen and salt forms have similar structures of the $[P(As)UO_6]^{n-}_{\infty\infty}$ two-dimensional layer. The differences are manifested only in the positions of the alkali metal cations and the proton. Thus, when the proton is replaced by a lithium ion, no changes are observed in the structure and the number of water molecules is also retained. However, in the case of the larger K^+ ions, the H^+ or Li^+ positions become inaccessible. Therefore, when H^+ is replaced by K^+, the hydroxonium ion H_3O^+ is displaced from the structure and the K^+ cation occupies the position of one of the water molecules. As a result, the potassium salt contains one H_2O molecule less. This substitution mechanism probably operates also in the case of the sodium and rubidium compounds. However, direct structural studies on the above crystal phases have not been carried out. There are only numerous results of X-ray phase analysis and of the indexing of the X-ray diffraction powder patterns comprising the phospho- and arseno-uranate derivatives of hydrogen, lithium, sodium, potassium, and rubidium. The contradictory and ambiguous nature of the available results may be judged by analysing the crystallographic characteristics presented in Table 1 and calculated by different workers. The uncertainty in the available information applies both to the choice of the crystal system and symmetry space group and to the determination of the number of water molecules per formula unit of the compound. There is no information whatever in the literature about the composition and structure of the caesium derivatives.

The X-ray diffraction studies carried out on the $HPUO_6 \cdot 4H_2O$ and $HAsUO_6 \cdot 4H_2O$ single crystals at the beginning of the 1980s elucidated to a large extent the nature and position of the water in the above compounds. During the preceding period, frequent attempts were made to investigate the nature of the water in $M^IP(As)UO_6 \cdot nH_2O$ by means of other methods. One of the early publications[69] describes a simplified treatment of the IR spectra of $HPUO_6 \cdot 4H_2O$, in which bands belonging to the 'uranyl' group were differentiated. Another communication[70] gives a fuller description of the state of water based on the analysis of the IR spectra and it is concluded that the hydroxonium ion $H_9O_4^+$ is present in the $HPUO_6 \cdot 4H_2O$ structure. Kobets et al.,[28] who noted that the proton is localised in the hydroxonium ion, arrived at the same conclusion. It is noteworthy that this was an incorrect conclusion, because the IR spectra quoted in the above communications contained the band due to the deformation vibrations of H_2O in the region of 1625 cm^{-1}. This band shows that a proportion of the water does not belong to hydroxonium ions. Subsequent direct structural studies showed that only two out of the four water molecules are involved in the interaction with the proton, affording a hydroxonium ion of the type $H_5O_2^+$.[60]

Thus one may conclude that the characteristics of the structure and the state of the water molecules in $M^IP(As)UO_6 \cdot nH_2O$ have been established reliably only for a small number of compounds, namely for $HPUO_6 \cdot 4H_2O$, $HAsUO_6 \cdot 4H_2O$, $LiAsUO_6 \cdot 4H_2O$, $KPUO_6 \cdot 3H_2O$, and $KAsUO_6 \cdot 3H_2O$. Only X-ray phase analysis has been carried out for the compounds $NaP(As)UO_6 \cdot 3H_2O$ and $RbP(As)UO_6 \cdot \cdot 3H_2O$, indicating that they may belong to a single structural type. The analogous caesium compounds have not been investigated and there are no reports in the literature about their structure.

Studies on the structures of the crystalline phases of $HPUO_6 \cdot 4H_2O$, $HAsUO_6 \cdot 4H_2O$, and their derivatives with all the alkali metals (including the caesium derivatives which we obtained), carried out at the beginning of the 1990s (Tables 2 and 3), indicate that the X-ray diffraction patterns of all the compounds contain similar sets of reflection maxima with similar p ɔsitions and relative intensities. Lower relative intensities of a series of diffraction peaks and a reduction in the number of the latter have been observed only in the case of $CsPUO_6 \cdot 3H_2O$ and $CsAsUO_6 \cdot 3H_2O$. These findings may be a consequence of the steric strain arising in the crystal lattices after the incorporation in the latter of the large caesium ions.

Table 1. Crystallographic characteristics of the compounds $M^IP(As)UO_6 \cdot nH_2O$ with a tetragonal crystal system.

Compound	Space group	Unit cell parameters/Å		Z	Ref.	Compound	Space group	Unit cell parameters/Å		Z	Ref.
		a	*c*					*a*	*c*		
α-$HPUO_6 \cdot 4H_2O$	*P4/ncc*	6.995	17.491	4	30	$HAsUO_6 \cdot 4H_2O$	*P4/ncc*	7.153	17.607	–	67
$HPUO_6 \cdot 4H_2O$	*P4/ncc*	6.979	17.465	4	67	$HAsUO_6 \cdot 4H_2O$	–	7.12	8.77	2	51
$HPUO_6 \cdot 4H_2O$	*P4/ncc*	6.973	17.414	–	45	$HAsUO_6 \cdot 4H_2O$	–	7.157	17.612	–	45
$LiPUO_6 \cdot 4H_2O$	–	6.93	9.07	2	51	$LiAsUO_6 \cdot 4H_2O$	*P4/n*	7.097	9.190	2	62
$NaPUO_6 \cdot 3H_2O$	–	7.00	8.72	2	51	$LiAsUO_6 \cdot 4H_2O$	–	7.13	9.21	2	51
$NaPUO_6 \cdot (3-4)H_2O$	–	6.97	8.69	1	51	$NaAsUO_6 \cdot 3H_2O$	*P4/ncc*	7.152	17.292	4	67
$NaPUO_6 \cdot 4H_2O$	–	7.04	8.46	–	51	$NaAsUO_6 \cdot 3\frac{1}{2}H_2O$	–	7.15	8.73	2	51
$KPUO_6 \cdot 3H_2O$	*P4/ncc*	6.994	17.784	4	61	$NaAsUO_6 \cdot 4H_2O$	*P4/n*	7.12	8.70	–	51
$KPUO_6 \cdot 3H_2O$	–	6.99	8.9	2	51	$KAsUO_6 \cdot 3H_2O$	*P4/ncc*	7.176	18.126	4	13
$KPUO_6 \cdot 3H_2O$	–	6.99	8.89	1	51	$KAsUO_6 \cdot 3H_2O$	*P4/n*	7.17	9.07	2	13
$KPUO_6 \cdot 3H_2O$	*P4/ncc*	6.991	17.806	4	67	$KAsUO_6 \cdot 3H_2O$	*P4/ncc*	7.163	17.846	4	67
$RbPUO_6 \cdot 3H_2O$	*P4/ncc*	7.02	18.24	4	67	$KAsUO_6 \cdot 3H_2O$	–	7.19	8.99	2	51
$HAsUO_6 \cdot 4H_2O$	*P4/nmm*	7.16	8.80	–	51	$RbAsUO_6 \cdot 3H_2O$	*P4/ncc*	7.19	17.65	4	67

Table 2. X-Ray diffraction data for the compounds $M^IPUO_6 \cdot nH_2O$.[71]

$HPUO_6 \cdot nH_2O$			$LiPUO_6 \cdot nH_2O$			$NaPUO_6 \cdot nH_2O$			*hkl*	$KPUO_6 \cdot nH_2O$			$RbPUO_6 \cdot nH_2O$			$CsPUO_6 \cdot nH_2O$			*hkl*
d_c/Å	d_e/Å	I(%)	d_c/Å	d_e/Å	I(%)	d_c/Å	d_e/Å	I(%)		d_c/Å	d_e/Å	I(%)	d_c/Å	d_e/Å	I(%)	d_c/Å	d_e/Å	I(%)	
8.720	8.672	100	9.121	9.118	100	8.577	8.588	100	002	8.915	8.974	33	9.041	9.025	71	8.814	8.801	44	002
5.451	5.438	28	5.526	5.522	31	5.409	5.405	36	102	5.494	5.505	45	5.532	5.522	30	–	–	–	102
4.938	4.941	17	4.911	4.901	23	4.928	4.914	36	110	4.933	4.928	36	4.946	4.941	36	4.953	4.955	33	110
4.297	4.301	23	4.324	4.322	38	4.273	4.270	47	112	4.317	4.311	38	4.339	4.332	45	4.318	4.32	22	112
3.698	3.700	70	3.812	3.818	77	3.652	3.655	81	104	3.756	3.754	100	3.793	3.801	100	3.730	3.731	100	104
3.492	3.243	35	3.245	3.243	51	3.228	3.226	51	202	3.249	3.249	73	3.262	3.261	98	3.255	3.255	67	202
2.940	2.940	17	2.940	2.940	34	2.929	2.931	29	212	2.945	2.945	55	2.945	2.954	54	2.952	2.954	22	212
2.684	2.683	28	2.785	2.784	31	2.645	2.644	24	106	2.732	2.734	31	–	–	–	–	–	–	106
2.539	2.539	11	2.567	2.567	15	–	–	–	214	–	–	–	2.574	2.578	18	–	–	–	116
2.505	2.505	7	–	–	–	–	–	–	116	–	–	–	2.473	2.475	18	–	–	–	220
2.376	2.374	9	2.371	2.374	22	–	–	–	222	2.377	2.377	36	2.385	2.386	30	–	–	–	222
2.208	2.206	9	2.1967	2.198	28	2.204	2.204	24	310	2.206	2.209	31	2.212	2.214	36	–	–	–	310
2.141	2.141	7	–	–	–	2.134	2.134	21	312	2.142	2.146	45	–	–	–	–	–	–	312
2.128	2.129	21	2.173	2.173	29	–	–	–	216	–	–	–	2.151	2.151	36	–	–	–	108
2.081	2.080	10	–	–	–	–	–	–	108	2.062	2.062	27	–	–	–	–	–	–	304
2.054	2.053	11	–	–	–	–	–	–	304	1.831	1.831	17	–	–	–	–	–	–	306
1.1994	1.994	11	–	–	–	–	–	–	118										
–	–	–	1.842	1.841	17	–	–	–	306										
1.788	1.787	7	–	–	–	–	–	–	218										
1.746	1.746	7	–	–	–	–	–	–	400										
1.644	1.645	14	–	–	–	–	–	–	1.1.10										

Note. The following notation has been adopted: d_c and d_e are the calculated and experimental interplanar spacings and I is the relative intensity.

Table 3. X-Ray diffraction data for the compounds $M^IAsUO_6 \cdot nH_2O$.[72]

$HAsUO_6 \cdot nH_2O$			$LiAsUO_6 \cdot nH_2O$			$NaAsPUO_6 \cdot nH_2O$			*hkl*	$KAsUO_6 \cdot nH_2O$			$RbAsUO_6 \cdot nH_2O$			$CsAsUO_6 \cdot nH_2O$			*hkl*
d_c/Å	d_e/Å	I(%)	d_c/Å	d_e/Å	I(%)	d_c/Å	d_e/Å	I(%)		d_c/Å	d_e/Å	I(%)	d_c/Å	d_e/Å	I(%)	d_c/Å	d_e/Å	I(%)	
8.797	8.801	100	8.904	8.845	100	8.560	8.547	100	002	9.069	8.845	100	8.797	8.715	100	9.187	8.801	100	002
5.544	5.539	25	5.575	5.574	7	5.484	5.488	10	102	5.625	5.574	9	5.562	5.556	7	–	–	–	102
5.049	5.039	12	5.055	5.039	5	5.050	5.049	5	110	5.072	5.071	4	5.076	5.007	5	–	–	–	110
4.379	4.385	22	–	–	–	–	–	–	112	4.427	4.440	22	4.397	4.396	43	4.430	4.428	80	112
–	–	–	4.452	4.439	24	4.280	4.301	22	004	3.883	3.788	22	3.750	3.746	31	3.865	3.762	33	104
3.745	3.746	53	3.779	3.778	19	3.671	3.685	36	104	3.586	3.576	7	3.589	3.590	8	3.576	3.583	13	200
3.570	3.569	22	3.575	3.576	5	3.571	3.596	10	200	–	–	–	3.324	3.326	14	–	–	–	114
3.308	3.308	34	3.317	3.314	12	3.295	3.296	14	202	3.335	3.320	9	–	–	–	3.332	3.314	20	202
3.001	2.998	16	3.009	3.010	5	2.993	2.993	5	212	–	–	–	3.016	3.013	8	–	–	–	212
2.772	2.771	6	2.787	2.789	5	–	–	–	204	2.023	2.003	4	–	–	–	–	–	–	006
2.713	2.710	16	–	–	–	2.650	2.663	13	106	2.786	2.743	9	2.715	2.718	10	–	–	–	106
2.584	2.662	9	–	–	–	2.560	2.560	5	214	2.597	2.596	4	2.539	2.543	8	–	–	–	116
–	–	–	2.559	2.560	5	–	–	–	116	2.536	2.537	4	–	–	–	–	–	–	220
2.524	2.529	14	–	–	–	2.525	2.527	5	220	–	–	–	2.439	2.442	5	–	–	–	22
2.426	2.426	11	2.432	2.433	6	–	–	–	222	–	–	–	–	–	–	2.221	2.219	33	303
2.199	2.196	12	2.226	2.225	31	2.484	2.151	12	008	–	–	–	2.199	2.201	32	–	–	–	008
2.160	2.161	12	2.175	2.176	7	–	–	–	216	–	–	–	2.165	2.163	10	–	–	–	216
2.093	2.017	16	2.037	2.040	12	1.940	1.918	10	118	2.162	2.176	5	2.103	2.103	8	–	–	–	108
–	–	–	1.781	1.780	7	–	–	–	0.0.10	–	–	–	2.018	2.019	10	–	–	–	118
1.661	1.661	12	1.680	1.681	10	–	–	–	1.1.10	2.029	2.040	9	–	–	–	2.029	2.032	15	314
1.578	1.576	16	–	–	–	–	–	–	2.0.10	1.814	1.812	4	–	–	–	–	–	–	0.0.10
										–	–	–	1.662	1.665	11	–	–	–	1.1.10
										–	–	–	1.580	1.581	7	–	–	–	2.0.10

The analytical indexing of the X-ray powder diffraction patterns presented in Table 4 shows that all the compounds have similar structures and have close unit cell parameters. Analysis of the IR spectra permits a fuller interpretation of the structures of the test compounds. The number of absorption bands, their positions, and their relative intensities are similar in the spectra of all the compounds in each of the series of phosphates and arsenates of the uranium derivatives. They confirm not only the structural similarity but also the similar functional composition and the identical nature of the distortion in the compounds of the principal coordination tetrahedra of phosphorus and arsenic (tetrahedra), uranium(VI) (octahedron), and the alkali metal. The assignment of the absorption bands in the spectra of the compounds $M^IPUO_6 \cdot nH_2O$ and $M^IAsUO_6 \cdot nH_2O$ is presented in Tables 5 and 6. The partial superposition of the stretching vibrations of the arsenate tetrahedron and of the shortened U⋯O⋯U linkages of the UO_6 octahedron in the 800–900 cm^{-1} region does not hinder their assignment because of their highly characteristic nature.

Table 4. The tetragonal unit cell parameters of the compounds $M^IP(As)UO_6 \cdot nH_2O$ (space group $P4/ncc$, $Z = 4$).[71,72]

Compound	a/Å	c/Å
$HPUO_6 \cdot 4H_2O$	6.984 ± 0.001	17.440 ± 0.004
$LiPUO_6 \cdot 4H_2O$	6.945 ± 0.002	18.242 ± 0.013
$NaPUO_6 \cdot 3H_2O$	6.949 ± 0.001	17.154 ± 0.007
$KPUO_6 \cdot 3H_2O$	6.977 ± 0.002	17.829 ± 0.010
$RbPUO_6 \cdot 3H_2O$	6.994 ± 0.002	18.083 ± 0.011
$CsPUO_6 \cdot 3H_2O$	7.005 ± 0.003	17.629 ± 0.014
$HAsUO_6 \cdot 4H_2O$	7.140 ± 0.002	17.594 ± 0.007
$LiAsUO_6 \cdot 4H_2O$	7.149 ± 0.006	17.808 ± 0.012
$NaAsUO_6 \cdot 3H_2O$	7.142 ± 0.002	17.119 ± 0.009
$KAsUO_6 \cdot 3H_2O$	7.172 ± 0.008	18.138 ± 0.042
$RbAsUO_6 \cdot 3H_2O$	7.178 ± 0.005	17.594 ± 0.018
$CsAsUO_6 \cdot 3H_2O$	7.151 ± 0.031	18.374 ± 0.080

The characteristic vibrations of the water of crystallisation can be distinguished in the spectra. The most striking feature is the separation into components of the ν_2 deformation vibration bands of water in the $HPUO_6 \cdot 4H_2O$ and $HAsUO_6 \cdot 4H_2O$ spectra. The ν_2 vibration of water in the $HPUO_6 \cdot 4H_2O$ spectrum at 1637 cm^{-1} is accompanied by a band with an intensity equal to that of the band at 1737 cm^{-1} corresponding to the deformation vibrations of the hydroxonium ion.[74] A similar separation of the ν_2 vibrations into bands at 1626 and 1737 cm^{-1} occurs in the $HAsUO_6 \cdot 4H_2O$ spectrum. The ν_2 doublets with comparable relative intensities permit the assumption that two water molecules form the hydroxonium ion $H_5O_2^+$, while the remaining water molecules retain their molecular individuality.[73]

The ν_2 vibrations of water in the IR spectra of $LiPUO_6 \cdot 4H_2O$ and $LiAsUO_6 \cdot 4H_2O$ are also represented by doublets at 1635 and 1675 cm^{-1} for the first compound and at 1614 and 1659 cm^{-1} for the second. The appearance of the doublets is a consequence of the nonuniformity of the water molecules in the lithium compounds and indicates the isolation of part of the water in the form of complex ions of the type $(H_2OLiOH_2)^+$ owing to the formation of the familiar Li bond. Thus the small size of the H^+ and Li^+ ions and their high electrostatic fields are the cause of the increased content of water molecules in the $HP(As)UO_6 \cdot 4H_2O$ and $LiP(As)UO_6 \cdot 4H_2O$ crystal lattices and are responsible for the incorporation of water molecules in the hydroxonium and 'lyonium' ions. The ν_2 deformation vibration bands of H_2O at 1600 cm^{-1} in the sodium, potassium, rubidium, and caesium compounds indicate the typically molecular form of water.

The ν_1 and ν_3 stretching vibrations of water in the region of 3400 cm^{-1} are not resolved in the spectra of any of the test compounds. They are represented in a broad band due to the presence of branched hydrogen bonds between the molecules of water of crystallisation.

The Cs^+ ions, among alkali metals, are characterised by the highest crystal-chemical radius and an extremely weak force field. Because of this, the X-ray diffraction patterns of the compounds $CsPUO_6 \cdot 3H_2O$ and $CsAsUO_6 \cdot 3H_2O$ reveal the disappearance of a series of diffraction peaks due to steric causes, indicating a degree of structural disorder.

Thus all the compounds considered with the composition $M^IP(As)UO_6 \cdot nH_2O$, where $M^I = H^+$, Li^+, Na^+, K^+, Rb^+, or Cs^+, are individual crystalline phases belonging to a single structural type. The composition of the coordination polyhedra of their structural-forming elements is based on the same principle and they differ from one another only in the number of molecules of water of crystallisation.

Table 5. Frequency assignments in the IR spectra of $M^IPUO_6 \cdot nH_2O$.[71]

Assignment	Vibration frequencies/cm^{-1}					
	$HPUO_6 \cdot nH_2O$	$LiPUO_6 \cdot nH_2O$	$NaPUO_6 \cdot nH_2O$	$KPUO_6 \cdot nH_2O$	$RbPUO_6 \cdot nH_2O$	$CsPUO_6 \cdot nH_2O$
$\nu(H_2O)$	3350 m	3390 m	3400 m	3440 m	3440 m	3390 m
$\delta(H_2O)$	1637 m	1675 m	1633 m	1640 m	1603 m	1645 m
		1635 m				
$\delta(H_3O^+)$	1737 m					
$\nu(PO_4)$	1090 w	1106 w	1103 w	1107 w	1106 w	1104 w
	985 s	993 s	997 s	997 s	997 s	993 s
$\delta(PO_4)$	600 w	610 w	610 w	590 w	590 w	590 w
$\nu(U{=}O)$	907 s	905 s	903 s	903 s	897 s	900 s
	809 w	800 w	803 w	800 w	783 w	803 w

Note. s = intense (strong), m = moderate, w = weak.

Table 6. Frequency assignments in the IR spectra of $M^IAsUO_6 \cdot nH_2O$.[72]

Assignment	Vibration frequencies/cm^{-1}					
	$HAsUO_5 \cdot nH_2O$	$LiAsUO_5 \cdot nH_2O$	$NaAsUO_5 \cdot nH_2O$	$KAsUO_5 \cdot nH_2O$	$RbAsUO_5 \cdot nH_2O$	$CsAsUO_5 \cdot nH_2O$
$\nu(H_2O)$	3350 m	3425 m	3395 m	3420 m	3400 m	3395 m
$\delta(H_2O)$	1626 m	1659 m	1626 m	1621 m	1618 m	1626 m
		1614 m				
$\delta(H_3O^+)$	1737 m					
$\nu(AsO_4)$	895 w	889 w	886 w	885 w	881 w	885 w
	803 s	805 s	802 s	805 s	804 s	802 s
$\delta(AsO_4)$	451 m	453 m	445 m	453 m	447 m	449 m
$\nu(U{=}U)$	916 m	918 m	917 m	919 m	921 m	919 m

IV. Thermographic study of the compounds $M^IP(As)UO_6 \cdot nH_2O$

The presence of water of crystallisation is responsible for important properties of the compounds $M^IP(As)UO_6 \cdot nH_2O$ with a layered structure. The capacity of compounds of this kind for hydration has two characteristic features: the unequal water contents for different alkali metals and the different nature of the water in the compounds under consideration. The same compound from the series considered can exist in states with different susceptibilities to hydration depending on the formation conditions. The number of water molecules changes stepwise on passing from one degree of hydration to another and the nature, location, and the role of water in the structure of each hydrate differ. The stability of a particular hydrate is determined by the size of the alkali metal cation. The removal of water from compounds with different cations under conditions where the water content is the same is accompanied by energy effects of different magnitude. This is associated with the nature of the ordered arrangement of the water molecules in the structure of the compound — their bonds both with the interlayer cation and the uranium phosphate (uranium arsenate) layer and with one another. Water determines in its turn the order in the packing of the anionic uranium layers and its removal leads to a shift of the layers relative to one another. The complete removal of water can lead to maximum disorder and hence to the retention of only two-dimensional order within the limits of the anionic uranium layer.

Despite the fact that the study of the dehydration of a number of the compounds $M^IP(As)UO_6 \cdot nH_2O$ has continued for more than 30 years, information about the temperature ranges in which water is removed is contradictory. Thus according to Karpov and Ambartsumyan,[75] 3.5 water molecules per formula unit are removed from $HPUO_6 \cdot 4H_2O$ in the temperature range 30–180 °C and four water molecules are removed at 230–250 °C. On the other hand, according to Weiss et al.,[76] three water molecules are removed from $HPUO_6 \cdot 4H_2O$ at 60 °C. The removal of 2.5 water molecules from the same compound at 60–70 °C and the removal of total water at 220 °C have been reported.[77] The most complete information about the dehydration of $HPUO_6 \cdot 4H_2O$ has been presented by Kobets and coworkers.[78,79] These results are presented in Table 7.

Table 7. Characteristics of the $HPUO_6 \cdot nH_2O$.[78,79]

Compound	Dehydration temperature range/K	Number of water molecules removed	$\Delta_r H°(T)$/ kJ mol^{-1}
$UO_2HPO_4 \cdot 4H_2O$	323–353	2	51.5 ± 2.5
$UO_2HPO_4 \cdot 2H_2O$	373–388	$\frac{1}{2}$	56.5 ± 3.3
$UO_2HPO_4 \cdot 1\frac{1}{2}H_2O$	443–463	$1\frac{1}{2}$	65.3 ± 2.9
$UO_2HPO_4 \cdot H_2O$	833–873	$\frac{1}{2}$	–

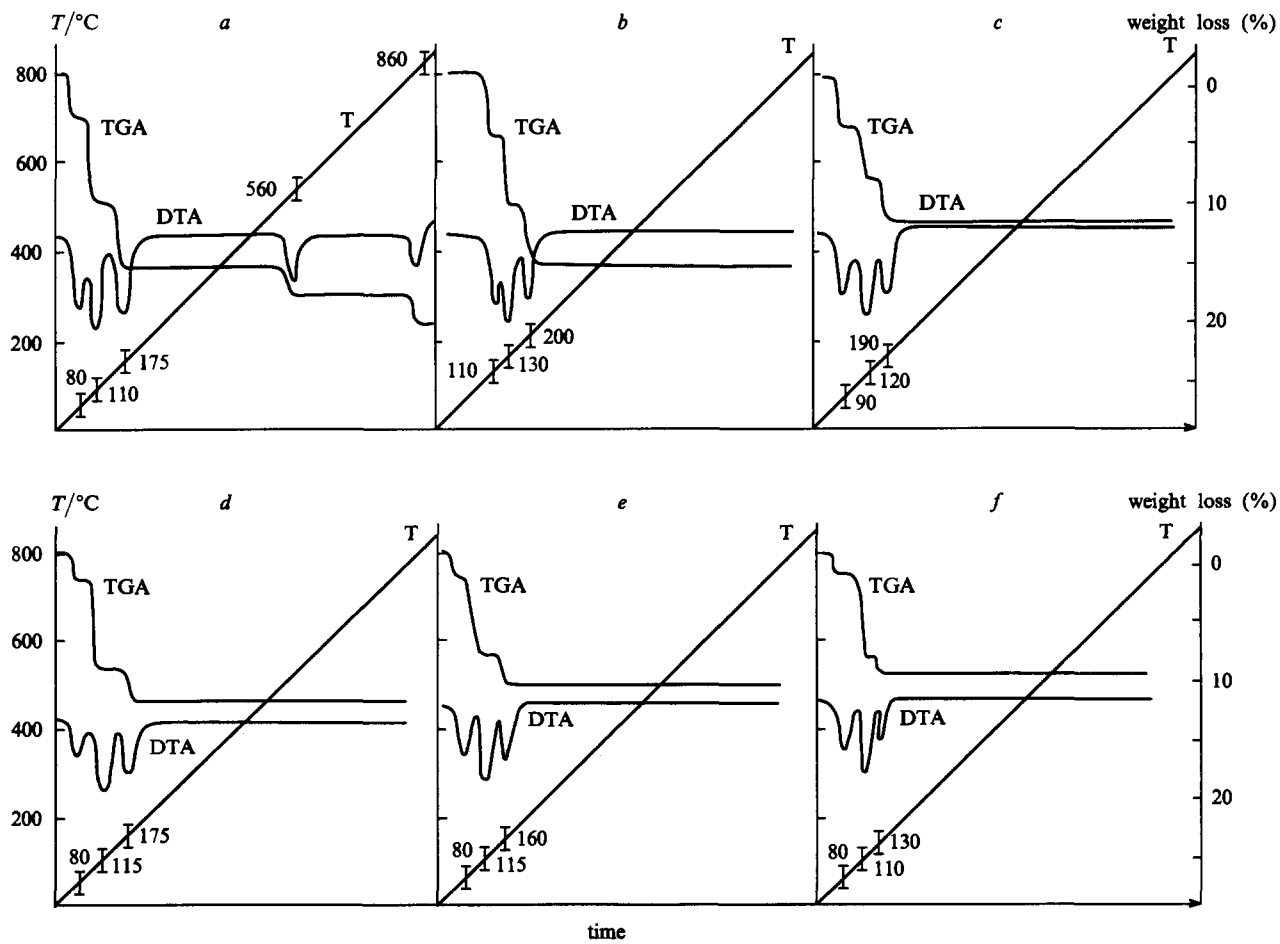


Figure 2. Derivatograms for the compounds $M^IPUO_6 \cdot nH_2O$: (*a*) $HPUO_6 \cdot 4H_2O$; (*b*) $LiPUO_6 \cdot 4H_2O$; (*c*) $NaPUO_6 \cdot 3H_2O$; (*d*) $KPUO_6 \cdot 3H_2O$; (*e*) $RbPUO_6 \cdot 3H_2O$; (*f*) $CsPUO_6 \cdot 3H_2O$.

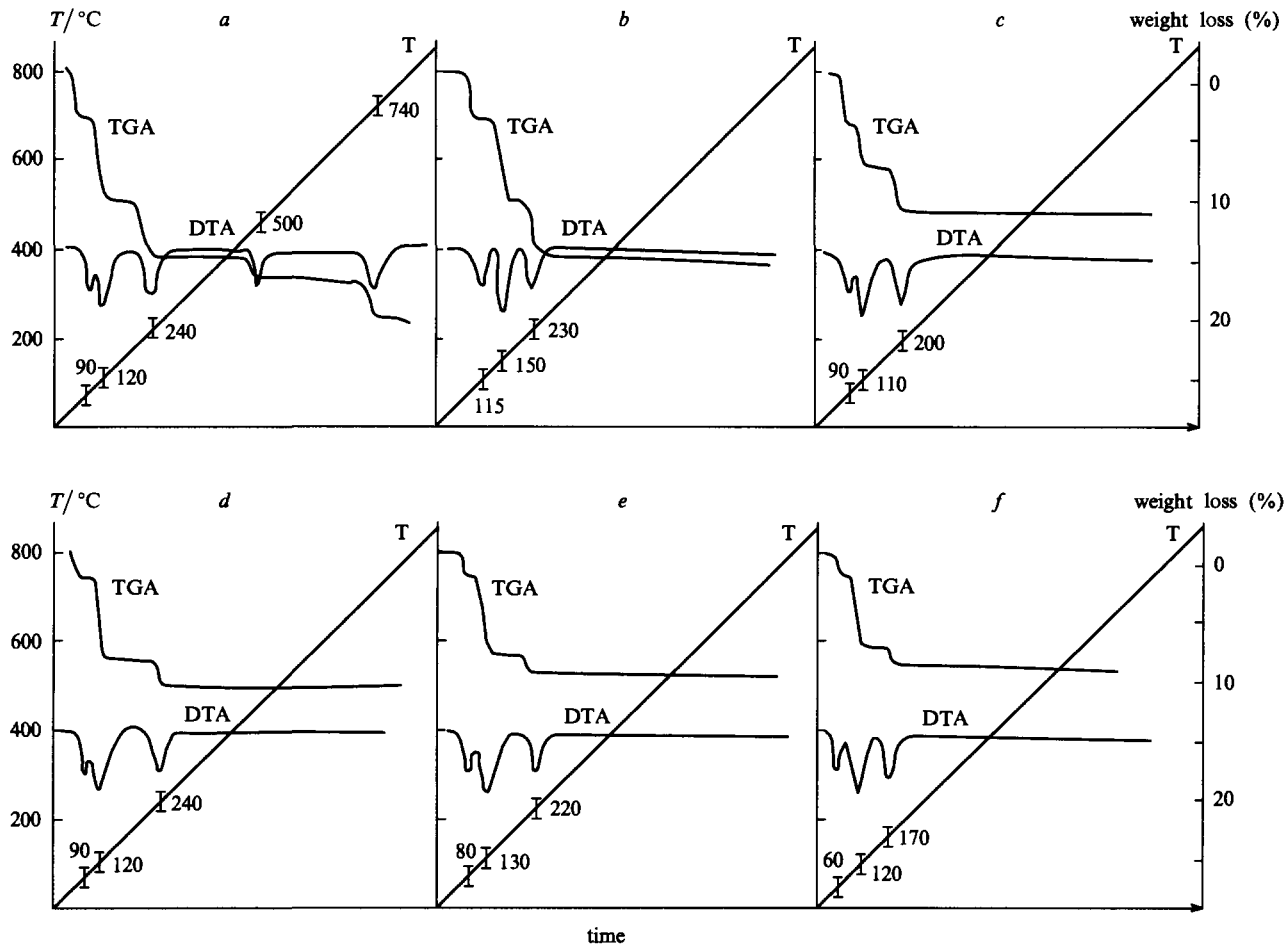


Figure 3. Derivatograms for the compounds $M^IAsUO_6 \cdot nH_2O$: (*a*) $HAsUO_6 \cdot 4H_2O$; (*b*) $LiAsUO_6 \cdot 4H_2O$; (*c*) $NaAsUO_6 \cdot 3H_2O$; (*d*) $KAsUO_6 \cdot nH_2O$; (*e*) $RbAsUO_6 \cdot 3H_2O$; (*f*) $CsAsUO_6 \cdot 3H_2O$.

The results quoted conflict with the data of other workers both as regards the temperature ranges and as regards the number of water molecules removed. However, they make it possible to estimate the enthalpy of the overall dehydration reaction of the crystalline compound $HPUO_6 \cdot 4H_2O$.

$$HPUO_6 \cdot 4H_2O \rightarrow HPUO_6(\text{solid}) + 4H_2O(\text{liq.}) \quad (1)$$

When account is taken of corrections for the enthalpy of vaporisation of water,[80] the enthalpy of the removal of four H_2O molecules calculated in terms of liquid water is $\Delta_r H^\circ_1(298) = 16.7$ kcal mol^{-1} [69.9 kJ mol^{-1}]. The soundest available information (from the scientific point of view) about the dehydration reactions of the compounds $M^IP(As)UO_6 \cdot nH_2O$ is in essence restricted to these results. One may note in addition only isolated studies, carried out at different times, on the dehydration of $LiPUO_6 \cdot 4H_2O$,[3] $NaPUO_6 \cdot 4H_2O$, $NaAsUO_6 \cdot 4H_2O$, $KPUO_6 \cdot 4H_2O$, and $KAsUO_6 \cdot 4H_2O$.[2] However, the different experimental conditions, the uncertainty in the determination of the number of water molecules in the formula units of the same compounds, and the limited number of representatives of the $M^IP(As)UO_6 \cdot nH_2O$ structural series investigated have led to the problem of their dehydration being little studied.

The thermal stability of the compounds $M^IP(As)UO_6 \cdot nH_2O$ has been studied to an even lesser extent. Identical decomposition mechanisms have been put forward only for the compound $HPUO_6 \cdot 4H_2O$ by virtually all the workers who have investigated it (see, for example, Refs 25, 59, 79, and 81). The thermal stabilities of other compounds $M^IP(As)UO_6 \cdot nH_2O$ have not been studied.

The thermographic study of the compounds $M^IP(As)UO_6 \cdot nH_2O$ which we carried out by the derivatographic method combined with X-ray phase analysis of the intermediate and final dehydration thermal decomposition products showed that the acids $HPUO_6 \cdot 4H_2O$ and $HAsUO_6 \cdot 4H_2O$ are thermally least stable.[71-73] In conformity with the derivatograms presented in Figs 2 and 3, their thermal decomposition can be represented by the following reaction:

$$HPUO_6 \cdot 4H_2O \xrightarrow[-H_2O]{80\ ^\circ C} HPUO_6 \cdot 3H_2O \xrightarrow[-2H_2O]{110\ ^\circ C}$$
$$\rightarrow HPUO_6 \cdot H_2O \xrightarrow[-H_2O]{175\ ^\circ C} HPUO_6 \xrightarrow[-\frac{1}{2}H_2O]{560\ ^\circ C}$$
$$\rightarrow \tfrac{1}{2}(UO_2)_2P_2O_7 \xrightarrow[-\frac{1}{2}O_2]{>\ 860\ ^\circ C} \tfrac{1}{2}U_2O_3P_2O_7,$$

$$HAsUO_6 \cdot 4H_2O \xrightarrow[-H_2O]{90\ ^\circ C} HAsUO_6 \cdot 3H_2O \xrightarrow[-2H_2O]{120\ ^\circ C}$$
$$\rightarrow HAsUO_6 \cdot H_2O \xrightarrow[-H_2O]{240\ ^\circ C} HAsUO_6 \xrightarrow[-\frac{1}{2}H_2O]{500\ ^\circ C}$$
$$\rightarrow \tfrac{1}{2}(UO_2)_2As_2O_7 \xrightarrow[-\frac{1}{2}O_2]{740\ ^\circ C} \tfrac{1}{2}U_2O_3As_2O_7.$$

Analysis of the above data shows that the mechanisms of the dehydration and thermal decomposition of both compounds are the same with the sole difference that water is removed from $HAsUO_6 \cdot 4H_2O$ at a higher temperature and requires a larger

energy expenditure. On the other hand, the condensation of the acid group in $HAsUO_6$ takes place with a smaller energy expenditure than in the case of $HPUO_6$. The higher temperature ranges corresponding to the dehydration of $HAsUO_6 \cdot 4H_2O$ compared with $HPUO_6 \cdot 4H_2O$, despite their analogous composition and total structural similarity, may be due to the coordinative unsaturation of the arsenic in the AsO_4 polyhedron, which results in a redistribution of the electron density in the As ← O ← H chains, strengthening the hydrogen bonds. This property of arsenic(V) is characteristic of many arsenates[82] and is manifested even in As_2O_5, in the crystal lattice of which 50% of the arsenic atoms are involved in tetrahedral coordination, whilst the remaining 50% are involved in octahedral coordination,[77] which is completely uncharacteristic of oxygen compounds of phosphorus.

The higher temperatures of the condensation of the acid phosphate groups with formation of pyrophosphates are entirely reasonable and are a consequence of the coordinative saturation of the phosphorus in the PO_4 tetrahedron, which is responsible for the stability of the latter.

The compounds $M^IP(As)UO_6 \cdot nH_2O$, where M^I = Li, Na, K, Rb, or Cs, are distinguished by a higher thermal stability compared with the corresponding acids. After the multistage removal of molecular water, they all have the composition $M^IP(As)UO_6$. However, the elimination of water molecules from the coordination environment of the alkali metal cation leads to the disruption of the coordination polyhedron of the latter and to the breakdown of the structure of the compounds as a whole. The dehydration reactions of $M^IPUO_6 \cdot nH_2O$ and $M^IAsUO_6 \cdot nH_2O$ are presented below (Scheme 1).

Several trends are manifested in the dehydration reactions of the compounds $M^I(P)AsUO_6 \cdot nH_2O$, where M^I = H, Li, Na, K, Rb, or Cs, presented in Scheme 1. Firstly, the dehydration reactions of the phosphouranate and arsenouranate compounds of the same univalent element have the same stages. Secondly, lower temperature ranges of the dehydration reaction are characteristic of the phosphouranate derivatives, which may be a consequence of the weaker binding of water in these compounds. Thirdly, the temperature ranges of the dehydration reactions decrease on passing from lithium to caesium derivatives of both phosphouranate and arsenouranate compounds. This effect corresponds to a decrease in the enthalpies of dehydration of the alkali metal ions with increase in their size and indicates the inclusion of water molecules in the coordination environment of the univalent elements. Fourthly, the condensation of the acid groups in $HAsUO_6$ takes place with smaller energy expenditures than happens in the case of $HPUO_6$. This difference may be due to the coordinative unsaturation of the arsenic in the AsO_4 tetrahedron, which is the reason for its lower stability.

In connection with the thermal decomposition, it is necessary to consider yet another feature mentioned above. The complete dehydration of the compounds $M^IP(As)UO_6 \cdot nH_2O$ leads to their conversion into an amorphous form, i.e. to the breakdown of the long-range order and hence to the appearance of disorder in the crystal lattice. This is an extremely important feature because it involves a change in the energy state of the compounds and should influence their standard enthalpies of formation. The question arises of the reason for such conversion into an amorphous form. Direct structural studies on $KAsUO_6 \cdot 3H_2O$,[13] $KPUO_6 \cdot 3H_2O$,[61] and $LiAsUO_6 \cdot 4H_2O$ [62] single crystals have shown that the coordination environment of the alkali metal atoms includes the oxygen of the water of crystallisation. Since the oxygen atoms of the molecular water occupy the so-called crystallographic sites in the structure of the compounds, the removal of water leads to the disruption of the coordination polyhedra of the univalent elements and to the disordering of the structure as a whole. The possibility of the appearance of a new coordination environment around the alkali metal atoms is significantly hindered because the oxygen atoms present in the compounds $M^IP(As)UO_6$ now belong to the uranium octahedra and the phosphorus (arsenic) tetrahedra and are very rigidly fixed in the structure. As a result of this, instead of the stable lattice of the crystalline hydrate $M^IP(As)UO_6 \cdot nH_2O$, the less stable structure of the anhydrous compound with a highly polarised $M^{\delta+}[P(As)UO_6]^{\delta-}$ bond, similar to that which occurs in ionic melts, appears.

Scheme 1

$$LiPUO_6 \cdot 4H_2O \xrightarrow[-H_2O]{110\ ^\circ C} LiPUO_6 \cdot 3H_2O \xrightarrow[-2H_2O]{130\ ^\circ C} LiPUO_6 \cdot H_2O \xrightarrow[-H_2O]{200\ ^\circ C} LiPUO_6,$$

$$NaPUO_6 \cdot 3H_2O \xrightarrow[-H_2O]{90\ ^\circ C} NaPUO_6 \cdot 2H_2O \xrightarrow[-2H_2O]{120\ ^\circ C} NaPUO_6 \cdot H_2O \xrightarrow[-H_2O]{190\ ^\circ C} NaPUO_6,$$

$$KPUO_6 \cdot 3H_2O \xrightarrow[-\frac{1}{2}H_2O]{80\ ^\circ C} KPUO_6 \cdot 2.5H_2O \xrightarrow[-2H_2O]{115\ ^\circ C} KPUO_6 \cdot \tfrac{1}{2}H_2O \xrightarrow[-\frac{1}{2}H_2O]{175\ ^\circ C} KPUO_6,$$

$$RbPUO_6 \cdot 3H_2O \xrightarrow[-\frac{1}{2}H_2O]{80\ ^\circ C} RbPUO_6 \cdot 2.5H_2O \xrightarrow[-2H_2O]{115\ ^\circ C} RbPUO_6 \cdot \tfrac{1}{2}H_2O \xrightarrow[-\frac{1}{2}H_2O]{160\ ^\circ C} RbPUO_6,$$

$$CsPUO_6 \cdot 3H_2O \xrightarrow[-\frac{1}{2}H_2O]{80\ ^\circ C} CsPUO_6 \cdot 2.5H_2O \xrightarrow[-2H_2O]{110\ ^\circ C} CsPUO_6 \cdot \tfrac{1}{2}H_2O \xrightarrow[-\frac{1}{2}H_2O]{130\ ^\circ C} CsPUO_6,$$

$$LiAsUO_6 \cdot 4H_2O \xrightarrow[-H_2O]{115\ ^\circ C} LiAsUO_6 \cdot 3H_2O \xrightarrow[-2H_2O]{150\ ^\circ C} LiAsUO_6 \cdot H_2O \xrightarrow[-H_2O]{230\ ^\circ C} LiAsUO_6,$$

$$NaAsUO_6 \cdot 3H_2O \xrightarrow[-H_2O]{90\ ^\circ C} NaAsUO_6 \cdot 2H_2O \xrightarrow[-2H_2O]{110\ ^\circ C} NaAsUO_6 \cdot H_2O \xrightarrow[-H_2O]{200\ ^\circ C} NaAsUO_6,$$

$$KAsUO_6 \cdot 3H_2O \xrightarrow[-\frac{1}{2}H_2O]{90\ ^\circ C} KAsUO_6 \cdot 2.5H_2O \xrightarrow[-2H_2O]{120\ ^\circ C} KAsUO_6 \cdot 0.5H_2O \xrightarrow[-\frac{1}{2}H_2O]{240\ ^\circ C} KAsUO_6,$$

$$RbAsUO_6 \cdot 3H_2O \xrightarrow[-\frac{1}{2}H_2O]{80\ ^\circ C} RbAsUO_6 \cdot 2.5H_2O \xrightarrow[-2H_2O]{130\ ^\circ C} RbAsUO_6 \cdot 0.5H_2O \xrightarrow[-\frac{1}{2}H_2O]{220\ ^\circ C} RbAsUO_6,$$

$$CsAsUO_6 \cdot 3H_2O \xrightarrow[-\frac{1}{2}H_2O]{60\ ^\circ C} CsAsUO_6 \cdot 2.5H_2O \xrightarrow[-2H_2O]{120\ ^\circ C} CsAsUO_6 \cdot 0.5H_2O \xrightarrow[-\frac{1}{2}H_2O]{170\ ^\circ C} CsAsUO_6.$$

V. Thermodynamic properties of the compounds $M^IP(As)UO_6 \cdot nH_2O$

Before our investigations, there were virtually no literature data concerning the determination of the standard thermodynamic functions of formation of the compounds $M^IP(As)UO_6 \cdot nH_2O$. Attempts have been made in a number of studies[5,16,17,75,83-85] to calculate the standard Gibbs free energies of formation of a series of compounds of this type at 298.15 K ($\Delta_fG°$, kJ mol^{-1}) from the solubility products (K_s) in aqueous solutions. The calculation was based on the idea that the following equilibria exist at the precipitate $\rightleftharpoons$ solution interface:

$$HP(As)UO_6 \cdot 4H_2O\,(cryst.) \rightleftharpoons UO_2^{2+}\,(soln) + HP(As)O_4^{2-}\,(soln) + 4H_2O, \quad (2)$$

$$M^IP(As)UO_6 \cdot nH_2O\,(cryst.) \rightleftharpoons M^+(soln) + UO^{2+}(soln) + P(As)O^{3-}(soln) + nH_2O, \quad (3)$$

where M^I are alkali metals.

Bearing in mind the low concentration of ions in solution and assuming that the activity of the solid phase is unity, one can postulate that the equilibrium constants of reactions (2) and (3) are equal to the solubility products of the corresponding compounds. Then we have

$$\Delta_rG^\circ_{2,3}(298) = 298.15 \times 8.314 \times \ln K_s/J.$$

The solubility products K_s of the compounds are listed in Table 8.

Table 8. The solubility products (K_s) of certain compounds $M^IP(As)UO_6 \cdot nH_2O$.

Compound	K_s	Ref.
$HPUO_6 \cdot 4H_2O$	2.14×10^{-11}	20, 23, 27
$HAsUO_6 \cdot 4H_2O$	3.17×10^{-11}	17
$LiPUO_6 \cdot 4H_2O$	2.4×10^{-26}	3, 21
$LiAsUO_6 \cdot 4H_2O$	1.5×10^{-19}	17
$NaPUO_6 \cdot 4H_2O$	6.4×10^{-24}	21, 27
$NaAsUO_6 \cdot 3H_2O$	1.35×10^{-22}	17
$KPUO_6 \cdot 3H_2O$	8×10^{-24}	21, 23, 27
$KAsUO_6 \cdot 3H_2O$	2.25×10^{-23}	17
$RbPUO_6 \cdot 3H_2O$	1×10^{-27}	21, 27

Table 9 presents the [standard] free energies [of formation] $\Delta_fG°(298)$ for a series of compounds calculated from the following relations:

$$\Delta_fG°[298,\ HP(As)UO_6 \cdot 4H_2O,\ cryst.] = \Delta_fG°(298, UO_2^{2+}, soln) + \Delta_fG°[298, HP(As)O_4^{2-}, soln] + 4\Delta_fG°(298,\ H_2O,\ liq.) + RT\ln K_s,$$

$$\Delta_fG°[298,\ M^IP(As)UO_6 \cdot nH_2O,\ cryst.] = \Delta_fG°(298, M^{I+}, soln) + \Delta_fG°(298, UO_2^{2+}, soln) + \Delta_fG°[298, P(As)O_4^{3-}, soln] + n\Delta_fG°(298, H_2O, liq.) + RT\ln K_s.$$

Langmuir[85] calculated the standard enthalpies of formation of $NaPUO_6$ (−2536 kJ mol^{-1}) and $KPUO_6$ (−2561 kJ mol^{-1}) from $\Delta_fG°(298)$ and the standard entropy of formation evaluated by the method of contributions. It is noteworthy that these values can be regarded as only estimates. For this reason, in the subsequent sections of the review we shall deal in greater detail with the determination of the standard enthalpies of formation of the compounds $M^IP(As)UO_6 \cdot nH_2O$ and their dehydration products.†

VI. Standard enthalpies of formation of the compounds $M^IP(As)UO_6$ and their crystalline hydrates

Detailed schemes for the determination of the standard enthalpies of formation of the compounds $M^IP(As)UO_6$, where M^I = H, Li, Na, K, Rb, or Cs, and their crystalline hydrates having the general formula $M^IP(As)UO_6 \cdot nH_2O$, where n = 4 for M^I = H or Li and n = 3 for M^I = Na, K, Rb, or Cs, have been put forward.[87-96] In the present review, we shall therefore consider only the general approach to the solution of the problem in relation to the calculation of the standard enthalpies of formation $\Delta_fH°(298)$ of the compounds $M^IP(As)UO_6$, where M^I = Li, Na, K, Rb, or Cs.

The standard enthalpies of the following processes were determined in an adiabatic calorimeter:

$$[KH_2P(As)O_4\,(cryst.) + UO_3\,(cryst.) + M^INO_3\,(cryst.)] + 4HF\,(soln) \rightarrow KF\,(soln) + UO_2F_2\,(soln) + M^IF\,(soln) + H_3PO_4\,(soln) + HNO_3\,(soln) + H_2O, \quad (4)$$

$$[M^IP(As)UO_6\,(solid) + KNO_3\,(cryst.)] + 4\,HF\,(soln) \rightarrow KF\,(soln) + M^IF\,(soln) + UO_2F_2\,(soln) + H_3PO_4\,(soln) + HNO_3\,(soln). \quad (5)$$

The design of the calorimeter and its use have been described in detail.[97] The standard enthalpies of reactions (4) and (5) are presented in Table 10.

The reactant ratios in reactions (4) and (5) were constant at 1 mol of the mixture: 260 mol of HF : 800 mol of H_2O.

† We carried out these investigations in 1990-1994, but unfortunately they cannot be compared with any other data because of the lack of the latter in the literature.

Table 9. The standard Gibbs free energies of formation of the compounds $M^IP(As)UO_6$ and their crystalline hydrates of 298.15 K.

Compound	$-\Delta_fG°$/kJ mol^{-1}	Ref.	Compound	$-\Delta_fG°$/kJ mol^{-1}	Ref.
$HPUO_6$	2112	83	$HAsUO_6$	1764	17
$HPUO_6$	2109	85	$HAsUO_6 \cdot 4H_2O$	2679	a
$HPUO_6$	2090	86	$LiAsUO_6 \cdot 4H_2O$	2950	84
$HPUO_6 \cdot 4H_2O$	3052	a	$NaAsUO_6 \cdot 4H_2O$	2941	84
$LiPUO_6 \cdot 4H_2O$	3358	84	$NaAsUO_6 \cdot 3H_2O$	2703	a
$NaPUO_6 \cdot 3H_2O$	3102	84	$KAsUO_6 \cdot 4H_2O$	2961	84
$KPUO_6$	2391	83	$KAsUO_6 \cdot 3H_2O$	2728	a
$KPUO_6 \cdot 3H_2O$	3102	83	$KAsUO_6$	2021	83
$RbPUO_6 \cdot 3H_2O$	3121	a			

[a] Calculated by the authors from literature data.

Table 10. The standard enthalpies of reactions (4) and (5).[87,88,94]

M^I	$-\Delta_r H^\circ_4(298)$/kJ mol^{-1}		$-\Delta_r H^\circ_5(298)$/kJ mol^{-1}	
	phosphates	arsenates	phosphates	arsenates
Li	107.4 ± 1.1	138.5 ± 1.2	82.2 ± 0.2	129.9 ± 0.8
Na	70.8 ± 0.8	125.3 ± 1.2	39.0 ± 0.9	116.4 ± 1.3
K	64.5 ± 1.9	112.1 ± 1.6	32.8 ± 0.1	99.2 ± 0.6
Rb	61.1 ± 0.8	112.5 ± 1.4	31.0 ± 1.2	95.4 ± 0.8
Cs	58.8 ± 2.4	107.0 ± 1.0	25.2 ± 1.0	89.5 ± 1.4

When Eqn (5) is subtracted from Eqn (4), we arrive at the following process:

$$KH_2P(As)O_4\,(cryst.) + UO_3\,(cryst.) + M^INO_3\,(cryst.) \rightarrow M^IP(As)UO_6\,(solid) + KNO_3 + H_2O\,(liq.), \quad (6)$$

the standard enthalpy of which is $\Delta_r H^\circ_6(298) = \Delta_f H^\circ_4(298) - \Delta_r H^\circ_5(298)$ according to Hess's law.

On the other hand, the quantity $\Delta_r H^\circ_6(298)$ is equal to the algebraic sum of the $\Delta_r H^\circ(298)$ of all the participants in reaction (6). The standard enthalpies of formation of the compounds investigated (Table 12) can then be calculated from the quantities $\Delta_r H^\circ_6(298)$ and the literature values of the standard enthalpies of formation of the corresponding reactants (Table 11).

Table 11. The standard enthalpies of formation of the reactants in reaction (6) at 298.15 K.

Compound	$-\Delta_f H^\circ(298)$/kJ mol^{-1}	Ref.
KH_2PO_4	1567.46 ± 2.32	83, 84, 98, 102
KH_2AsO_4	1184.79 ± 1.89	83, 84, 99
UO_3	1228.3 ± 3.0	83, 84, 100, 102
H_2O	285.83 ± 0.04	98
$LiNO_3$	483.2 ± 0.5	84
$NaNO_3$	468.2 ± 0.5	84
KNO_3	494.6 ± 0.5	84
$RbNO_3$	495.1 ± 0.5	84
$CsNO_3$	505.7 ± 0.5	84

Table 12. The standard enthalpies of formation of the compounds M^IPUO_6 and M^IAsUO_6.[87,88]

Compound	$-\Delta_f H^\circ(298)$/ kJ mol^{-1}	Compound	$-\Delta_f H^\circ(298)$/ kJ mol^{-1}
$HPUO_6$	2275 ± 7	$HAsUO_6$	1868 ± 7
$LiPUO_6$	2524 ± 8	$LiAsUO_6$	2125 ± 8
$NaPUO_6$	2515 ± 8	$NaAsUO_6$	2110 ± 8
$KPUO_6$	2539 ± 7	$KAsUO_6$	2140 ± 8
$RbPUO_6$	2541 ± 8	$RbAsUO_6$	2145 ± 8
$CsPUO_6$	2555 ± 10	$CsAsUO_6$	2156 ± 9

The following additional experiments were performed in order to test the results. Firstly, the enthalpies of reactions (4) and (5) were determined for two other reactant ratios (1 mol of mixture : 130 mol of HF and 1 mol of mixture : 520 mol of HF). It was established that the enthalpies $\Delta_r H^\circ_{4,5}(298)$ are independent of the molar reactant ratio within experimental error (1.5%–3.0%). Secondly, the enthalpies of reactions (4) and (5) were determined for two acids participating in the reaction — HF and HCl. It was established that the enthalpies of reaction (6) are identical within experimental error. This is in fact the reason why the products of reactions (4) and (5) are indicated as the most probable. Their chemical nature may be different but the important feature is that they are the same in the corresponding pairs of reactions.

Analysis of the results shows that reactions (4) and (5) are exothermic (Table 10); the absolute values of $\Delta_r H^\circ_4(298)$ for both phosphorus and arsenic compounds decrease on passing from lithium to caesium. Such variation of the enthalpies of the above processes in the series of alkali metals can be accounted for as follows.

Since the participants in reaction (4) — phosphorus or arsenic derivatives — differ only in the chemical nature of the alkali metal nitrate (M^INO_3) and the alkali metal ion in solution [$M^IF(soln) \rightleftharpoons M^+ + F^-$], the changes in the overall enthalpies $\Delta_r H^\circ_4(298)$ in the direction Li → Na → K → Rb → Cs are caused by the different crystal lattice energies of M^INO_3 and the different hydration energies of the M^+ ions in solution. The first term is always positive (endothermic process), diminishing on passing from lithium to caesium. Thus the endothermicity of this stage of the overall process (4) should decrease in the direction Li → Cs. On the other hand, the hydration of the M^+ ions in aqueous solutions is an exothermic process. With increase in the ionic radius of M^+, the hydration enthalpy diminishes (the exothermicity decreases in the direction Li → Cs). The experimental data therefore permit the following conclusions: the overall enthalpy $\Delta_r H^\circ_4(298)$ is negative, because the term associated with the enthalpy of hydration of the M^+ ions in aqueous solution exceeds the energy of the disruption of the M^INO_3 crystal lattice; the decrease in the absolute enthalpy of hydration of the M^+ on passing from lithium to caesium is the decisive factor governing the decrease in the exothermicity of the overall process (4) in the same direction.

The variation of the overall enthalpies $\Delta_r H^\circ(298)$ of reactions (5) can be accounted for similarly. The reactions differ only in the chemical nature of $M^IP(As)UO_6$ and the M^+ ion in aqueous solution.

The linear variation of the enthalpies of reactions (4) and (5) with increase in the ionic radius (r) of the alkali metal or with decrease in the hydration enthalpy [$\Delta_h H^\circ(298, M^+, soln)$] of the alkali metal ion in aqueous solution can be accounted for by the same causes. The corresponding relations assume the form

$$\Delta_r H^\circ(298) = a + b(X),$$

where X is a characteristic of the alkali metal or its ion (ionic radius, enthalpy of hydration). The quantities r and $\Delta_h H^\circ$ for alkali metals are presented in Table 13 and the coefficients a and b are listed in Table 14.

The significantly lower exothermicity of reactions (4) and (5) involving the same alkali metal in phosphorus compounds compared with arsenic compounds can be explained in the following manner. As a consequence of the greater, compared with arsenic, coordinative saturation of phosphorus in the oxygen compounds, the effective charge on the alkali metal atom is lower, which leads ultimately to an increase in the K–O bond energy in KH_2PO_4 [reaction (4)] or the M^I–O bond energy in M^IPUO_6 [reaction (5)] compared with the analogous arsenic compounds. On the other hand, the higher effective charge of the AsO_4^{3-} ion compared with PO_4^{3-} is responsible for the higher energy of dehydration of the AsO_4^{3-} ion in aqueous solution. Allowance for

Table 13. The characteristics X of the alkali metal according to Glushko and Pauling.[84,101]

M^I	r/Å	$\Delta_h H^\circ(M^+)$/ kJ mol^{-1}	$\Delta_f H^\circ(M^+)$/ kJ mol^{-1}	I_1/ eV[a]
Li	0.60	534	–	–
Na	0.95	426	609.60	5.138
K	1.33	341	513.91	4.339
Rb	1.48	316	490.16	4.176
Cs	1.69	284	458.81	3.893

[a] I_1 is the first ionisation potential.

Table 14. The coefficients a and b in the equations $\Delta_r H°(298) = a + bX$ for reactions (4) and (5).[103]

X	a		b	
	phosphates	arsenates	phosphates	arsenates
Reaction (4)				
r/Å	−122.8	−154.0	41.57	28.8
$\Delta_h H°(298, M^+, soln)$/ kJ mol^{-1}	−0.90	−71.12	0.188	0.126
Reaction (5)				
r/Å	−99.31	−152.3	47.32	38.16
$\Delta_h H°(298, M^+, soln)$/ kJ mol^{-1}	39.46	−43.53	0.214	0.165

these two factors actually makes it possible to understand the greater exothermicity of reactions (4) and (5) for the same alkali metal in the case of the arsenic compounds compared with the phosphorus compounds (Table 10).

The greater stability of the M^IPUO_6 structure compared with the M^IAsUO_6 structure is manifested by the fact that the absolute values of $\Delta_f H°(298)$ for the phosphorus compounds are higher than the corresponding values for the arsenic compounds. For all the alkali metals investigated (M^I = Li, Na, K, Rb, or Cs), the difference $\Delta_f H°(298, M^IAsUO_6) - \Delta_f H°(298, M^IPUO_6) = 400 \pm 5$ kJ mol^{-1} is virtually constant.

The absolute values of $\Delta_f H°(298)$ for the phosphorus and arsenic compounds exhibit a distinct tendency to increase in the direction Na → K → Rb → Cs. The linear relations $\Delta_f H°(298) = a + bX$, where X is a characteristic of the alkali metal, have been established. The corresponding coefficients a and b are presented in Table 15.

Table 15. The coefficients in the equation $\Delta_f H°(298) = a + bX$.

X	a		b	
	phosphates	arsenates	phosphates	arsenates
r, A	−2466	−2053	52.605	−62.279
$\Delta_f H°(298, M^+, gas)$/ kJ mol^{-1}	−2668	−2294	0.252	0.302
I_1/eV	−2673	−2299	30.83	36.84

Analogous schemes have been used to calculate the standard enthalpies of formation of the crystalline compounds of the $M^IP(As)UO_6 \cdot nH_2O$ series (Table 16).

Table 16. The standard enthalpies of formation of the compounds $M^IP(As)UO_6 \cdot nH_2O$.[90,91]

Compound	$-\Delta_f H°(298)$/ kJ mol^{-1}	Compound	$-\Delta_f H°(298)$/ kJ mol^{-1}
$HPUO_6 \cdot 4H_2O$	3473 ± 8	$HAsUO_6 \cdot 4H_2O$	3086 ± 7
$LiPUO_6 \cdot 4H_2O$	3707 ± 9	$LiAsUO_6 \cdot 4H_2O$	3311 ± 8
$NaPUO_6 \cdot 3H_2O$	3392 ± 9	$NaAsUO_6 \cdot 3H_2O$	2998 ± 8
$KPUO_6 \cdot 3H_2O$	3413 ± 8	$KAsUO_6 \cdot 3H_2O$	3022 ± 8
$RbPUO_6 \cdot 3H_2O$	3412 ± 9	$RbAsUO_6 \cdot 3H_2O$	3023 ± 7
$CsPUO_6 \cdot 3H_2O$	3423 ± 11	$CsAsUO_6 \cdot 3H_2O$	3030 ± 7

For example, the enthalpies of the reactions of equimolecular mixtures of $M^IAsUO_6 \cdot nH_2O$ and potassium nitrate with an aqueous solution at HF at 298.15 K have been determined for the ratios 1 mol of the mixture : 260 mol of the HF : 800 mol of H_2O.[91]

$$[M^IAsUO_6 \cdot nH_2O(\text{cryst.}) + KNO_3(\text{cryst.})] + 4HF(\text{soln}) \rightarrow KF(\text{soln}) + M^IF(\text{soln}) + UO_2F_2(\text{soln}) + H_3P(As)O_4(\text{soln}) + HNO_3(\text{soln}) + nH_2O \quad (7)$$

Subtraction of Eqn (7) from Eqn (4) yields the process

$$KH_2AsO_4(\text{cryst.}) + UO_3(\text{cryst.}) + M^INO_3(\text{cryst.}) + (n-1)H_2O \rightarrow M^IAsUO_6 \cdot nH_2O(\text{cryst.}) + KNO_3(\text{cryst.}), \quad (8)$$

the enthalpy of which $\Delta_r H°_8(298) = \Delta_r H°_4(298) - \Delta_r H°_7(298)$. The enthalpies $\Delta_f H°(298)$ for the crystalline hydrates investigated can be calculated from the values of $\Delta_r H°_8(298)$ and the standard enthalpies of formation of the corresponding reactants (Table 10).

$$\Delta_f H°(298, M^IAsUO_6 \cdot nH_2O, \text{cryst.}) = +\Delta_r H°_8(298) + \Delta_f H°(298, KH_2AsO_4, \text{cryst.}) + \Delta_f H°(298, UO_3, \text{cryst}) + \Delta_f H°(298, M^INO_3, \text{cryst.}) + (n-1)\Delta_f H°(298, H_2O, \text{liq.}) - \Delta_f H°(298, KNO_3).$$

Analysis of the quantities presented in Table 16 permits the following conclusions: the enthalpies $\Delta_f H°(298)$ for the phosphorus derivatives are greater in absolute magnitude, as in the case of anhydrous compounds, than the corresponding values for the arsenic derivatives. For all the alkali metals investigated, the difference $\Delta_f H°[298, M^IAsUO_6(\text{cryst.})] - \Delta_f H°[298, M^IPUO_6(\text{cryst.})]$ is almost constant and equal to 393 ± 3 kJ mol^{-1}; in the series of phosphorus and arsenic derivatives, the absolute value of $\Delta_f H°$ increases in the direction Na → K → Rb → Cs; the linear relations $\Delta_f H°[298, M^IP(As)UO_6 \cdot nH_2O] = a + bX$ have been established (Table 17); in the series of the phosphorus and arsenic compounds (M^I = Na, K, Rb, Cs), the difference between the enthalpies $\Delta_f H°(298)$ for the anhydrous compounds and their crystalline hydrates $\Delta_f H°[298, M^IP(As)UO_6] - \Delta_f H°[298, M^IP(As)UO_6 \cdot 3H_2O]$ per mole of the water of crystallisation is virtually constant and equal to 293 ± 3 kJ (mol H_2O)$^{-1}$; the analogous difference in the case of the hydrogen and lithium compounds is also constant but it exceeds the above value, i.e. $\Delta_f H°[298, M^IP(As)UO_6] - \Delta_f H°[298, M^IP(As)UO_6 \cdot 4H_2O] = 300 \pm 4$ kJ (mol H_2O)$^{-1}$, which emphasises yet again the stronger binding of the water of crystallisation in the hydrogen and lithium derivatives compared with other Group I elements.

Table 17. The coefficients in the equations $\Delta_f H°[298, M^IP(As)UO_6 \cdot 3H_2O, \text{cryst.}] = a + bX$ (M^I = Na, K, Rb, Cs).

X	a		b	
	phosphates	arsenates	phosphates	arsenates
r/Å	−3355	−2959	−40.441	−43.238
$\Delta_f H°(298, M^+, gas)$/ kJ mol^{-1}	−3511	−3128	0.196	0.213
I_1/eV	−3515	−3132	23.99	25.96

1. The enthalpies of the dehydration reactions of the compounds $M^IP(As)UO_6 \cdot nH_2O$

We shall examine the methods for the determination of the enthalpies of dehydration of the test compounds in relation to the phosphorus derivatives.

The enthalpies of the reactions of M^IPUO_6 or their crystalline hydrates with an aqueous solution of hydrofluoric acid have been determined calorimetrically.

$$M^IPUO_6(\text{solid}) + 3HF(\text{soln}) \rightarrow M^IF(\text{soln}) + UO_2F_2(\text{soln}) + H_3PO_4(\text{soln}), \quad (9)$$

$$M^{I}PUO_6 \cdot nH_2O\,(cryst.) + 3HF\,(soln) \rightarrow$$
$$\rightarrow M^{I}F\,(soln) + UO_2F_2\,(soln) + H_3PO_4\,(soln) \cdot nH_2O. \quad (10)$$

Subtraction of Eqn (9) from Eqn (10) yields the dehydration process [see Eqn (1)], the enthalpy of which is equal to the difference $\Delta_r H^\circ_{10}(298) - \Delta_r H^\circ_9(298)$ (Table 18).

Table 18. The standard enthalpies of reactions (1), (7), (9), and (10) (the $\Delta_r H^\circ$ are expressed in kJ mol^{-1}).[87,90]

M^I	$-\Delta_r H^\circ_9(298)$	$-\Delta_r H^\circ_{10}(298)$	$-\Delta_r H^\circ_1(298)$	$-\Delta_r H^\circ_7(298)$
H	65.5 ± 1.0	9.63 ± 0.08	53.8 ± 1.1	–
Li	89.0 ± 0.3	49.3 ± 0.2	39.7 ± 0.5	86.9 ± 0.8
Na	77.9 ± 0.3	58.4 ± 0.6	19.5 ± 0.9	85.4 ± 1.4
K	59.7 ± 0.6	43.0 ± 0.1	16.7 ± 0.7	75.1 ± 1.2
Rb	57.8 ± 0.3	44.4 ± 0.3	13.4 ± 0.6	74.7 ± 0.5
Cs	55.8 ± 0.2	45.2 ± 0.2	10.6 ± 0.4	72.7 ± 0.5

Since all the crystalline hydrates investigated differ in the amount of water of crystallisation, Table 19 presents the enthalpies of the dehydration reactions per mole of water evolved.

The higher binding energy of the water of crystallisation in the $M^{I}AsUO_6 \cdot nH_2O$ structures compared with $M^{I}PUO_6 \cdot nH_2O$ is striking. This happens despite their analogous functional composition and complete structural similarity, including identical locations of the water molecules around the univalent element. These results are fully consistent with the thermographic determinations of the temperature ranges in the stage-by-stage and complete elimination of water from the phosphorus and arsenic compounds (see Section IV). The cause of these differences, which consists in the unequal coordination capacities of phosphorus(V) and arsenic(V), was investigated in detail by the present authors in an earlier study.

Table 19. The enthalpies of the dehydration reaction[103] $(1/n)M^{I}P(As)UO_6 \cdot nH_2O(cryst.) \rightarrow (1/n)M^{I}P(As)UO_6\,(solid) + H_2O\,(liq.)$.

Compound	$-\Delta_r H^\circ(298)$/ kJ mol^{-1}	Compound	$-\Delta_r H^\circ(298)$/ kJ mol^{-1}
$HPUO_6 \cdot 4H_2O$	13.5	$HAsUO_6 \cdot 4H_2O$	19.0
$LiPUO_6 \cdot 4H_2O$	10.0	$LiAsUO_6 \cdot 4H_2O$	11.0
$NaPUO_6 \cdot 3H_2O$	6.5	$NaAsUO_6 \cdot 3H_2O$	10.0
$KPUO_6 \cdot 3H_2O$	5.5	$KAsUO_6 \cdot 3H_2O$	8.0
$RbPUO_6 \cdot 3H_2O$	4.5	$RbAsUO_6 \cdot 3H_2O$	7.0
$CsPUO_6 \cdot 3H_2O$	3.5	$CsAsUO_6 \cdot 3H_2O$	5.5

The significantly higher energy of the dehydration of the hydrogen forms compared with their salt analogues confirms the nonequivalent nature of the water in compounds $HP(As)UO_6 \cdot 4H_2O$, which is indicated by the results of an IR spectroscopic study of these compounds (see Section III). It has also been established that the decrease in the enthalpy of dehydration of the crystalline hydrates $M^{I}P(As)UO_6 \cdot nH_2O$ in the series of alkali metal compounds is equivalent to the decrease in this series of the enthalpies of dehydration (in kJ mol^{-1}) of the ions of the corresponding elements in aqueous solution:

$$\Delta_r H^\circ(298) = [-3.5 + 0.0245\Delta_h H^\circ(298,\ M^+,\ soln) \pm 0.2];$$

for the phosphates;

$$\Delta_r H^\circ(298) = [-3.0 + 0.0305\Delta_h H^\circ(298,\ M^+,\ soln) \pm 0.2].$$

for the arsenates.

2. Enthalpies of ion-exchange reactions

The substitution of a proton in the compounds $HP(As)UO_6 \cdot 2H_2O$ by alkali metal ions constitutes the basis of the synthesis of the crystalline compounds $M^{I}P(As)UO_6 \cdot nH_2O$. Knowledge of the energy relations governing the ion-exchange reactions is therefore necessary.

The standard enthalpies of the exchange reactions

$$M^+(soln) + HP(As)UO_6 \cdot 4H_2O$$
$$\rightleftharpoons M^{I}P(As)UO_6 \cdot nH_2(cryst) + H^+(soln) + (4-n)H_2O, \quad (11)$$

were calculated from the standard enthalpies of formation of the crystalline hydrates (Table 6) and the literature values of the standard enthalpies of formation of alkali metal ions in aqueous solution. The results are presented in Table 20.

Table 20. The ionic radii and standard enthalpies of formation of alkali metal ions and the standard enthalpies of reaction (11).[96]

M^I	R/A	$-\Delta_r H^\circ(M^+)$/ kJ mol^{-1}	$\Delta_r H^\circ_{11}(298)$/kJ mol^{-1}	
			$M^{I}PUO_6 \cdot nH_2O$	$M^{I}AsUO_6 \cdot nH_2O$
Li^+	1.28	278.45 ± 0.21	44.5	54.5
Na^+	1.61	240.41 ± 0.13	35.5	42.5
K^+	2.01	252.25 ± 0.13	26.5	30.5
Rb^+	2.17	251.04 ± 0.13	26.0	28.5
Cs^+	2.42	255.56 ± 0.13	22.5	28.5

The standard enthalpies of the ion-exchange reactions presented are positive i.e. the above processes proceed with absorption of energy. The enthalpies $\Delta_r H^\circ(298)$ decrease on passing from lithium to caesium in the series of alkali metals. In order to establish the causes of such variation, we shall consider the energy relations for the ion-exchange reactions in greater detail.

The overall enthalpy of the ion-exchange reactions can be represented by the following terms:

$$\Delta_r H^\circ = \Delta H^\circ_{M^+} + \Delta \bar{H}^\circ_{M^+} + \Delta H^\circ_{H^+} + \Delta \bar{H}^\circ_{H^+} + \Delta H^\circ_{O-H}$$
$$+ \Delta H^\circ_{O-M} + \Delta H^\circ_{lat}, \quad (12)$$

where $\Delta H^\circ_{M^+}$ is the enthalpy of hydration of the M^+ ion in the crystalline $M^{I}P(As)UO_6 \cdot nH_2O$ phase, $\Delta \bar{H}^\circ_{M^+}$ is the enthalpy of dehydration of the M^+ ion in solution, $\Delta H^\circ_{H^+}$ is the enthalpy of hydration of the proton in solution, $\Delta \bar{H}^\circ_{H^+}$ is the enthalpy of dehydration of the proton in the crystalline $HP(As)UO_6 \cdot 4H_2O$ phase, ΔH°_{O-H} is the enthalpy of dissociation of the O–H bond in the crystalline $HP(As)UO_6 \cdot 4H_2O$, ΔH°_{O-M} is the enthalpy of formation of the O–M bond in the crystalline $M^{I}P(As)UO_6 \cdot nH_2O$ phase, and ΔH°_{lat} is the enthalpy of the disruption of the $HP(As)UO_6 \cdot 4H_2O$ crystal lattice and of the formation of the $M^{I}P(As)UO_6 \cdot nH_2O$ crystal lattice.

During the ion-exchange reaction, dehydration of the M^+ ion takes place before the transfer of the latter from solution to the crystalline $HP(As)UO_6 \cdot 4H_2O$ phase becomes possible. Such a process is associated with the expenditure of energy, so that $\Delta \bar{H}^\circ_{M^+} \gg 0$. In the series of alkali metal ions ranging from lithium to caesium, the enthalpy of dehydration diminishes from 534 kJ mol^{-1} for the lithium ion to 284 kJ mol^{-1} for the caesium ion.[101] A proportion of this energy expenditure is compensated by the energy of hydration of the corresponding M^+ ion in the crystalline $M^{I}P(As)UO_6 \cdot nH_2O$ phase ($n = 4$ in the case of M^I = Li and $n = 3$ in the case of all other alkali metals). In the stage involving the transfer of a proton from the crystalline $HP(As)UO_6 \cdot 4H_2O$ phase to the solution, the proton is hydrated with a considerable evolution of energy, amounting to $\Delta H^\circ_{H^+} = -1090$ kJ mol^{-1}.[84] Thus, from the standpoint of the ion hydration-dehydration processes, reaction (11) should be significantly exothermic. However, together with the energetic processes considered, other terms of Eqn (12) must also be taken into account.

As shown above, the four water molecules in $HP(As)UO_6 \cdot 4H_2O$ are not equivalent. Two of them form the hydroxonium ion $H_5O_2^+$, whilst the other two retain their molecular individuality. Whereas the removal of molecular water from $HP(As)UO_6 \cdot 4H_2O$ involves a considerable energy expenditure, at the level of the energy of hydrogen bonds, the decomposition of the hydroxonium ion into $2H_2O$ and H^+ is associated with an appreciable endothermic effect, i.e. $\Delta\overline{H}^\circ_{H^+} > 0$. An appreciable energy expenditure is also necessary for the dissociation of the P(As)O–H bond in the $HP(As)UO_6 \cdot 4H_2O$ crystals. Thus the average O–H bond dissociation energy is 463 kJ mol^{-1}. Finally, an energy expenditure is necessary to increase the interlayer distance on passing from the crystalline $HP(As)UO_6 \cdot 4H_2O$ phases to the crystalline $M^IP(As)UO_6 \cdot nH_2O$ phases. For example, this distance increases from 17.440 Å in the $HPUO_6 \cdot 4H_2O$ phase to 18.242 Å in the $LiPUO_6 \cdot 4H_2O$ phase. The analogous distances for the arsenic compounds are 17.594 and 17.808 Å (Table 4). Furthermore, it is necessary to take into account additional energy expenditures as a consequence of the structural rearrangement caused by the decrease in the number of water molecules from four to three in the $M^IP(As)UO_6 \cdot nH_2O$ formula unit on passing from lithium compounds to sodium, potassium, rubidium, and caesium compounds, i.e. $\Delta H^\circ_{lat} > 0$.

Thus the predominance of the energy expenditure over the exothermic effect, due to ion hydration processes ($\Delta H^\circ_{H^+} < 0$, $\Delta H^\circ_{M^+} < 0$) and the formation of new P(As)O–M bonds in the crystalline phase (ΔH°_{O-M}), is the cause of the endothermicity of the ion-exchange reactions (11). In this case, the quantities $\Delta_r H^\circ(298)$ decrease linearly with increase in the radius of the alkali metal ion (R) in aqueous solution (Table 20):

$$\Delta_r H^\circ(298) = [(67.5 - 19.35R) \pm 1.5]/\text{kJ}$$

for reactions involving $HPUO_6 \cdot 4H_2O$, and

$$\Delta_r H^\circ(298) = [(82.5 - 24.12R) \pm 3.0]/\text{kJ}$$

for reactions involving $HAsUO_6 \cdot 4H_2O$.

The observed greater endothermicity of the ion-exchange reactions (11) for arsenouranic acid compared with the analogous processes for phosphouranic acid is associated with the higher dehydration energy of $HAsUO_6 \cdot 4H_2O$ compared with that of $HPUO_6 \cdot 4H_2O$ and the lower packing density of the crystal lattice of the latter compound.

The considerable endothermicity of the reactions involving the exchange of hydrogen for alkali metal ions in the crystalline compounds $HP(As)UO_6 \cdot 4H_2O$ shows that the displacement of the equilibrium towards the formation of the exchange products requires that the entropy term $T\Delta_r S^\circ$ in the equation for the standard Gibbs free energy function $\Delta_r G^\circ = \Delta_r H^\circ - T\Delta_r S^\circ$ should be positive and should exceed the enthalpy term. However, an estimate of $\Delta_r G^\circ(298)$ for reactions (8) shows that the ion-exchange enthalpy makes the main contribution to the Gibbs free energy of the given process. For example, for the reaction

$$Li^+ \text{ (st. soln)} + HAsUO_6 \cdot 4H_2O \text{ (cryst.)} \rightleftharpoons LiAsUO_6 \cdot 4H_2O \text{ (cryst.)} + H^+ \text{ (st. soln)},$$

the free energy $\Delta_r G^\circ$ is given by

$$\Delta_r G^\circ(298) = \Delta_f G^\circ(298, LiAsUO_6 \cdot 4H_2O, \text{cryst.}) + \Delta_f G^\circ(298, H^+, \text{st. soln}) - \Delta_f G^\circ(298, HAsUO_6 \cdot 4H_2O, \text{cryst.}) - \Delta_f G^\circ(298, Li^+, \text{st. soln}).$$

If we employ the data presented in Table 18 and the quantity $\Delta_f G^\circ(298, Li^+, \text{st. soln}) = -292.29 \pm 0.46$ kJ mol^{-1},[84] we obtain $\Delta_r G^\circ(298) = 21$ kJ mol^{-1}. Consequently the equilibrium constant of the process, from the equation $\Delta_r G^\circ = -RT\ln K_e$, is $K_e(298) = 2 \times 10^{-4}$. The displacement of the equilibrium in reaction (11) towards the formation of the exchange products is possible either as a result of an increase in temperature or as a result of the employment of reactions occurring with liberation of energy. Table 21 presents the results of the calculation of the standard enthalpies of the reactions of $HP(As)UO_6 \cdot 4H_2O$ with aqueous solutions of alkali metal hydroxides and also the enthalpies of the ion-exchange reactions with participation of the anhydrous acids.[103]

$$M^IOH \text{ (st. soln)} + HPUO_6 \cdot 4H_2O \text{ (cryst.)} \rightarrow M^IPUO_6 \cdot nH_2O \text{ (cryst.)} + (n-1)H_2O \text{ (liq.)}. \quad (13)$$

$$M^+ \text{ (st. soln)} + HP(As)UO_6 \text{ (solid)} \rightleftharpoons M^IP(As)UO_6 \text{ (solid)} + H^+ \text{ (soln)}. \quad (14)$$

The reactions of $HP(As)UO_6 \cdot 4H_2O$ with solutions of alkali metal hydroxides are exothermic, which ultimately permits the quantitative formation of the crystalline compounds $M^IP(As)UO_6 \cdot nH_2O$. These results confirm the legitimacy of the use of ion-exchange reactions for the synthesis of the compounds $M^IP(As)UO_6 \cdot nH_2O$.

Table 21. The standard enthalpies of reaction (13) and (14).

M^I	$-\Delta_r H^\circ_{13}(298)$/kJ mol^{-1}		$\Delta_r H^\circ_{14}(298)$/kJ mol^{-1}	
	$HPUO_6 \cdot 4H_2O$	$HAsUO_6 \cdot 4H_2O$	$HPUO_6$	$HAsUO_6$
Li^+	11.5	2.5	29.5	21.5
Na^+	20.5	13.5	0.5	−1.5
K^+	29.0	25.5	−12.0	−19.5
Rb^+	29.5	27.0	−15.0	−26.0
Cs^+	33.5	27.5	−22.0	−30.0

It has been established on the basis of the results of X-ray phase analysis that the dehydration of the compounds $M^IP(As)UO_6 \cdot nH_2O$ leads to the disordering of their structures as a consequence of the disruption of the coordination environment of the ion of the univalent element. We used this finding to assess the role of structural factors from the standpoint of their contribution to the energy relations of the ion-exchange reactions.

The exclusion of contributions of the type ΔH°_{lat} from the energy relations of the ion-exchange reactions [see Eqn (12)] leads to a decrease in the overall energy expenditure in the processes under consideration and, in the case of the sodium, potassium, rubidium, and caesium compounds, the exchange reactions proceed with liberation of energy.

VII. Conclusion

The study of the crystalline compounds $HPUO_6 \cdot 4H_2O$ and $HAsUO_6 \cdot 4H_2O$ as well as their alkali metal derivatives by X-ray diffraction showed that the diffraction patterns of all the compounds have analogous sets of reflection maxima with similar positions and relative intensities. In terms of the results of the analytical indexing of the X-ray powder diffraction patterns, the compounds are structurally similar and have similar tetragonal unit cell parameters, which are virtually identical with the results of direct structural studies on $HPUO_6 \cdot 4H_2O$, $HAsUO_6 \cdot 4H_2O$, $LiAsUO_6 \cdot 4H_2O$, $KPUO_6 \cdot 3H_2O$, and $KAsUO_6 \cdot 3H_2O$ single crystals.

The numbers of bands, and their positions and relative intensities in the IR spectra of all the compounds in each of the series of phospho- and arseno-uranate derivatives are similar, which confirms not only the structural similarity of the compounds but also indicates their identical functional composition and the similar nature of the distortion of the principal coordination polyhedra: of phosphorus (tetrahedron), of arsenic (tetrahedron), and or uranium(VI) (octahedron).

A more detailed analysis of the IR spectra, especially in the region of the deformation vibrations of the so-called water of crystallisation, shows that its nature in the test compounds is not the same. In the compounds $HP(As)UO_6 \cdot 4H_2O$ and $LiP(As)UO_6 \cdot 4H_2O$, part of the water is present in the form of the complex hydroxonium ions $H_5O_2^+$ and the lyonium ions $(H_2OLiOH_2)^+$, whilst another part exists in the molecular form. In the compounds of other alkali metals, the entire water is molecularly homogeneous. The different nature of the water in the hydrogen and lithium derivatives, on the one hand, and the sodium, potassium, rubidium, and caesium derivatives, on the other, does not introduce fundamental differences into the structures of the principal coordination polyhedra of phosphorus, arsenic, and uranium or into the structures of the compounds as a whole.

The results of thermographic study of the compounds $M^IP(As)UO_6 \cdot nH_2O$ by the derivatographic method combined with X-ray phase analysis of the intermediate and final dehydration and thermal decomposition products showed that the temperature ranges corresponding to the dehydration of the $HAsUO_6 \cdot 4H_2O$ (363–513 K) are higher compared with $HPUO_6 \cdot 4H_2O$ (353–448 K), which is due to the excess force field of the arsenic in the coordinatively unsaturated AsO_4 polyhedron. On the other hand, the higher temperatures of the condensation of the phosphate groups in $HPUO_6$ with formation of pyrophosphates (833–1133 K) are a consequence of the coordinative saturation of the phosphorus in the PO_4 tetrahedron, which is responsible for the greater stability of the latter (the analogous condensation of the arsenic groups takes place in the range 773–1013 K). After the removal of water in stages, the alkali metal phospho- and arseno-uranate derivatives are converted into the compounds $M^IP(As)UO_6$. The elimination of water molecules from the coordination environment of the alkali metal cation leads in this instance to the conversion of the compound into an amorphous form, i.e. to the breakdown of the long-range order and hence to the disordering of the crystal lattices of the test compounds.

Higher dehydration temperature ranges are also characteristic of alkali metal arsenouranate derivatives compared with the corresponding phosphates, which is a consequence of the stronger binding of the water in $M^IAsUO_6 \cdot nH_2O$. A decrease in the dehydration temperature ranges is observed in both series of compounds on passing from lithium to caesium compounds. This effect is fully consistent with the decrease in the enthalpies of dehydration of alkali metal ions with increase in their size and indicates the incorporation of water molecules in the coordination environment of the univalent element.

The standard enthalpies of formation at 298.15 K of the compounds $M^IP(As)UO_6$ and their crystalline hydrates have been determined from calorimetric data. Quantitative rules governing the variation of the quantities $\Delta_fH°(298)$ for the compounds as a function of the physical characteristics of the alkali metal ions (ionic radius, enthalpy of formation of the ion in the gas phase, ionisation potential) have been established. The results have been compared with the structural characteristics of the same compounds. In particular, the structural similarity of the compounds is manifested by the fact that the standard enthalpies of formation of the phosphorus and arsenic derivatives obey the similarity principle proposed by M Kh Karapetyants.

$$\Delta_fH°(298, M^IPUO_6)$$

$$= \{[-463.5 + 0.97\Delta_fH°(298, M^IAsUO_6)] \pm 2\}/\text{kJ mol}^{-1}$$

$$\Delta_fH°(298, M^IPUO_6 \cdot nH_2O)$$

$$= \{[-351.5 + 1.01\Delta_fH°(298, M^IAsUO_6 \cdot nH_2O)] \pm 3\}/\text{kJ mol}^{-1}.$$

In the series of phosphates and arsenates with M^I = Na, K, Rb, or Cs, the difference between the $\Delta_fH°(298)$ for the anhydrous compounds and their crystalline hydrates per mole of water of crystallisation is virtually constant at 293 ± 3 kJ mol^{-1}. The analogous difference in the case of the hydrogen and lithium forms is also constant, but exceeds the above quantity and amounts to 300 ± 4 kJ mol^{-1}, which emphasises yet again the stronger binding of the water of crystallisation in the hydrogen and lithium derivatives compared with the derivatives of the other Group I elements. This is also indicated by the enthalpies of the dehydration reactions of the crystalline hydrates investigated.

The study of the energy relations of the ion-exchange processes showed that they are all endothermic. This is due to the predominance of the energy expenditure associated with the change in structure on passing from the compounds $HP(As)UO_6 \cdot 4H_2O$ to $M^IP(As)UO_6 \cdot nH_2O$ compared with the overall exothermic effect in the accompanying process involving the dehydration-hydration of the alkali metal ions and the proton in the aqueous phase. The enthalpies of the ion-exchange reactions decrease in this instance in the series of alkali metal derivatives from lithium to caesium for both $HPUO_6 \cdot 4H_2O$ and $HAsUO_6 \cdot 4H_2O$. The results lead to prospects for the practical use of the ion-exchange reactions in order to isolate the compounds and also to prevent the entry of the ecologically dangerous (including radioactive) elements into the human habitat.

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102. V N Yaglov, Doctoral Thesis in Chemical Sciences, Ivanovo Chemical Engineering Institute, Ivanovo, 1980
103. G N Chernorukov, Candidate's Thesis in Chemical Sciences, Nizhnii Novgorod State Technical University, Nizhnii Novgorod, 1995

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Isoureas: synthesis, properties, and applications

A A Bakibaev, V V Shtrykova

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Abstract. Data on the methods of synthesis, chemical properties, and applications of isoureas are surveyed. Promising ways of using isoureas in organic synthesis are demonstrated. The bibliography includes 166 references.

I. Introduction

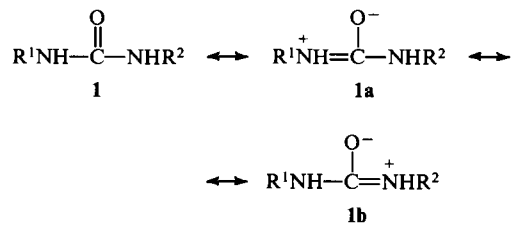
Ureas and isoureas (urea derivatives with *O*-functional-group substituents) are genetically related classes of organic compounds. This claim is based on the fact that they can be obtained from the same starting materials (carbodiimides, cyanamides, and organic cyanates) and also on their ability to be interconverted.

One of the promising aspects of the chemistry of ureas is their synthesis from compounds of different classes with an amide group activated beforehand. A transition of this kind from the amide to the iminoester group has already yielded excellent results. Thus imidates have been obtained from amides,[1,2] while lactim esters have been obtained from lactams.[3] The lactim esters were subsequently used in new ways which had not been employed before. There are virtually no reviews on the chemistry of isoureas apart from Hegarty's paper,[4] but the description of the methods of synthesis of isoureas in the latter is more in the way of a summary. This led to the writing of the present review in which information about the methods of synthesis, chemical properties, and applications of isoureas is compiled.

II. Methods of synthesis of isoureas

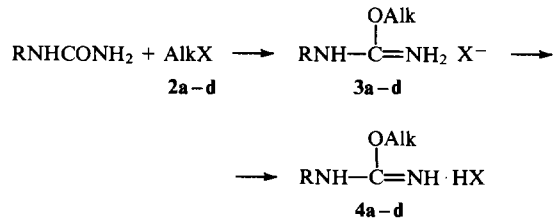
1. Syntheses from ureas

The delocalisation of π electrons in the R^1N-C-O and R^2N-C-O fragments in the ureas **1** is responsible for their weak basicity. The structure of the ground state of ureas can be expressed as a hybrid of the resonance forms **1**, **1a**, and **1b**.



1 **1a** **1b**

Nevertheless, among the multiplicity of the reactions which ureas tend to undergo, the most characteristic are those involving nucleophilic attack on the oxygen or nitrogen atom of the ureas **1** by electrophiles or neutral reagents, the resonance forms **1a** and **1b** being the most probable reactive species in these reactions. One of the specific examples of nucleophilic attack on the oxygen atom of ureas is provided by the direct *O*-alkylation of urea by various alkylating agents **2a–d**. The isoureas **4a–d** are apparently formed via the isouronium intermediates **3a–d**.



2a–d **3a–d** **4a–d**

R = H, Alk, Ar;

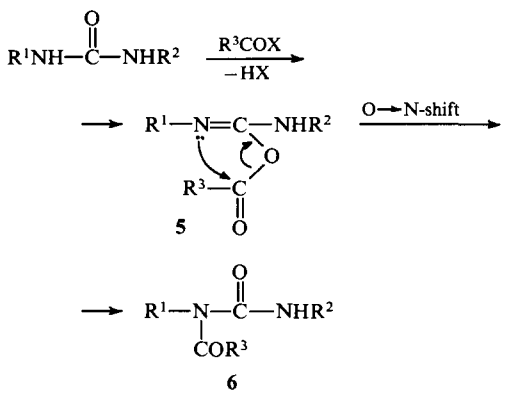
X = $AlkSO_4^-$ (**a**), $NaSO_3^-$ (**b**), I^- (**c**), $AlkSO_3^-$ (**d**).

The reaction involving the *O*-alkylation of ureas is carried out as a rule in neutral media at low temperatures (up to 100 °C), because the alkylating agents AlkX are extremely reactive. Alkyl sulfates **2a**,[5–7] alkanesulfonates **2b**,[5] alkyl iodides **2c**,[8] and aryl alkanesulfonates **2d**[5] are usually employed as the *O*-alkylating agents for ureas. *O*-Alkylisoureas **4a–d** are as a rule isolated as the corresponding salts, but in some cases the free bases can also be obtained by careful neutralisation. The isoureas **4** with easily removeable groups ($AlkO^-$) tend to undergo elimination readily in a basic medium.

Many investigators believe[9–13] that the *N*-acylation of ureas proceeds via the initial *O*-acylated intermediate **5**.

A A Bakibaev, V V Shtrykova Research Laboratory for Problems in the Synthesis of Medicinal Drugs, Tomsk Polytechnic University, prosp. Lenina 30, 634004 Tomsk, Russian Federation.
Fax (7-382) 221 90 80. Tel. (7-382) 249 28 61 (A A Bakibaev)

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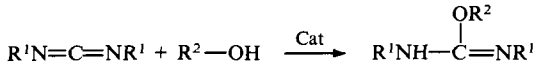
6

However, the kinetically controlled adduct **5** has not so far been isolated in the classical acylation reactions of ureas, only the *N*-acylureas **6** being found among the reaction products.[14-16] *N*-Acylureas **6** are formed as a result of the intramolecular thermodynamically more favourable O → N shift (migration) of the acyl group. For example, the acylation of *N*-methylurea by acetyl chloride affords *N*-acetyl-*N*-methylurea **6**,[13] which agrees with the formation of the *O*-acetyl intermediate **5**, although the secondary nitrogen atom should be more nucleophilic in the direct attack by the acylating agent.

2. Synthesis from carbodiimides

Carbodiimides (CDI) constitute one of the most important types of unsaturated compounds with a heterocumulated bond system. By virtue of thoroughly developed and reliable methods of synthesis, CDI have found extensive applications, mainly in peptide synthesis and for the immobilisation of biomolecules.[17,18] The close relationship between CDI and ureas is emphasised by the fact that ureas are one of the traditional sources of CDI[17-22] and the latter can be readily converted, in their turn, into ureas. CDI are obtained from 1,3-disubstituted ureas by dehydration with P_2O_5,[19] metal carbonyls [$Fe(CO)_5$, $Fe_2(CO)_4CNPh$, $Fe_2(CO)_9$, $W(CO)_6$, $Mo(CO)_6$],[20] triphenylphosphine dibromide,[21] or triphenylphosphine[22] in triethylamine and aromatic sulfonic acid chlorides under conditions of phase transfer catalysis,[23] or by the interaction of *N*-alkylideneureas with PCl_5.[24]

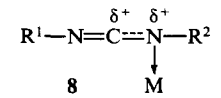
By virtue of their comparatively ready availability and high reactivity in reactions with nucleophiles, CDI have proved to be perhaps the principal synthons for the synthesis of *O*-alkyl(aryl)isoureas. The reactions of CDI with alcohols and certain phenols in the presence of specific catalysts or alkoxides in the synthesis of *O*-alkyl(aryl)isoureas do not even require heating.[25-32] The noncatalytic addition of alcohols and phenols to CDI is relatively ineffective because of the weak nucleophilic properties of these reagents.



7

R^1, R^2 = Alk, Ar.

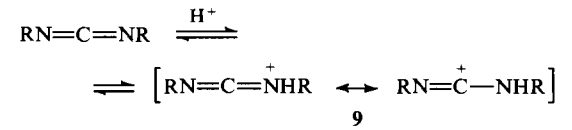
The relatively low nucleophilicity of alcohols (phenols), on the one hand, and the known tendency of CDI to undergo spontaneous or initiated polymerisation[33] during the synthesis of isoureas **7**, on the other, can be readily overcome by employing a series of synthetic procedures designed to increase the electrophilicity of the heterocumulene fragment of the CDI towards nucleophiles. In this part of the review, we shall quote only the studies which were published after the reviews of Bocharov[34] and Pankratov,[35] where reactions involving CDI, including the reactions of CDI with alcohols, were surveyed. The interaction of CDI with alcohols (phenols) is usually catalysed by copper salts (CuCl, $CuCl_2$, Cu_2O) or Zn^{2+}.[36-41] The catalytic action of metal ions apparently consists in the formation of a coordination complex between the CDI and the metal ion (via the imine nitrogen atom).



8

M = Cu(I), Cu(II), Zn(II).

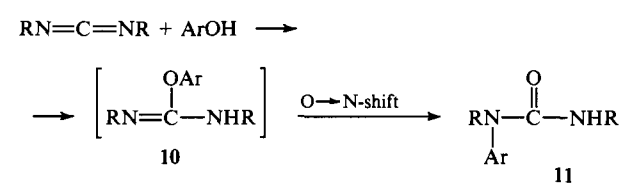
The formation of the coordination complex **8** leads to an increase in the electrophilicity of the central carbon atom of the CDI. Another method for the activation of CDI in reactions with nucleophiles, including alcohols, involves the use of proton-donors.[42,43] The protonation of CDI results in the formation of the electrophilic species **9**.



9

The preliminary *N*-functionalisation of the CDI by electron-accepting groups (acyl, sulfoxyl, and phosphoryl) significantly facilitates subsequent nucleophilic addition.[44]

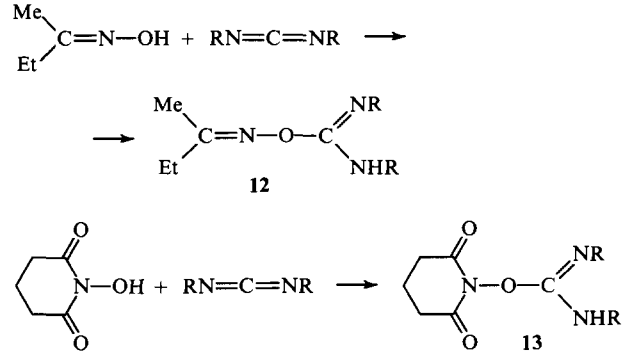
Proceeding now to certain characteristic features of the reactions of CDI with alcohols (phenols), we note in the first place that the interaction of CDI with alcohols affords the corresponding isoureas **7**, whilst the analogous reactions with phenols do not proceed unambiguously. The usual phenols react with CDI to form in most cases *N*-arylureas **11**[45-48] and many workers are inclined to assume that these reactions proceed via the *O*-aryl intermediate **10**, although there is no reliable evidence for this.



10 11

The fact that phenols with distinct acid properties react with CDI to form stable *O*-arylisoureas **10** may serve as indirect evidence in support of the existence of the intermediate **10**.[49-55] Such compounds have been isolated in the reactions of CDI with 2,6-dichloronitrophenol,[55] pentachlorophenol,[51,52] and 2-carboxy-4,6-dinitrophenol. It has been postulated that *ortho* substituents in the phenols mentioned above inhibit the usual O → N shift as a result of their steric influence on the reaction centre.

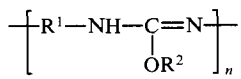
It has been shown in a number of studies[37,56-59] that the non-traditional isoureas **12** and **13** can be obtained from CDI and *N*-hydroxy-compounds.



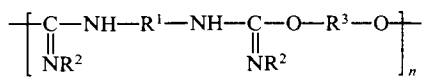
12 13

R = Alk, Ar.

Polycarbodiimides react with aliphatic alcohols to form the corresponding poly-*O*-alkylisoureas with structures **14** and **15**.[60–63]



14

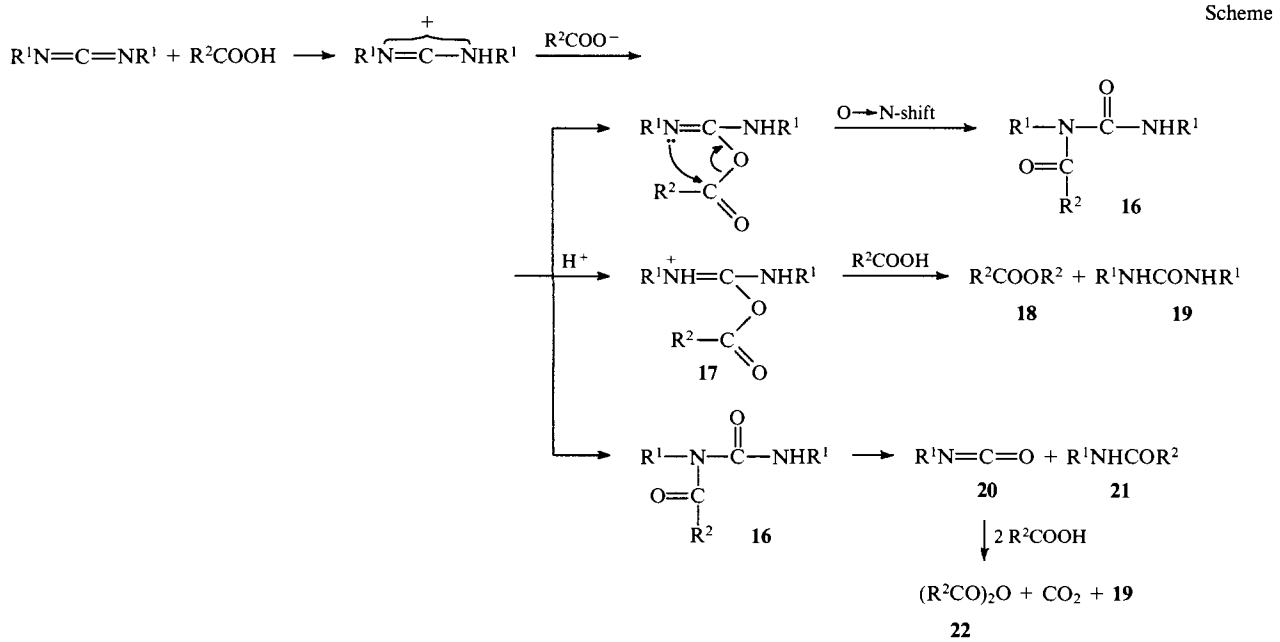


15

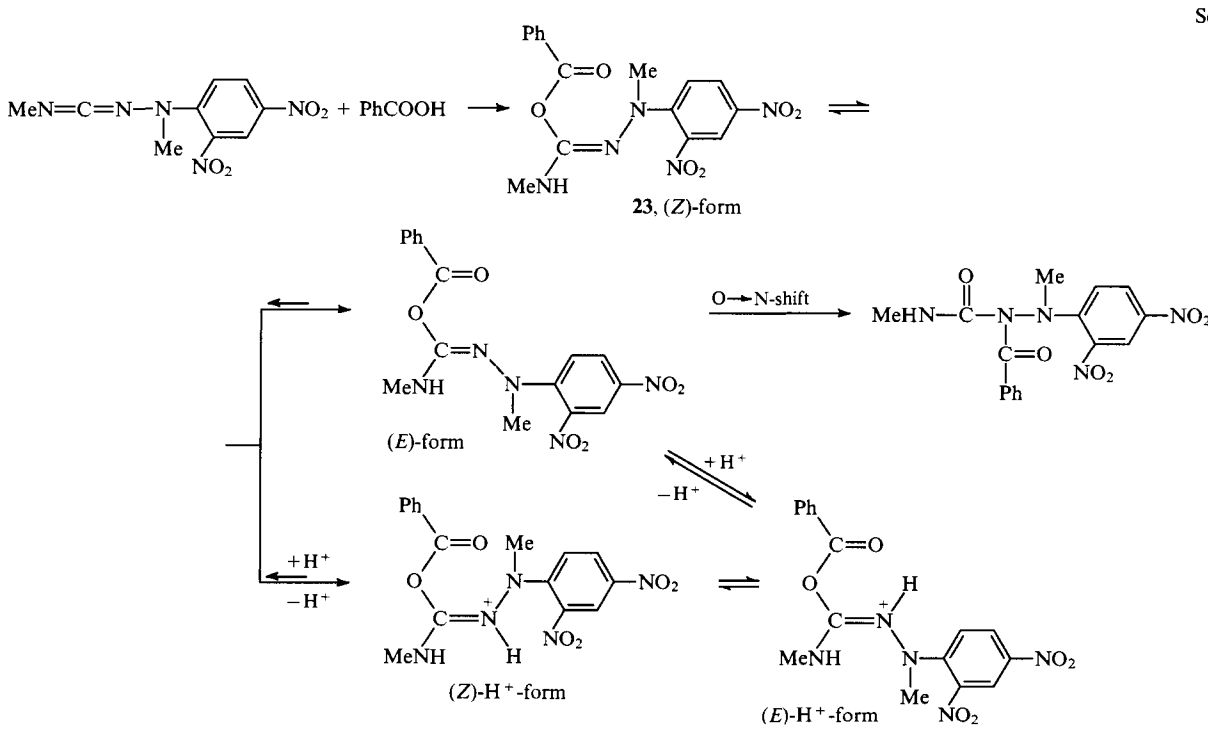
It is of interest that the polyisoureas **14** and **15** are more soluble and have lower melting points than the initial polycarbodiimides.

The attractive features of CDI in peptide synthesis stimulated detailed investigation of the reactions of CDI with carboxylic acids, including the kinetics of these processes.[18,64–70] The reactions of CDI with carboxylic acids (Scheme 1) are completed, depending on the acidity of the medium, temperature, and the amount of reactant, by the formation of either the *N*-acylurea **16**, or of the ester **18** and the urea **19**, or of the amide **21** and the anhydride **22** via the intermediate isocyanate **20**. The formation of the *N*-acylurea **16** is usually observed at elevated temperatures or when the reaction is carried out for a long time.[71] A highly acid medium promotes the formation of the esters **18** via the protonated intermediate **17**; sterically cumbersome groups R^1 or the use of a high temperature lead to decomposition of the *N*-acylurea **16** into the isocyanate **20** and the amide **21**, while the isocyanates **20** react with two molecules of a carboxylic acid to produce two molecules of the urea **19** and the anhydride **22** (Scheme 1).

Scheme 1



Scheme 2



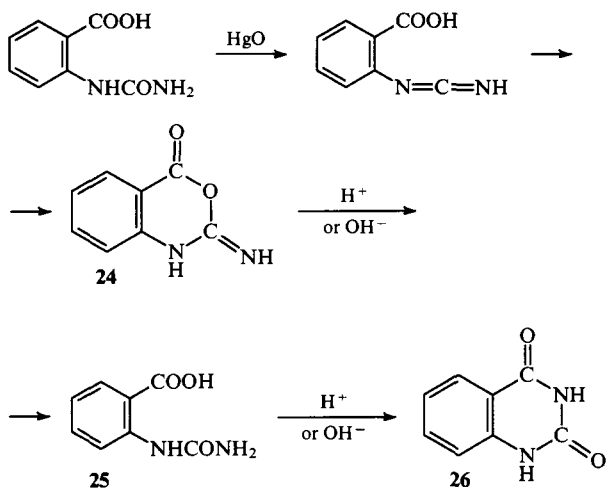
In order to eliminate the racemisation of the acid substrate, which is undesirable in peptide synthesis, and the competing O → N shift in reactions with carboxylic acid, one may employ *N*-hydroxysuccinimide or 1-hydroxybenzotriazole.[72,73]

It is believed[74,75] that poly-*N*-acylureas are formed from polycarbodiimides and carboxylic acids via the corresponding poly-*O*-acylated intermediate.

Comparatively recently, it has been possible to synthesise and isolate the stable *O*-acylisourea **23** (Scheme 2).[76,77]

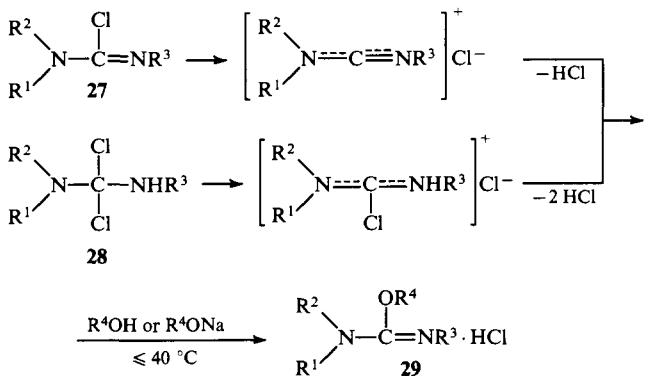
The stability of the *O*-acylisourea **23** is attributed to the (*Z*)-configuration relative to the C=N bond, while the (*E*)-isomer undergoes the spontaneous O → N shift of the acyl group.

The synthesis of 1,2-dihydro-2-imino-3,1,4-*H*-benzoxazolin-4-one **24**, which can be converted into the quinazolinedione **26** via the urea **25**, is a remarkable example of the intramolecular stabilisation of *O*-acylisoureas.[78]



3. Syntheses from chloroformamidines

Mono- and di-chloroformamidines **27** and **28** can be readily synthesised from the corresponding CDI and dry HCl.[17,18,33,34] They are sometimes obtained by treating *N,N,N'*-trisubstituted ureas with PCl_5.[4] Being highly reactive in dissociative reactions, the chloroformamidines **27** and **28** smoothly substitute the chloride anion by alkoxide anions, affording *O*-alkylisoureas **29** in a high yield.[79–82]

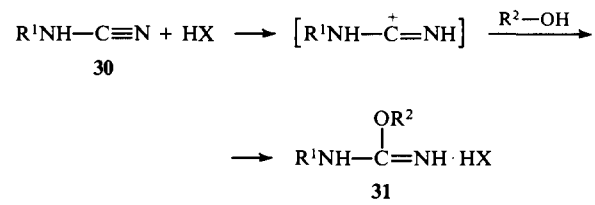


R^1–R^4 = Alk, Ar.

Despite the simplicity of the formation of the isoureas **29**, the methods of their synthesis based on chloroformamidines have not come to be widely used in preparative chemistry, which is evidently associated with the greater availability of CDI and ureas, although in certain cases (for trisubstituted isoureas) chloroformamidines are preferable.

4. Syntheses from cyanamides

The close relationship between ureas and cyanamides **30** can be seen on the basis of their interconversion: the dehydration of *N*-substituted ureas in basic media results in the formation of cyanamides **30**, whilst the reverse reaction affords ureas.[82] Cyanamides may be regarded also as a tautomeric form of CDI and the latter, as noted above, are 'genetically' close to ureas. Consequently cyanamides **30** tend to undergo the same addition reactions as CDI. As was in fact expected, cyanamides **30** react with alcohols in the presence of acids to form the isoureas **31** with a free imine group.[83–88]

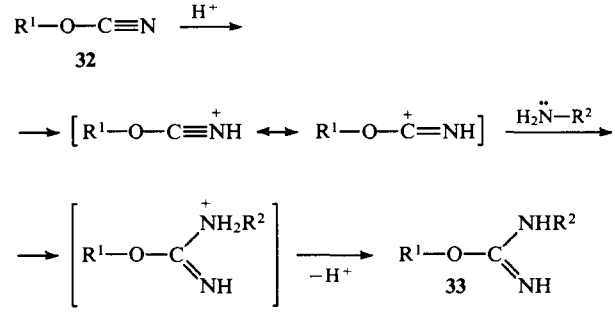


R^1, R^2 = Alk, Ar.

Both inorganic and organic acids are used as proton catalysts, whilst the isoureas **31** are isolated respectively as the halides and the sulfate, phosphate, carbonate, and nitrate salts or in the form of aliphatic and aromatic carboxylates.[83–88] ^{14}C-Labelled *O*-methylisourea has been obtained for biochemical research from the corresponding cyanamide and methanol in the presence of hydrogen chloride.[89]

5. Syntheses from organic cyanates

The methods of synthesis of isoureas examined above were based on the initial attack by nucleophilic alcohols (alkoxides) on the electrophilic carbon of the substrates, while the formation of isoureas from organic cyanates **32** is based on attack by a nucleophilic amine.



R^1, R^2 = Alk, Ar.

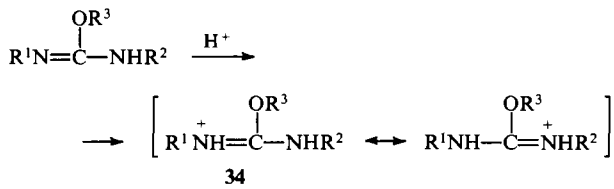
The reactions of organic cyanates **32** with amines or their salts are carried out as a rule in inert organic solvents at −50 to +150 °C, the best yields of the isoureas **33** being attained for equimolar proportions of the substrate and the reagent.[90–93]

6. Other methods of synthesis of isoureas

A series of examples of the synthesis of isoureas, not related directly to the methods of synthesis examined above, have been described in the literature.[94–97] However, analysis of these methods showed[94–97] that they definitely imply the intermediate formation of species the conversion of which into isoureas was examined above. Bearing this factor in mind and taking into account the fact that these examples of the synthesis of isoureas[94–97] represent isolated instances, we believe that they do not require detailed comments.

III. Chemical properties

Isoureas, which contain the iminoester functional group, are stronger bases (the pK_a values for isoureas are from 6 to 10) than ureas. Thus pK_a for *O*-methylisourea is 9.80, while that for the isomeric *N*-methylurea is 0.82.[98,99] The increased basicity of isoureas can be accounted for by the higher stability of their conjugate acids as a result of the resonance of the isouronium cation **34**, which gives rise to a fundamental difference between isoureas and *N*-substituted ureas.



34

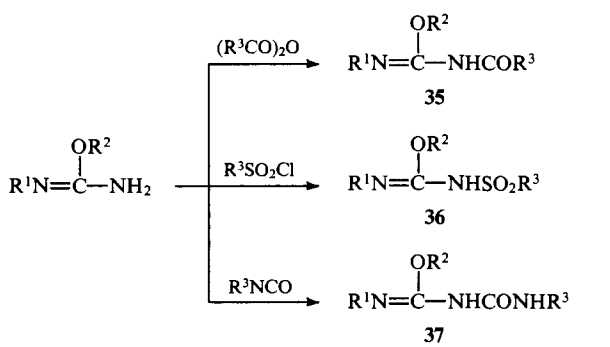
R^1-R^3 = Alk, Ar.

As was to be expected, isoureas are extremely reactive with respect to nucleophiles, but their free bases are themselves effective nucleophiles. The above general properties of isoureas make it possible to specify certain characteristic reactions which isoureas tend to undergo.

1. Reactions with participation of a nucleophilic nitrogen atom

In synthetic practice, *N*-acylation processes (Scheme 3) have been most widely investigated among the reactions of isoureas with widely the particpation of a nucleophilic nitrogen atom.[100-106]

Scheme 3



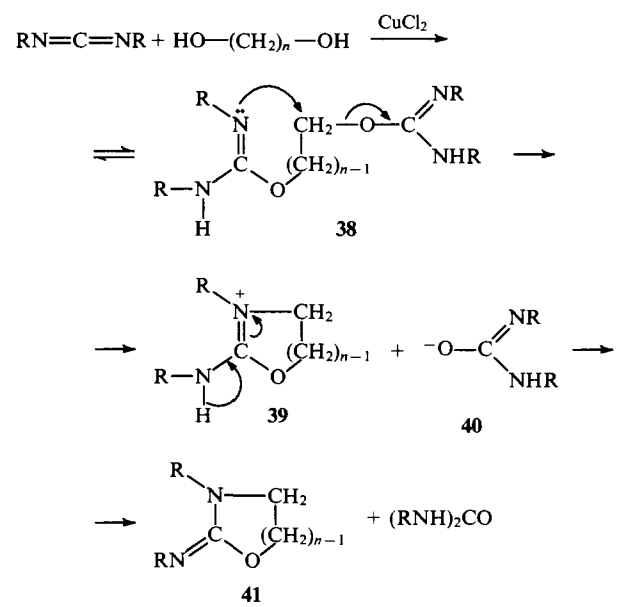
35 **36** **37**

R^1, R^3 = Alk, Ar; R^2 = Alk.

Examples of the synthesis of derivatives of bisisourea from phthalic acid dichloride and the corresponding isoureas are known.

N-Acylisoureas **35-37** are as a rule formed smoothly and in high yields, the procedure for their isolation not requiring special conditions. The key stage in the formation of type **41** 1,3-oxazolidines involves nucleophilic attack by the imine nitrogen atom on the methylene group. Thus the interaction of glycols with CDI, catalysed by copper chloride,[107,108] is completed by the cyclisation of the intermediate bisisoureas **38** via intramolecular nucleophilic attack by the imine nitrogen atom on the terminal methylene group and the transfer of the proton in the cyclic isouronium ion **39** to the highly basic anion **40**.

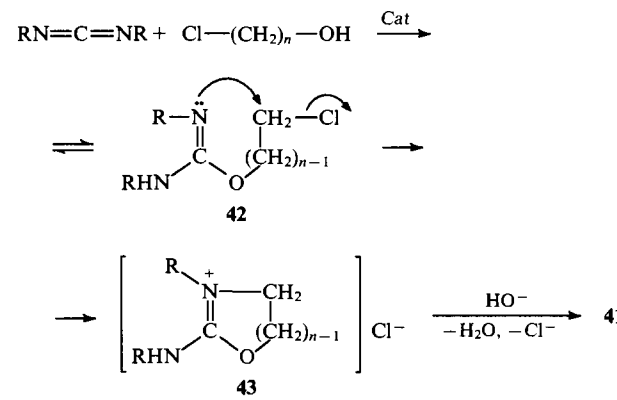
The reactions of cyclohexanediols with CDI afford the corresponding oxazolidines with the *trans*-configuration.[109] It has been established that the type **41** oxazolidines are also formed in the reaction of CDI with certain haloalcohols.[103,105]



38 **39** **40** **41**

R = Alk, Ar; n = 2, 3.

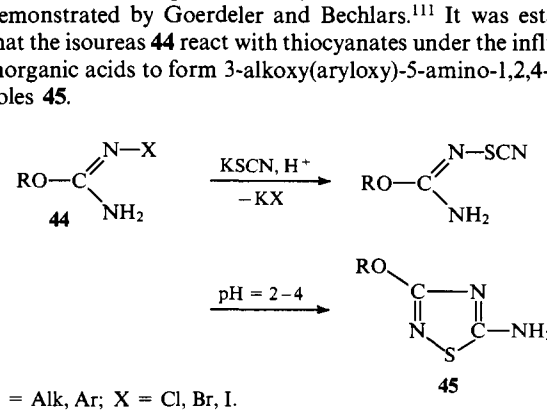
It has been suggested that the hydrochloride **43** is formed as a result of intramolecular nucleophilic substitution of the chlorine atom by the imine nitrogen in the isourea **42** and the subsequent dehydrochlorination in a basic medium leads to the oxazolidines **41**.[110]



42 **43**

R = Alk, Ar; n = 2,3; Cat = $CuCl_2$,[103] HBF_4.[105]

Another example of the cyclisation of isoureas has been demonstrated by Goerdeler and Bechlars.[111] It was established that the isoureas **44** react with thiocyanates under the influence of inorganic acids to form 3-alkoxy(aryloxy)-5-amino-1,2,4-thiadiazoles **45**.

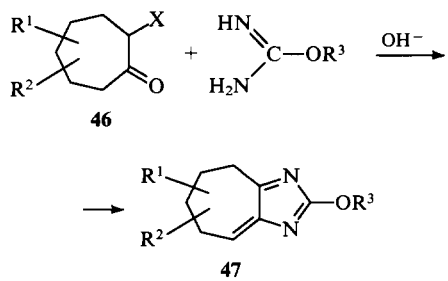


44 **45**

R = Alk, Ar; X = Cl, Br, I.

The thiadiazoles **45** proved to be extremely stable compounds, which are readily acylated and give rise to nitrosoamines capable of azo-coupling in an acid medium.[111]

The reactions of derivatives of the tropones **46** having functional-group substituents in the 2-position with isoureas or their salts in the presence of bases result in the formation of the cyclic 2-alkoxyimidazole derivatives **47**.[112]

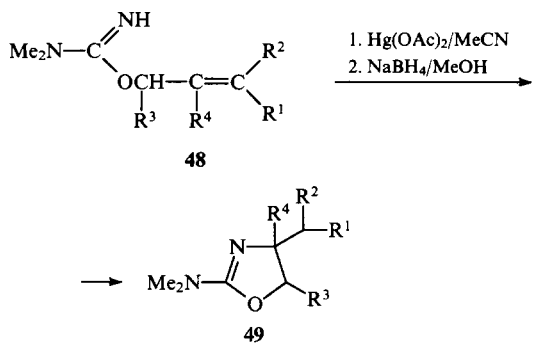


46 **47**

$R^1 = R^2$ = H, Alk, Ar, $PhCH_2$, Hal, OH, CN, NHY;

X = Br, Cl, AlkO, TsO; R^3 = Me, Et.

The intramolecular electrophilic cyclisation of alkyl-substituted 1,1-dimethylisoureas **48**, obtained from the corresponding alcohols and cyanamide, leads to the formation of the oxazole derivatives **49**.[113]



48 **49**

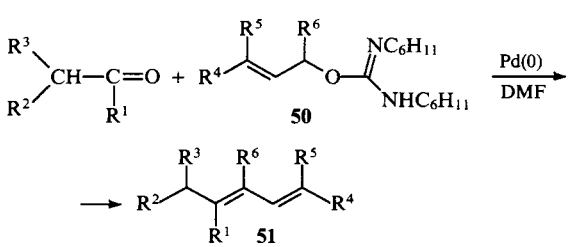
R^1–R^4 = H, Ar, Alk.

The relatively unstable *N*-haloisoureas RO–C(=NX)–NH_2 have been synthesised.[111] Their relative stability was found to depend on the nature of the substituent R (Me < Et < β-ClC_2H_4 < Ph < $PhCH_2$ ≪ cyclo-C_6H_{11}) and on the halogen X (I < Br < Cl). It was shown that the condensation of *O*-alkylisoureas with cyanamide gives rise to *O*-alkyl-*N*-cyanoisoureas and dicyandiamide.[114]

2. Reactions accompanied by the elimination of the *O*-alkyl(aryl) fragment

a. *C*-Alkylation

There are few examples of the *C*-alkylation of *O*-alkylisoureas in the literature. A convenient method of synthesis of alkenes employing 2-allyl-isoureas **50** as an effective agent for the direct α-allylation of ketones and aldehydes in the presence of zerovalent palladium or with added triphenylphosphine (for aldehydes) has been developed comparatively recently.[115,116]

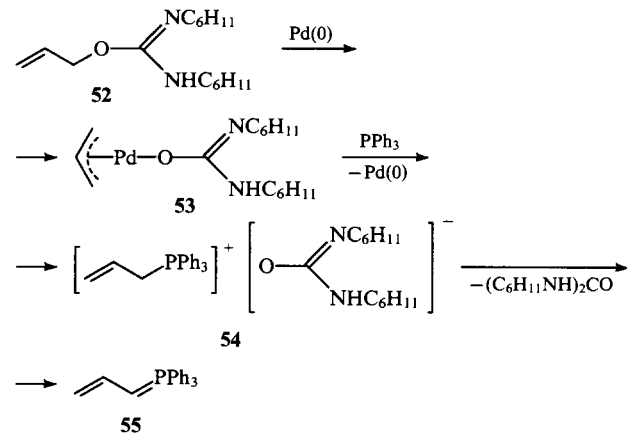


50 **51**

R^1 = H, Alk, Ph; R^2, R^3 = H, Alk, Ph;

R^4–R^6 = H, Me, Pr, C_6H_{11}, Ph.

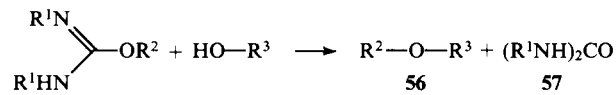
It has been suggested that the oxidative coupling of the isourea **52** with zerovalent palladium results in the formation of the π-allyl intermediate **53**. When triphenylphosphine is employed, the intermediate **53** reacts with the latter as a nucleophile, affording the phosphonium salt **54**. As a strong base, the isourea anion in compound **54** abstracts an α-proton, affording the allylidenetriphenylphosphorane **55** and the latter is then used as an agent for the introduction of the allylidene group into benzaldehydes via a Wittig type reaction.



52 **53** **54** **55**

b. *O*-Alkylation (arylation)

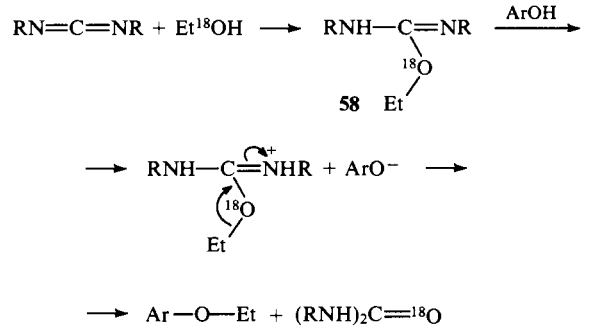
Isoureas react smoothly with alcohols or phenols, giving rise to the ethers **56**; the leaving groups are the ureas **57**.[108, 117–119]



56 **57**

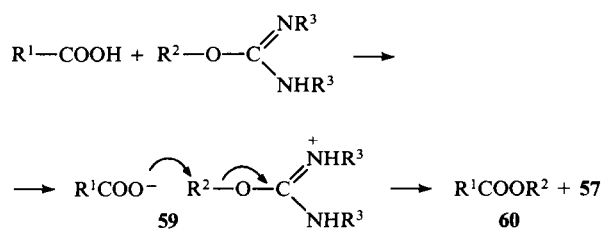
R^3 = Alk, Ar.

It has been established that type **56** ethers are formed in the interaction of ^{18}O-labelled ethanol with CDI by attack of the alkoxide or aryloxide anions on the alkyl group of the intermediate *O*-alkylisoureas **58**.[120]



58

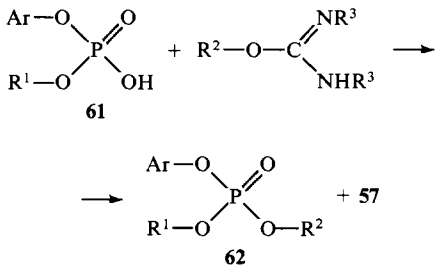
The esters **60** can be obtained in high yields by the reaction of *O*-alkylisoureas with carboxylic acids.[121,122]



59 **60**

The existing ideas about the mechanisms of the reactions of isoureas with carboxylic acids are based on the fact that the isoureas are initially protonated to give the intermediate **59** and the latter is then attacked by the carboxylate anion at the alkoxy-group with formation of a tetrahedral intermediate.

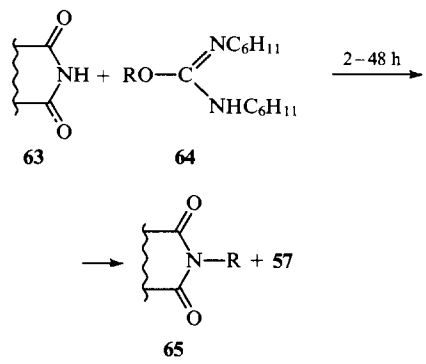
The phosphates **61** react readily with *O*-alkylisoureas to form the corresponding esters **62**.[123]



R^1, R^2 = H, Alk.

c. *N*-Alkylation

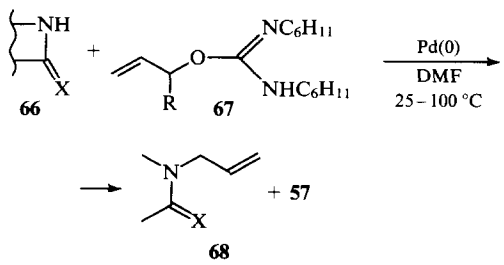
It has been found comparatively recently[124,125] that the refluxing of cyclic imides **63** with *O*-alkyldicyclohexylisoureas **64** in dimethylformamide (DMF) makes it possible to synthesise the *N*-alkylimides **65** in satisfactory yields.



R = Me, Bu, (±)-Bu^s, (±)-$C_6H_{13}CHMe$, $C_{12}H_{25}$.

According to the authors, the reaction proceeds via an S_N2 mechanism with 98% inversion of the configuration. This has been confirmed by the reaction of [(*R*)-(−)-1-methylheptyl]-isourea **64** with phthalimide, which leads to [(+)-1-methyl-heptyl]phthalimide. On treatment with hydrazine hydrate, the latter is converted into [(*S*)-(+)-1-methylheptyl]-amine.

The zerovalent palladium-catalysed direct *N*-allylation of amides, thioamides, and certain lactams **66** by *O*-allylisoureas **67** has been achieved.[126]



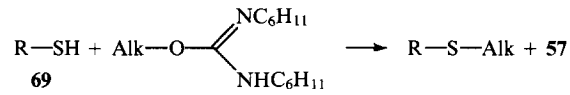
X = O, S.

The yields of the *N*-allyl derivatives **68** are in the range 27%–87%.

In the allylation of certain heterocyclic bases (thymine, thymidine, uridine) by *O*-alkylisoureas, it was established that this entails the exclusive *N*-alkylation of the azaheterocycles, while the isomeric *O*-alkyl derivatives were not detected even in trace amounts.[127,128]

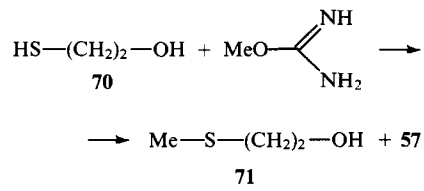
d. *S*-Alkylation

It has been shown in a number of studies[129,130] that *O*-alkyl-isoureas are excellent *S*-alkylating agents for mercaptans and thiophenols **69**.

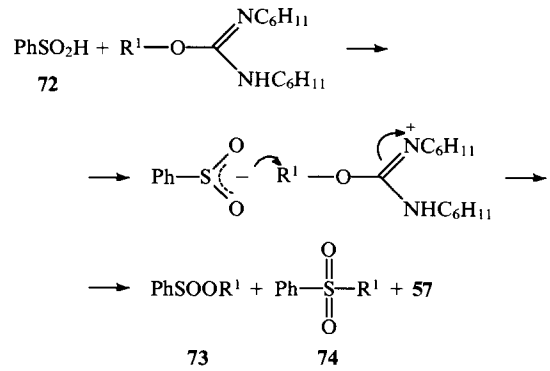


R = Alk, Ar.

It is remarkable that the reaction of *O*-methylisourea with 2-mercaptoethanol **70** affords selectively the *S*-methylated product **71**.[130]



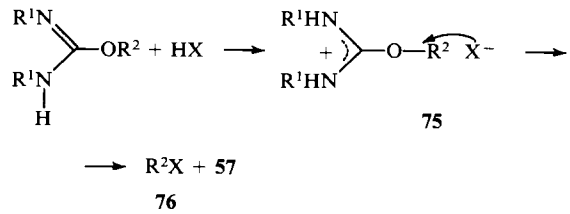
The interaction of *O*-alkylcyclohexylisoureas with benzene-sulfinic acid **72** leads to the preferential formation of the sulfinates **73** (*O*-alkylation products), although the formation of appreciable amounts of the sulfones **74** (*S*-alkylation products) has also been observed.[131]



The overall yield of the alkylation products was 60%–90%. The ratio of the sulfinates **73** and the sulfones **74**, determined from ^{1}H NMR spectroscopic data, depends on the nature of the group R and the solvent employed, branched groups R inducing the virtually 100% formation of the sulfinates **73**.

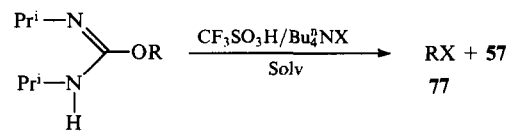
e. Synthesis of alkyl halides

Nucleophilic substitution in the protonated urea **75** on heating with hydrogen halides, where the leaving groups are neutral ureas **57** and alkyl halides **76** are the products, has long been known.[132–135]



X = Cl, Br, I.

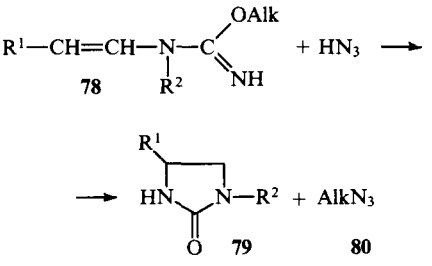
Since the traditional methods of synthesis of alkyl halides **76**, especially the bromides, frequently involve the formation of insufficiently pure target products, an effective modification of this reaction has been proposed,[136] permitting the synthesis, together with the usual alkyl halides, also of the unsaturated alkyl halides **77** in 57%–90% yields.



X = Br, I.

The use of trifluoromethanesulfonic acid instead of the traditional hydrogen halides made it possible to regulate accurately the amount of acid and to eliminate nucleophilic competition between the added halide and the acid residue. Kinetic study showed that this is a first-order reaction and that its rate depends on the concentration of the *O*-alkylisourea salt **75**. It has been established that, depending on the substituent, the reactivity of isoureas decreases in the following sequence: allyl = propargyl = benzyl > primary > secondary. Although the reaction involving nucleophilic substitution in solution in hexamethylphosphoramide and DMF proceeds more effectively, it is preparatively more convenient to employ dichloromethane or chloroform.

It has been shown[137] that the reaction of *O*-alkyl-*N*-alkenyl-isoureas **78** with hydrazoic acid does not lead to the expected aminotetrazoles, as in the case of iminoesters,[1] but affords *N*-alkylimidazolidin-2-ones **79** and alkyl azides **80**.



$R^1 = R^2$ = Alk, Ar.

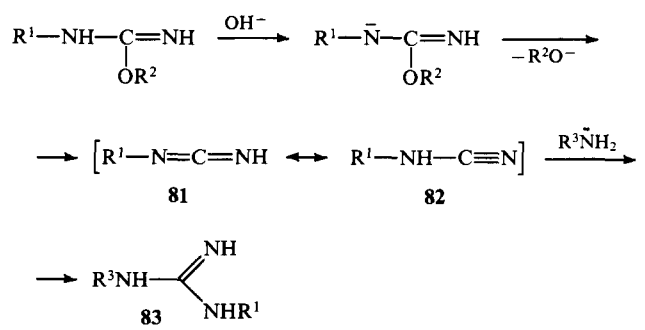
It has been suggested[137] that the heterolytic dissociation of the O–Alk bond accompanied by nucleophilic substitution by the azide anion takes place in the hydrazoate salt of the isourea **78**. The isourea residue undergoes heterocyclisation to compound **79** apparently via intramolecular electrophilic addition to the double bond.

The formation of *N*-substituted ureas **57** has been observed in a number of instances on heating *O*-alkylisoureas.[125,136] Compounds **57** are obtained by elimination of an alkene from the *O*-alkylisoureas.

3. Reactions accompanied by the elimination of the alkoxy-fragment

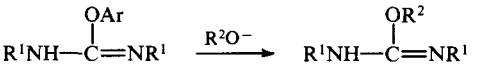
Among reactions of this type, the reactions of isoureas with amines, leading to guanidines, are best known.[83,138]

It has been suggested that the CDI **81** is formed initially via β-elimination and then undergoes a tautomeric transformation into the cyanamide **82**. The cyanamide undergoes nucleophilic attack by the amine.



R^1–R^3 = Alk, Ar.

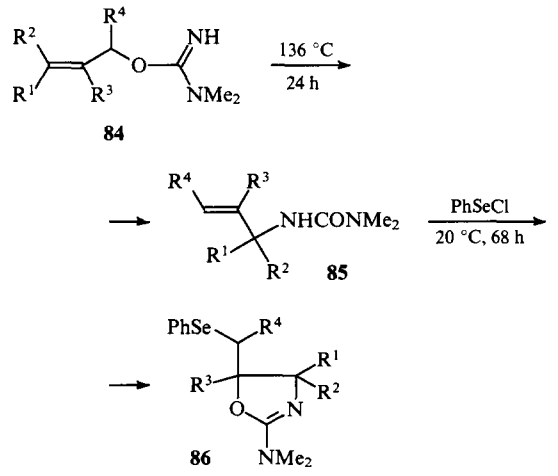
The exchange of the aryloxy-group for an alkoxy-group sometimes occurs in *O*-arylisoureas. It takes place on heating in the presence of the R^2O^- alkoxide ion via a mechanism involving a process similar to elimination-addition.[4]



It has been established that *N*-alkyl- and *O*-aryl-isoureas give rise to the corresponding alkanes and arenes on reduction with hydrogen over palladium.[139–141] Consequently, these reactions can be regarded as a general method for the reduction of alcohols and phenols to hydrocarbons. In a strongly basic medium, *N*-acylisoureas give rise to *N*-acylcyanamides,[142] whilst a high-temperature treatment of isoureas (250–300 °C) leads to the formation of isocyanates.[143]

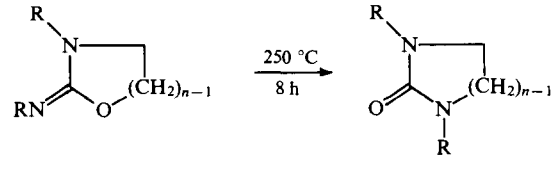
4. Other reactions

The isomerisation of the isoureas **84** on refluxing in xylene leads to the formation of *N*-substituted ureas **85**, which are converted into the oxazolines **86** on treatment with PhSeCl in chloroform in the presence of silica gel.[113]



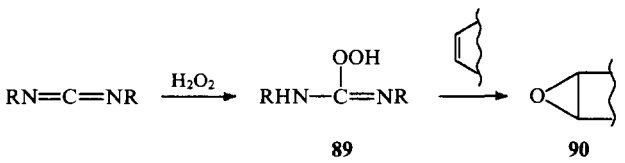
R^1–R^4 = H, Alk, Ar.

On heating to 250 °C, the isoureas **87** rearrange to the cyclic ureas **88**.[144]



n = 2, 3.

The interaction of CDI with hydrogen peroxide leads to the peroxycarboximidic acids **89**, which are effective agents for the oxidation of alkenes and especially arenes to the corresponding epoxides **90**.[145]



89 **90**

IV. Applications of isoureas

The principal fields in which isoureas are employed are agriculture, medicine, and biochemistry. Isoureas are used to a somewhat lesser extent in polymer and analytical chemistry.

Thus isoureas exhibit a high herbicidal activity,[146–148] are used as plant growth regulators,[146–153] and promote the acceleration of the growth of wool, improvement in the production of meat and milk from animals, and improvement in the assimilation of animal feed.[154]

The study of the biological activity of *O*-alkylisoureas established their stimulating effect on smooth muscles.[155] Certain isoureas are used as antiinflammatory medicinal drugs.[156] A few possess an anticancer activity.[157] Isoureas linked to purine or pyrimidine bases and containing fluorescent labels are used to detect deoxyribonucleic and ribonucleic acids and their fragments.[158]

Isoureas are employed in the synthesis of auxiliary agents for the dyeing of textiles and polymers[159] and for the synthesis of copolymers with a specified fibre shape.[60–63]

The pronounced basicity of isoureas made it possible to synthesise from them a large number of coloured coordination compounds and to investigate their properties.[160–166]

V. Conclusion

Unfortunately, new studies on the development of general methods of synthesis of isoureas have not been published recently. However, more vigorous investigation of the chemical properties of isoureas promises to yield important results both synthetically and theoretically. In this context, one of the promising procedures involves the study of the reactions of isoureas with various amino-derivatives which are potentially capable of giving rise to the synthesis of new heterocyclic systems. Analysis of literature data has shown that the reactions of isoureas with organometallic compounds, especially with Grignard reagents, have not been investigated. For example, the possibility of the addition of a Grignard reagent to the C=N bond and of the direct substitution of the alkoxy-group in isoureas by an alkyl residue may lead to interesting results, as has been shown for iminoesters.

The fairly large set and availability of the synthons for the preparation of a wide variety of isoureas have been by no means fully made use of, in our view, for the needs of medicine, biochemistry, and other purposes.

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Bifunctional complexones

K I Popov, N V Tsirul'nikova, N M Dyatlova

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Abstract. In the review, a systematic account is given of the methods of synthesis of bifunctional complexones and conjugates based on them, data on the physicochemical and biological properties of these compounds and their applications are analysed, and the prospects in the search for new ligands are examined. The bibliography includes 160 references.

I. Introduction

In the course of the development of the chemistry of complexones, attempts have been frequently made to construct molecules combining, together with the chelate fragment ensuring complex-forming properties, groups of atoms incapable of participating in the formation of complexes but imparting to the chelating agent new functions which were not previously characteristic of this compound.[1] The first 'hybrids' should legitimately include the analytical indicators synthesised at the beginning of the 1950s; Xylenol Orange **1**, phthalein complexone, alizarin complexone, thymolphthalexone, fluorexon, etc.[1,2] The chelating iminodiacetic acid (IDA or H_2ida) fragment and chromophoric groups are successfully combined in the molecules of these substances (Fig. 1, see over).

Later attempts were made to introduce into the complexone molecule a hydrophobic hydrocarbon group, imparting surface-active properties to the chelating agent,[3–6] paramagnetic spin labels,[7] etc.

However, complexones bound covalently to proteins, which appeared at the end of the 1970s, have aroused and continue to arouse the greatest interest.[8–12] This is associated with the fact that the products of the interaction of the protein of a bifunctional complexone and a cation — conjugates — have found extensive application in biology and medicine (see Fig. 2, p. 941).[1,8–13]

K I Popov Moscow State Academy of the Food Industries, Volokolamskoe shosse 11, 125080 Moscow, Russian Federation; State Institute for Chemical Reagents and Specially Pure Chemicals, Bogorodskii val 3, 107076 Moscow, Russian Federation. Fax (7-095) 963 74 83. Tel. (7-095) 963 74 60
N V Tsirul'nikova, N M Dyatlova State Institute for Chemical Reagents and Specially Pure Chemicals, Bogorodskii val 3, 107076 Moscow, Russian Federation. Fax (7-095) 963 74 83

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Despite the fact that all the 'hybrid compounds' mentioned above can perform simultaneously at least two fundamentally different functions, the term 'bifunctional complexones' became firmly established only after the introduction of the last variety of chelating agents.

At the present time, the term 'bifunctional complexones' embraces a range of substances containing, apart from the chelating fragment, a reactive group ensuring the covalent attachment of such a complexone to biological macromolecules (peptides, proteins).[1]

Various modifications of diethylenetriaminepentaacetic acid (DTPA or H_5dtpa), ethylenediaminetetraacetic acid (EDTA or H_4edta), and certain other complexones are usually employed to produce bifunctional complexones. Isothiocyanate, bromoacetamide, carboxymethoxy-, diazonium, or other similar groups are employed as groups with affinity for proteins.

So far as possible, the bifunctional complexones should satisfy the following requirements:

(i) To retain the ability to form thermodynamically highly stable complexes after immobilisation on the protein.

(ii) To become rapidly attached to the protein and to retain the cation in the chelating component for a sufficiently long time compared with the half-life of the radioactive label or the period required for natural elimination from the organism, which presupposes the existence also of kinetic stability (the lowest possible rates of dissociation of the complex in vivo), in addition to the thermodynamic stability.

(iii) Not to exert a significant influence on the biological properties of the antigen.

Furthermore, the conjugate obtained must have a low toxicity and must not accumulate in the organism.

By virtue of the ability of the chelating fragment to bind cations into highly stable complexes, the conjugates acquire properties characteristic of the given metal: radioactivity, paramagnetism, the ability to absorb or emit photons, the ability to catalyse certain chemical reactions, etc.,[14,15] whilst variation of the protein component in the conjugate, for example the combination of the bifunctional complexone with various monoclonal antibodies, significantly increases selectivity in the accumulation of the cation-label or the cation-base of the therapeutic preparation in an in vivo situation.[16,17]

The bifunctional complexone not only ensures the attachment of the cation to the protein but frequently lowers, as a result of complex formation, the toxicity of the metal and increases its 'acceptability' to the organism.[18]

Studies in the field of the synthesis and application of bifunctional complexones have been prosecuted extremely

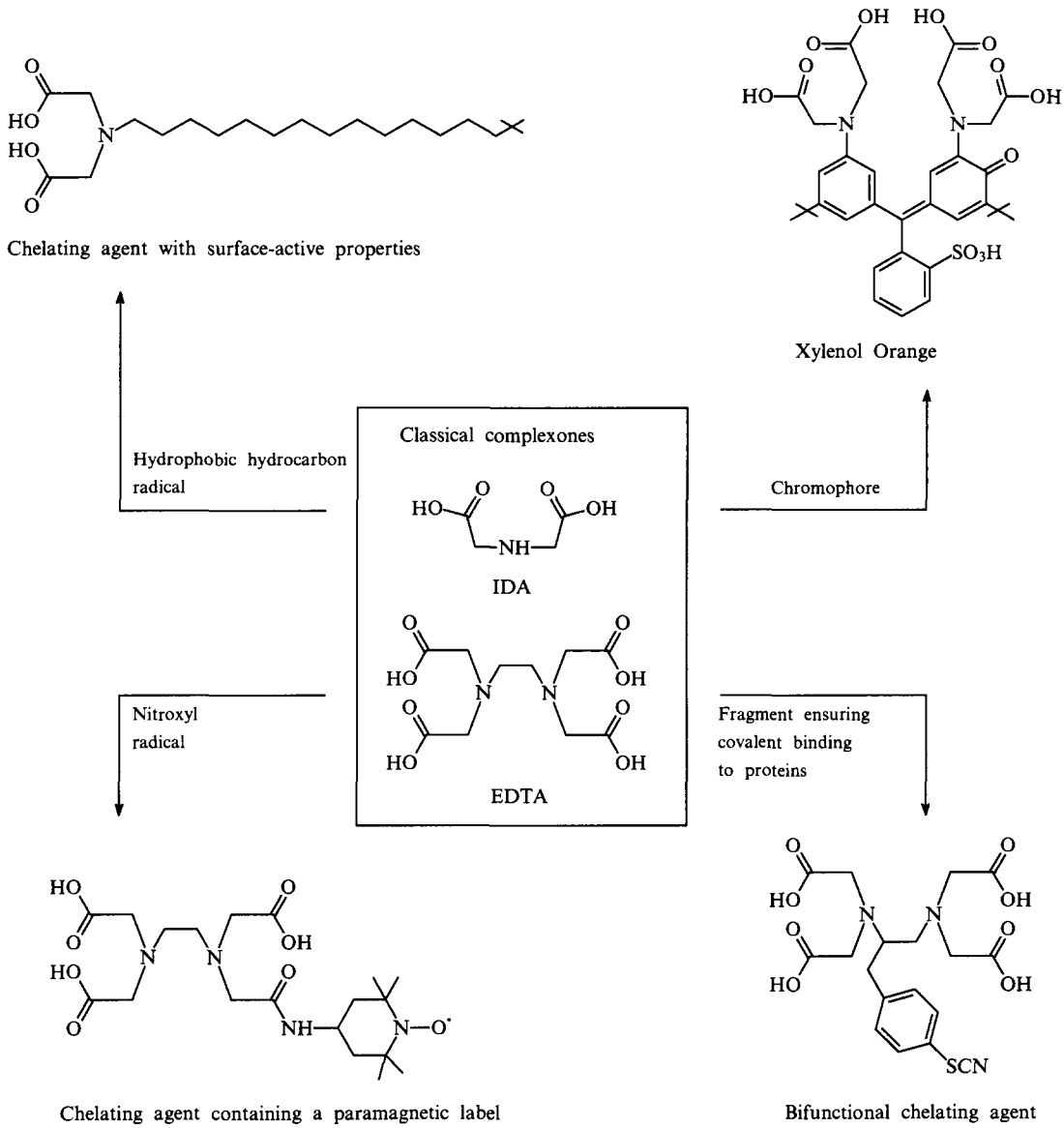


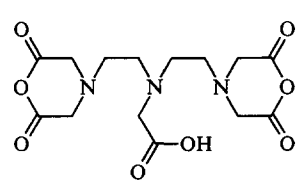
Figure 1. Different versions of the coupling of chelating and other functional fragments. IDA = iminodiacetic acid; EDTA = ethylenediaminetetraacetic acid.

vigorously. The possibility of the application of complexes of radioactive cations in the diagnosis and treatment of different forms of cancer,[19-24] in immunological research,[25-31] in the study of enzymes,[32-34] and in the study of various organs[35-37] has been discovered. Equally extensive prospects have arisen in connection with the complexes of paramagnetic (NMR tomography)[38-40] and fluorescent-active cations.[41-44]

II. Methods of synthesis of bifunctional complexones

Nowadays it is possible to differentiate two approaches to the modification of complexone molecules. The first ensures the formation of a covalent antigen–complexone bond as a result of chemical reactions involving at least one of the acetate groups of the complexone (Fig. 2*a*, compound **1**). The potential denticity of the chelating component of the bifunctional complexone can then be reduced, since the complex-forming capacity of the oxygen atom, arising when the acetamide group is bound to the antigens, is lower than that of the analogous atoms in the ionised carboxy-group.

The starting materials for the preparation of bifunctional complexones are mixed (A-DTPA) and bicyclic (B-DTPA) anhydrides of DTPA, the bicyclic anhydride of EDTA, the *N*-hydroxysuccinimidic ester of DTPA (E-DTPA),[10,45-47] and certain other ligands.[10,46,48,49]



B-DTPA

The synthesis of such complexones is distinguished by its simplicity. Thus B-DTPA is obtained under heterogeneous conditions by heating DTPA in an excess of acetic anhydride and pyridine at 65 °C for 24 h with subsequent filtration of the reaction mass in order to separate the deposit of the target product.[50] Sometimes a mixture of pyridine and dioxane is used as the reaction medium.[45]

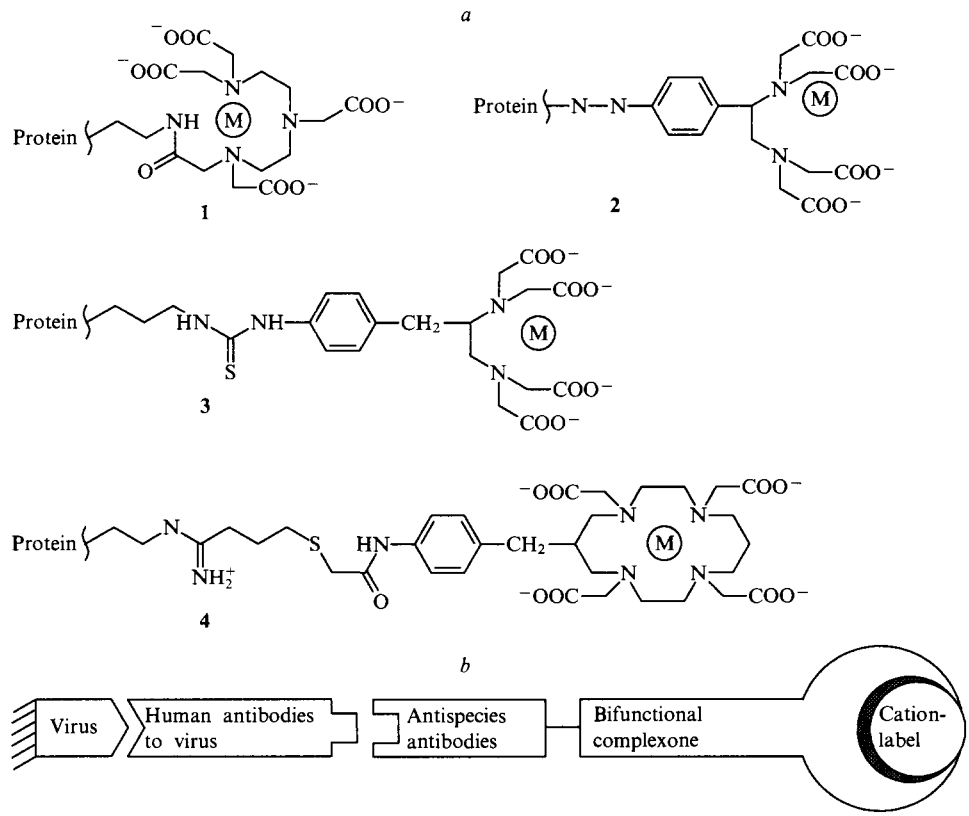
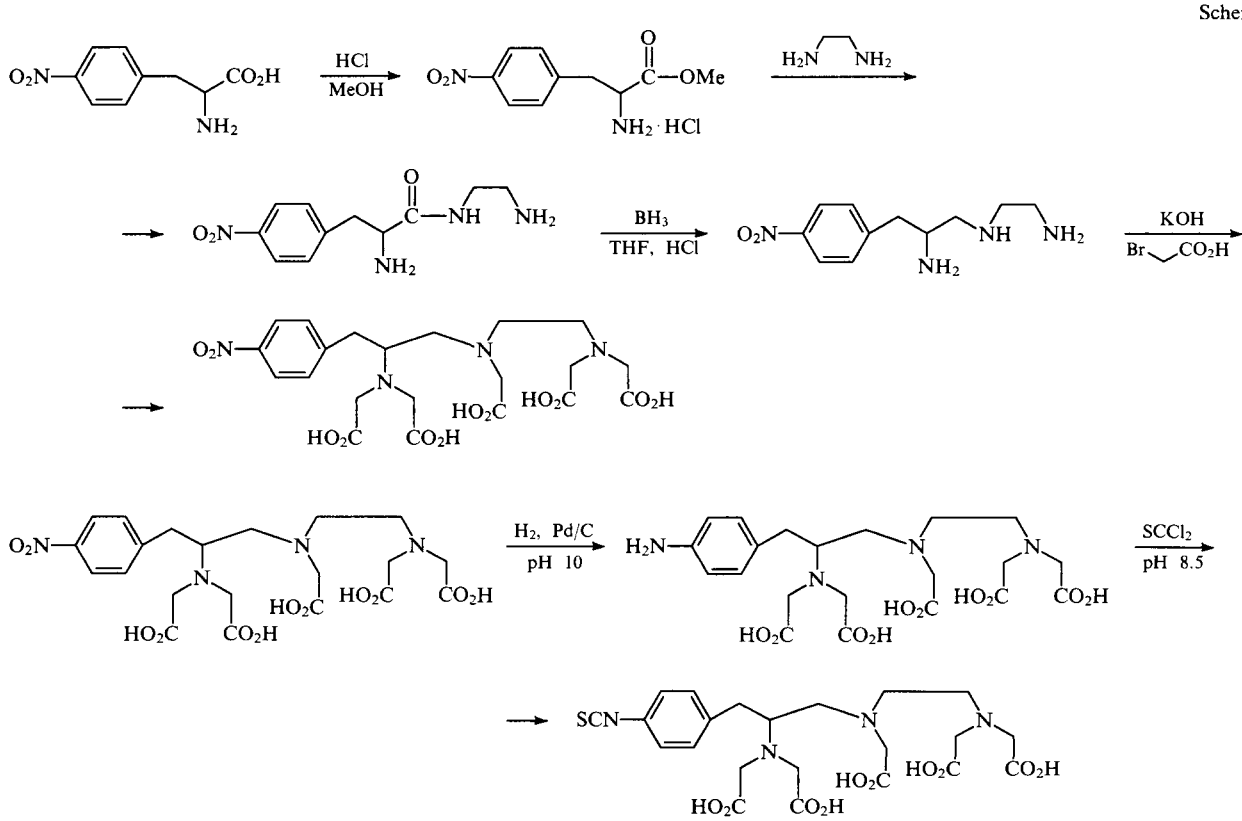
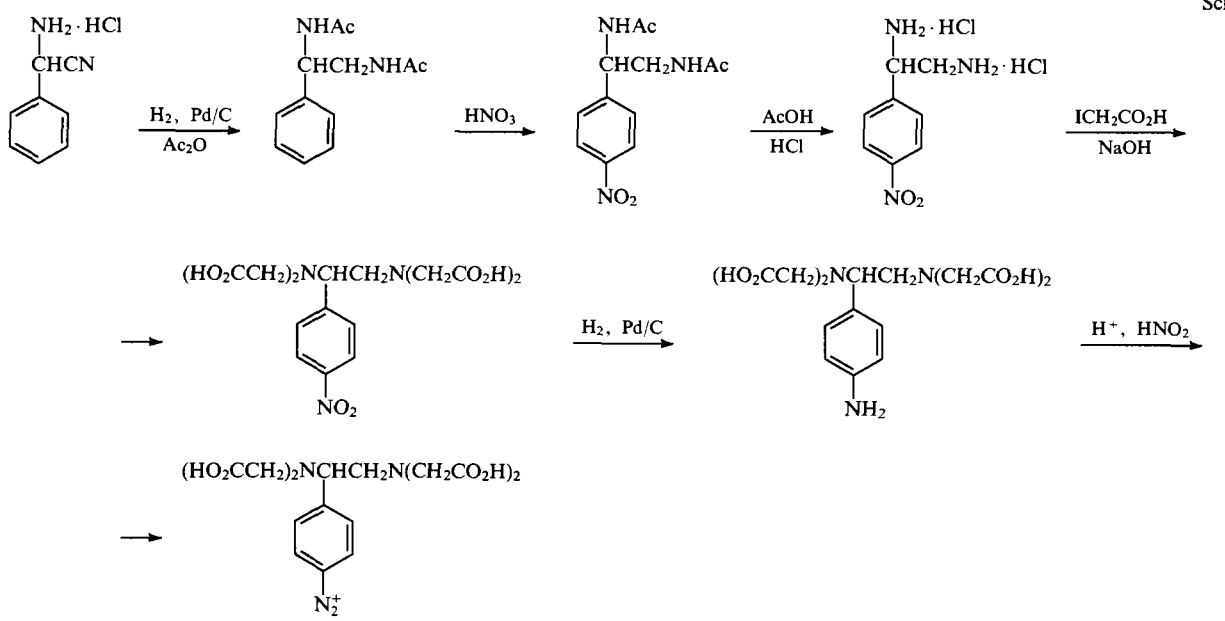


Figure 2. Conjugates formed by bifunctional complexones (*a*) and a general scheme for the diagnosis of viral diseases with the aid of bifunctional complexones (*b*).

Scheme 1



Scheme 2



E-DTPA is also synthesised under mild conditions by the reaction of DTPA with *N*-hydroxysuccinimide in the presence of triethylamine and dicyclohexylcarbodiimide.[27,51]

The possibility of obtaining carboxyalkylated derivatives of ethylenediamine, diethylenetriamine, and their analogues containing secondary amino-groups by the interaction of the above amines with monochloroacetic acid in the presence of calcium oxide is extremely promising.[52-54] The presence of the 'free' amino-group in the structures of such ligands gives rise to hope for their employment in the synthesis of bifunctional complexones with a specified structure.

Another approach in the creation of bifunctional complexones is based on the incorporation in the hydrocarbon skeleton of the complexone of a centre reactive in relation to proteins (Fig. 2*a*, compounds **2**–**4**). In this case, the chelating capacity of the complexone is retained after its immobilisation on proteins, but the synthesis itself is made significantly more complex. As a rule, either a phenyl or an alkylphenyl group with an isothiocyanate fragment in the *para*-position relative to the chelating component is introduced into the hydrocarbon skeleton of the complexone (EDTA, DTPA).[55,56] On subsequent conjugation, the isothiocyanate (diazonium, azide, haloacetamide) group participates in the formation of a covalent bond with the protein.

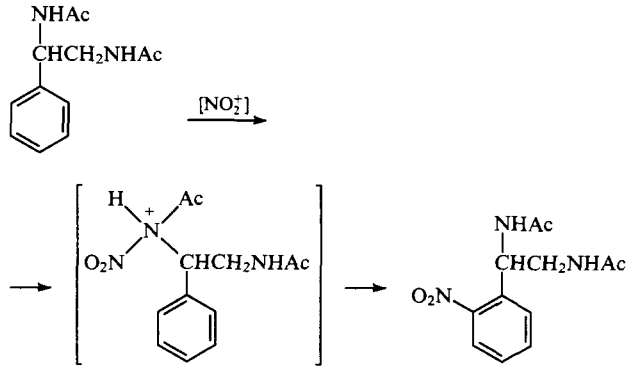
The synthesis of 1-benzyl-substituted derivatives of DTPA and EDTA is a two-stage process. The nitrobenzyl derivatives of the complexones are obtained initially, after which the functional group of the benzyl substituent is converted into the fragment employed for coupling to proteins, for example via Scheme 1 (see previous page).[34]

Scheme 2 represents the process involving the formation of a modified EDTA containing a benzenediazonium group in the ethylene bridge.[34]

It is noteworthy that the nitration of the amine, obtained by the catalytic hydrogenation of the hydrochloride of 1-phenylglycine nitrile in acetic anhydride, leads, according to NMR spectroscopic data, to the formation of a mixture of *ortho*- and *para*-isomers in molar proportions of 2:3. The formation of the *ortho*-isomer is probably preceded by the formation of an intermediate in the nitration of the diamine—an unstable *N*-nitroamide (Scheme 3).

A disadvantage of the method described above is also the low yield (< 30%) of diaminotetraacetic acid in the stage involving alkylation of the corresponding diamine dihydrochloride with an

Scheme 3



excess of iodoacetate or bromoacetate.[57] The use of methyl 2-amino-4-phenylbutyrate as the initial compound[10] instead of the hydrochloride of 1-phenylglycine nitrile makes it possible to reduce to a considerable extent the amount of the *ortho*-isomer formed on nitration and to obtain the analogous bifunctional complexone in a high yield. The small amount of the *ortho*-isomer (~10%) is easily removed by crystallisation.

The reason for the appreciable decrease in the yield of the *ortho*-isomer in this case is the separation from the aromatic ring of the chelating group produced by a distance equivalent to two hydrocarbon units and the consequent decrease in the risk of β-elimination.

New possibilities in the synthesis of bifunctional complexones have arisen by virtue of the use of α-aminoacids (α-AA) as the initial compounds.[34]

α-AA → α-AA ester → α-AA amide → α-AA diamine

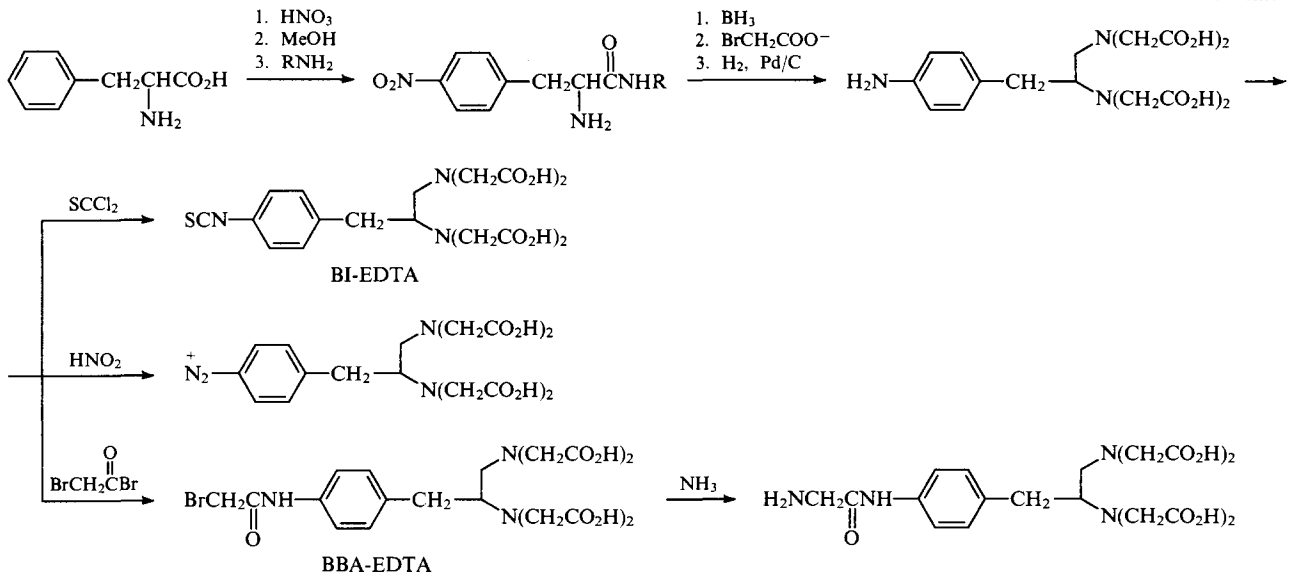
→ bifunctional complexone

By employing amines with different structures for the preparation of the amide, it is possible to vary widely the chelating properties of the target product.

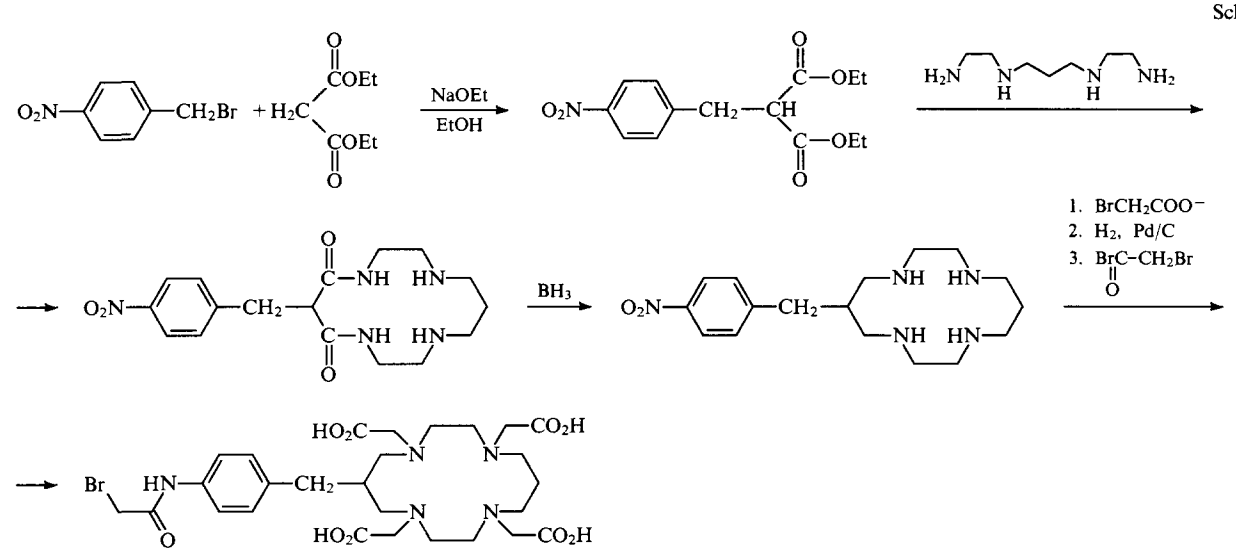
Scheme 4 illustrates the synthesis of bifunctional reagents in which phenylalanine is employed as the initial compound.[27]

The only serious disadvantage of the above synthesis is the need to use the toxic thiophosgene in the stage where the amino-group is substituted by the isothiocyanate group.

Scheme 4



Scheme 5



The multistage nature of the process is to a large extent compensated by the virtually quantitative yield of (*S*)-*N*-4-{2,3-bis[bis(carboxymethyl)amino]propyl}phenylbromoacetamide (BBA-EDTA) and its phenyl isothiocyanate analogue (BI-EDTA).[55]

Derivatives of tetraazacyclotetradecanetetraacetic acid (TATA of H_4tata) (Scheme 5) have also been obtained in a high yield using a readily available starting material.[58]

III. Synthesis of conjugates based on bifunctional complexones

In the preparation of conjugates, the sequence of reactions in the synthesis of the final products can be various. For BBA-EDTA, BI-EDTA, and the anhydrides of DTPA and E-DTPA, it is recommended that the chelating agent is initially coupled to the protein and then the cation-label is introduced into the system. For TATA, the synthesis is usually carried out in the opposite sequence,[10] but the first version is also permissible.

The coupling of the anhydrides of TATA and DTPA to proteins proceeds as a rule readily and under mild conditions. For example, in order to obtain the conjugates based on B-DTPA, the dried and purified anhydride of DTPA is treated with a bicarbonate buffer solution of the protein (10–15 mg ml^{-1} in 0.05 M solution of sodium bicarbonate at pH 8.5). The free DTPA is removed from the bound protein with Sephadex-650 molecular sieve or by centrifugation.[59]

The combination of B-DTPA with proteins is statistical in character: some of the protein molecules always remain free, whilst others combine with several B-DTPA fragments at once. Calculation shows that, for the average ratio [protein]:[B-DTPA] = 1:3, only a small proportion of the macromolecules remain unbound to the complexone, whereas for the 2:1 ratio more than 60% of the protein reacts with B-DTPA.[59]

It is quite evident that the proteins can lose activity as a result of immobilisation, the degree of degradation increasing with increase in the number of attached complexone molecules. It has been noted that the probability of side reaction involving so called 'cross' binding to the antibodies i.e. the 'cross linking' of the protein molecules with one another, is relatively high for A-DTPA. The chelating capacity of the complexone then diminishes sharply and it becomes necessary to carry out an additional purification of the reaction mixture in order to remove such 'blank' conjugates with a double molecular mass.[33]

Comparison of the relative effectiveness of the conjugation of B- and A-DTPA showed that the latter reagent is unstable, hydrolysing at an elevated temperature, and it is therefore not

possible to isolate and analyse it. Accordingly, the determination of the protein : anhydride ratio involves significant difficulties. On the other hand, B-DTPA is stable and the synthesis involving it is to a large extent susceptible to monitoring. A satisfactory reproducibility of the coupling reaction is attained as a result.[59]

It has been established that the effectiveness of the incorporation of the radioactive indium-111 into systems obtained by treating various proteins with B-DTPA ranges from 30% to 60% of the indium-111 isotope introduced, depending on the nature of the antibodies.[32]

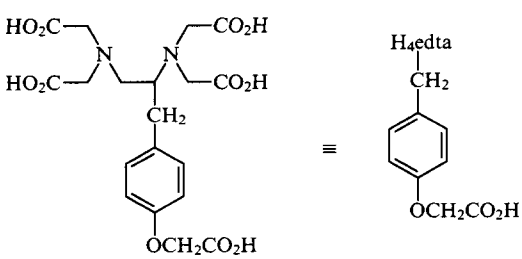
A minimal probability of cross-link formation has been noted for E-DTPA. For example, other conditions being equal, E-DTPA retains its antigen binding activity to a greater extent than B-DTPA — 100% and 70% respectively. Furthermore, the conditions needed to attain the maximum effectiveness of the coupling of E-DTPA to proteins are closer to the natural physiological conditions under which proteins exist than in the case of B-DTPA. In particular, maximum coupling efficiency has been noted for B-DTPA at pH 8.3, whereas in the case of E-DTPA it occurs in the region of pH 7.[60]

The number of variants of the coupling to proteins is much smaller for B-DTPA than for E-DTPA.[60] The bicyclic anhydride is capable of interacting mainly only with the accessible lysine residues, whereas E-DTPA adds also to the histidine and tyrosine fragments. Among the disadvantages of E-DTPA, one should include also its ability to form with proteins conjugates with a higher molecular mass and lower stability in vivo than the conjugates formed by B-DTPA. The practical consequences of this may be a higher degree of accumulation of the E–DTPA-labelled proteins in the liver and a considerable dose of the accumulated activity in the kidneys and in the bladder.[30]

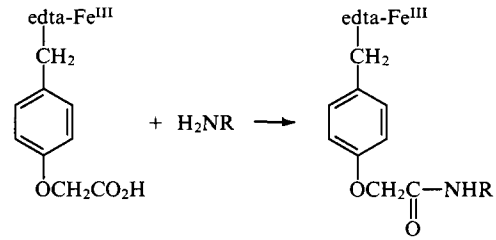
The coupling to proteins of the bifunctional complexones formed as a result of the modification of the hydrocarbon 'skeleton' is usually carried out by simple mixing of the components at pH 8–9 whilst cooling the mixture. The complexone is as a rule taken in excess. At the end of the coupling reaction, lasting on average several hours, the conjugate is separated from the reaction mixture by dialysis. It has been noted that in certain cases, when the average number of chelating molecules bound to the protein is greater than 3, a loss of the immune activity of the antibodies is observed.[10,20,35,37]

It has been established that the haloacetamide groups are distinguished by a low selectivity in reactions with natural macromolecules. These groups interact effectively with a wide range of nucleophilic centres of proteins, including the sulfhydryl and amino-groups. The resistance of these groups to hydrolysis under the conjugation conditions (37 °C, pH 9.5) makes it possible to obtain the necessary number of protein-bound chelating groups ($c > 10^{-5}$ M), which ensures, in its turn, the rapid and quantitative binding of the metal cations in the next stage of the synthesis of the conjugate.[23] The immune activity of the complexone–protein conjugates is retained for the group of compounds under considerations at a level of 77%–84% relative to control antibody specimens.[61]

1-(*p*-Carboxymethoxybenzyl)-EDTA occupies a special place in the overall series of benzyl derivatives of EDTA.



A necessary condition for the formation of the imide bond between this compound and the protein molecule is the preliminary formation of a complex with a metal, which protects the chelating fragment from undergoing the analogous reaction. A cation-label, for example the radioactive indium(III) or iron(III) isotopes, is usually selected as the complex-forming agent. The iron complexonate is obtained by the interaction of the complexone with iron(II) at pH 2. The complexonate produced is rapidly oxidised by atmospheric oxygen to the corresponding iron(III) derivative [subsequently the iron(III) complexonate must be protected against photodegradation]. The iron(III) chelate, taken in excess, readily reacts with human serum albumin at 20 °C and pH 5.[62]



R = protein

If necessary, the iron(III) may be removed from the conjugate by reduction during dialysis, by employing a buffer solution containing ascorbate and citrate ions and EDTA at pH 5. In the absence of ascorbate ions, the iron(III) is not removed from the conjugate.[62]

Cations can be easily introduced into the system by simple mixing of the components (with some excess of the metal) at pH 6, established with the aid of an acetate buffer solution.[10,63] Depending on the nature of the cation and of the chelating component of the immobilised protein, the reaction lasts from several minutes (indium-111)[10] to several hours (yttrium-90).[64] The conjugate is separated by dialysis from the excess unreacted components. It has been shown[30,65] that the addition of EDTA is extremely effective in the stage involving the elimination of the free radioisotope from the conjugate.

IV. Physicochemical properties and structures of bifunctional complexones and the conjugates based on them

There are virtually no literature data on the most important physical, chemical, and biological properties of the bifunctional complexones. This can be accounted for to a large extent by the difficulty of isolating such complexones and of eliminating the impurities from the latter (this is needed for accurate potentiometric and spectroscopic studies) and also by the low yield of the final products. Therefore, in constructing the bifunctional complexone molecule, designed to chelate a specific cation, and also in the initial quantitative and qualitative assessment of its complex-forming properties, one has to be guided by the information accumulated for the usual complexones and complexonates, introducing appropriate corrections into the latter.

1. Thermodynamics of the complex formation reaction

Bifunctional complexones, which constitute a special case of classical complexones, are capable of chelating the vast majority of the cations derived from the metals in the Periodic System.[1,10] For biological and medical purposes, the cations of radioactive isotopes (^{111}In, ^{99}Tc, ^{90}Y, ^{67}Cu, ^{46}Sc, ^{67,68}Ga, ^{153}Gd, ^{109}Pd),[10,66–71] paramagnetic cations (Gd^{3+}, Mn^{2+}, Fe^{3+}),[72–76] and fluorescent cations (Eu^{3+}, Tb^{3+})[77,78] are of greatest interest. The thermodynamics of the complex formation reaction is then considered taking into account the presence of the background biometals, for example calcium, which are present in vivo in an excess relative to the cation-label and behave as a competitor capable of displacing the label from the conjugate, reducing thereby the specificity of the action of the preparation introduced.[1,79–81]

For the estimation of the ability of the bifunctional complexone H_nL to form complexes with the cation of the metal M in a preliminary stage, use is made of the concentration stability constant K_{ML} measured at a fixed ionic strength I and a fixed temperature, i.e.

$$K_{ML} = \frac{[ML]}{[M][L]},$$

and also of the complex formation selectivity index — $K_{ML} : K_{CaL}$ (or $\Delta \lg K = \lg K_{ML} - \lg K_{CaL}$).

Our analysis of the literature values of the stability constants (see the stability constants handbooks[79-85] and the relevant reviews[86-88]) and inspection of the contents of the computer data bank produced for commercial use by the IUPAC Commission on Chemical Equilibria in 1993[89] revealed that the amount of thermodynamic data, permitting an indirect characterisation of the complex-forming capacities of the bifunctional complexones, is also extremely small. Direct thermodynamic studies on bifunctional complexones have been scarcely carried out. The first reports on this topic appeared comparatively recently.[90]

Table 1 presents certain data for EDTA and DTPA, which permit the qualitative estimation of the trends in the variation of the stabilities of the complexes on passing from classical complexones to their modifications modelling to some extent the bifunctional complexone.

The constants presented in Table 1 show that the introduction of aliphatic and aromatic groups into the ethylenediamine fragment of the complexone not only does not reduce the stability of the complexes but can actually tend to increase it. This effect is apparently associated with the stabilisation by the given group in solution of the ligand conformation most favourable for complex formation.

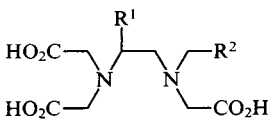
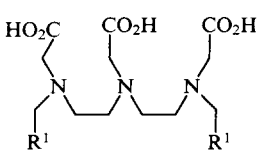
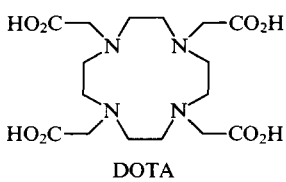
The replacement of one of the carboxy-groups by a hydrocarbon substituent leads unambiguously to a decrease in the overall stability of the complexes. However, there is then a possibility of an extremely significant increase in selectivity in complex formation by the typical cation-labels Cu^{2+} and Gd^{3+} relative to the endogenic background cations Zn^{2+} and Ca^{2+}.

It is remarkable that the replacement of the carboxylate fragment by the acetamide fragment also induces a sharp decrease in the stability constant. This suggests that in the case of gadolinium the decrease in the stability constant is associated with the decrease in the effective denticity of the ligand: the noninvolvement of the acetamide fragments in the formation of coordinate bonds with the lanthanide ion.

Ligands with 'built in' macrocycles are of considerable interest. Apart from the polychelating effect, the macrocyclic effect also makes an additional contribution in this case.[1,94-97] For example, the use of 1,4,7,10-tetraazacyclododecane-*N,N',N'',N'''*-tetraacetic acid (DOTA or H_4dota) instead of EDTA makes it possible to increase the stability of the europium(III) complexonate by ten orders of magnitude. The selectivity in relation to calcium ion increases simultaneously.[1] At the same time, the differences between the stabilities of the copper, calcium, and zinc complexes are abolished to a significant extent.

The next stage in the approach to a real system involves the consideration of the effective (and not concentration) stability constants K_{ef}, in which account is taken of the hydrolysis of the complexonate. The need for such allowance is due to the tendency of polyaminopolycarboxylic acids to be protonated at the physiological pH (7.2). For example, EDTA is present in the equilibrium mixture under such conditions both in the form of the complex and in the form of the anions $Hedta^{3-}$ and H_2edta^{2-}. This reduces significantly the fraction of the complex proper. Furthermore, the aquometal ions are also partly hydrolysed at the above pH and are present in solution in the form of monomeric and polymeric hydroxy-complexes. The constants K_{ef} make it possible to estimate the pH values most favourable for the complex formation reaction between the given ligand and the given cation.[1,98,99]

Table 1. Stability constants of the complexes formed by EDTA, DTPA, DOTA, and their derivatives (I = 0.1; 20–25 °C).

Ligand (H_nL)	R^1	R^2	$\lg K_{ML}$				Ref.
			Ca^{2+}	Zn^{2+}	Cu^{2+}	Gd^{3+}	
	H (EDTA)	COOH	10.79	16.68	18.86	17.27	88
	Et	COOH	11.75	18.23	20.6	18.6	85
	Ph	COOH	11.25	17.05	19.4	17.4	85
	H	Pr	16.1	–	12.7	13.07[a]	85, 91
	H	Ph	6.7	–	16.8	–	85
	COOH (DTPA)		10.89	18.55	21.53	22.56	88
	C(O)NHMe		7.17	12.04	13.03	16.85	18
	Py		7.97	14.02	17.50	16.83	18
 DOTA			15.85	18.90	19.06	28.21	92, 93

[a] Data for europium(III) (I = 1) are presented.

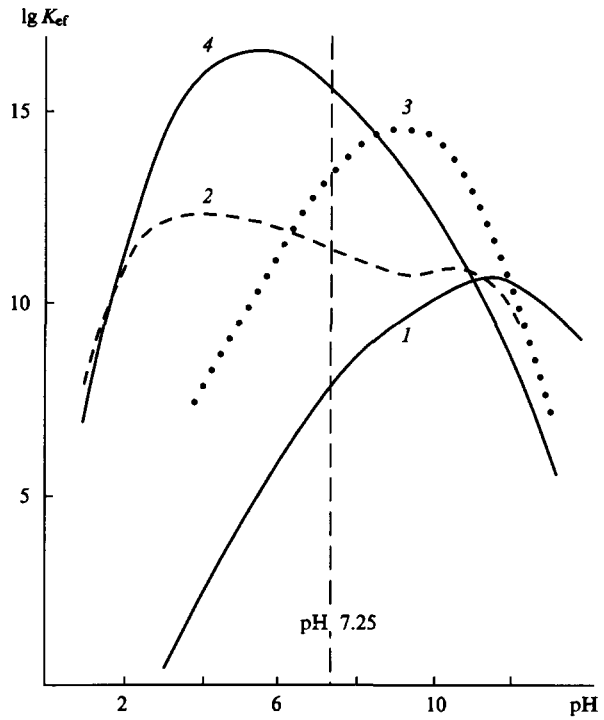


Figure 3. pH dependence of the effective stability constants of the complexes of EDTA with different ions: (*1*) Ca^{2+}; (*2*) Fe^{3+}; (*3*) Sm^{3+}; (*4*) In^{3+}.[100]

Fig. 3 presents the dependence of the logarithms of K_{ef} on pH for the complexes of EDTA with typical cation-labels: Fe^{3+}, Sm^{3+}, and In^{3+} (curves *2–4*). The corresponding values for the background element (calcium — curve *1*) are presented for comparison. The figure shows that in the alkaline region the complex formation reaction between EDTA and calcium becomes preferable to the reaction with indium or samarium.[100]

A clear idea about the ratio of the concentration and effective constants is provided by the following example. Despite the fact that the concentration stability constant of the iron(III) complex of EDTA is 10^6 times greater than that of the copper(II) complex of EDTA, at pH 7 the chelate $[Cuedta]^{2-}$ is 10^2 times more stable than $[Feedta]^-$ according to the calculations of the effective constants.[101]

It is also noteworthy that the calculations of the effective constants performed by different workers using different initial postulates can differ significantly[100,101] and as a rule require a critical analysis.

The problem of predicting the interaction between the complex-forming agent and the ligand in vitro in multicomponent systems, incorporating, apart from the bifunctional complexone, a series of bioligands and a wide range of background cations is much more complex.[79–81,101] Calculations have shown that the introduction of only one additional component into the In^{3+}–EDTA system reduces the K_{ef} at pH 7.4 by six orders of magnitude.[101]

Finally, difficulties which are truly impossible to overcome are faced by the experimenter when an attempt is made to assess quantitatively the thermodynamics of the complex formation reaction in vivo.[101,102] Nevertheless, on the whole knowledge of the thermodynamic stability constants makes it possible to predict fairly successfully the stability of the conjugate.[68,103]

2. Kinetic stability of the conjugates

Apart from the thermodynamic stability of the conjugates, when the latter are modified it is necessary to take into account also their kinetic stability: the rate of loss by the conjugate of the cation as a result of the dissociation of the complex or the substitution reaction between its 'own' cation-label and the competing biometals. Therefore, together with the problem of creating a complex with the bifunctional complexone which is thermodynamically as stable as possible, the problem of retarding the decomposition of the coordination compound appears no less important.

The rates of formation of the complexonates from the aquometal ions and also of the reverse process involving their dissociation are comparable to the rate of exchange of the water molecules in the aquo-ion, i.e. are determined to a first approximation by the properties of the aquo-ions.[1,104]

The introduction of an element of rigidity into the structure of the complexone molecule, in particular the introduction of macrocycles, makes it possible to retard significantly the dissociation of the complex formed by the complexone. For example, while the electrostatic charge on the anion is the same, the rate of dissociation diminishes sharply in the series EDTA–CDTA–DOTA (CDTA or H_4cdta = cyclohexanediaminetetraacetic acid).[1,104] It has been suggested that the kinetic features established in vitro for the classical complexones are also valid for their bifunctional analogues in vivo.

The kinetics of the loss of the metal atom by chelate complexes under the conditions of the living organism have been investigated.[10,34,105] The decomposition of the complex is a consequence of the operation of several factors at once, both kinetic and thermodynamic. In particular, it has been shown that the copper(II) complexes in human blood serum lose the metal in conformity with the prediction based on the analysis of the properties of simpler compounds. Thus the macrocyclic complexonate formed by TATA loses copper at a rate of 1%–3% in 24 h, the chelate based on the DTPA monoamide loses it at a rate of ~50% in 24 h, while the complex based on benzyl-EDTA loses the metal faster still.

The rate of loss of the metal by indium(III) complexonate has been investigated (Table 2).[105] It follows from the data presented that the coupling of the bifunctional complexone to albumin does not influence significantly the rate of biodegradation of the complex. At the same time, it is necessary to note that the ratio of the rate of degradation of the butylamides of EDTA and DTPA is directly opposite to that for EDTA and DTPA. Nevertheless, on the basis of the coordination possibilities of the modified ligands, the tendency in the variation of the rate of degradation of the modified ligands should be of the same type as for the rates of degradation of the corresponding unmodified ligands. The significant scatter of data between different series of experiments indicates the existence of a poorly monitored error.

Table 2. Kinetics of the in vitro loss of indium(III) by complexones, bifunctional complexones, and their conjugates with albumin.[105]

Ligand	Rate of loss of indium by the complexonate ML(%) in 24 h
1-(*p*-Carboxymethoxybenzyl)-EDTA	0.028 (0.041)
1-Methyl-EDTA	0.060 (0.052)
Albumin-phenyl-EDTA	0.060
Albumin-benzyl-EDTA	0.11
EDTA	0.53 (0.67)
EDTA mono-n-butylamide	29.0
DTPA mono-n-butylamide	0.93
Albumin-DTPA	1.6
	2.5[b]
DTPA	2.3 (2.6)

[a] The transfer of indium from the initial chelate complex ML to the complex with transferrin was investigated in human blood serum at pH 7.3 and 37 °C; the data for a repeated series of experiments are presented in brackets.

[b] A 0.01 M glycine solution was additionally introduced into the system.

3. The structure of the complexonates

Together with the thermodynamic, kinetic, and biological properties of the bifunctional complexones, their structure is an extremely important practical characteristic: the real denticity of the ligand and the coordination number of the cation. This is particularly important for the NMR-contrasted substances, since their capacity for paramagnetic interaction with the substrate is higher, other conditions being equal, the greater the number of water molecules retained in the coordination sphere of the paramagnetic cation incorporated in the conjugate.[106,107]

The structures of the metal complexonates have been examined in brilliant reviews.[108-110] Here we shall dwell only on two most important features discovered by analysing the results of more than 300 X-ray diffraction studies:

(i) The coordination number of the cation coordinated by the complexones frequently proves to be higher than those observed for the same ions in complexes with simple monodentate ligands. For example, manganese(II), cobalt(II), magnesium(II), and iron(III) in their EDTA and DTPA complexes exhibit a coordination number of 7, which is unusual for these metals. Because of this factor, the hexadentate EDTA ligand does not displace the entire water from the inner coordination sphere of iron(III), while the anion $[Fe(H_2O)edta]^-$ is a more effective relaxant than might have been expected. Indium(III) has a coordination number of 7 in its EDTA complex[108] and 8 in its DTPA complex.[111]

(ii) For all the structurally investigated crystalline normal complexonates ML and ML_2 with a coordination number greater than or equal to the denticity of the ligand, all the electron-donating ligand atoms are coordinated to the cation. Not a single case has been found in which the water molecule competed with the deprotonated carboxy-group for a site in the coordination sphere of the cation, i.e. a situation where the water molecule would have entered into the composition of the coordination sphere of the metal while one of the deprotonated carboxylate groups remained 'free'. On the basis of these data, one may predict, with a high degree of probability, the degree of shielding of the cation by the ligand on the basis of the structure of the molecule of the chelating agent itself.

Here it is appropriate to mention the lively discussion concerning the possibility of the retention of the structure of the complexonate when it passes from the crystalline phase to an aqueous solution.[112-118] Systematic radiospectroscopic[107,119-122] and EXAFS studies[123] in recent years have shown that the principal features of the structures of the complexonates, in particular the denticity of the ligand, are retained on dissolution. Thus the prediction of the structures of both simple complexonates and of the chelating component of the conjugates of bifunctional complexones in solution, based on X-ray diffraction structural data, is entirely correct.

V. Certain problems in the search for new effective ligands

In the general case, the isolation and analysis in a 'pure form' of any factors influencing the stability constants K_{ML} of polydentate, including bifunctional, complexones are extremely difficult. Thus any variation of the denticity of the ligand is as a rule coupled with the simultaneous variation of several parameters: the electrostatic charge, the size of the chelate ring, the ratios of the numbers of electron-donating atoms of different nature, etc.

Procedures such as variation of the denticity and of the dimensions of the rings potentially capable of being formed and the introduction into the structure of the chelating agents of elements of rigidity as well as heteroatoms, which ensure the selectivity of action in relation to the cation under consideration, are most widely used.[1]

For example, the introduction of the phosphonate group instead of the carboxylate group sharply increases the selectivity of the chelating agent in relation to copper(II) ions (Fig. 4). The tropicity (selectivity) in relation to bone tissue frequently

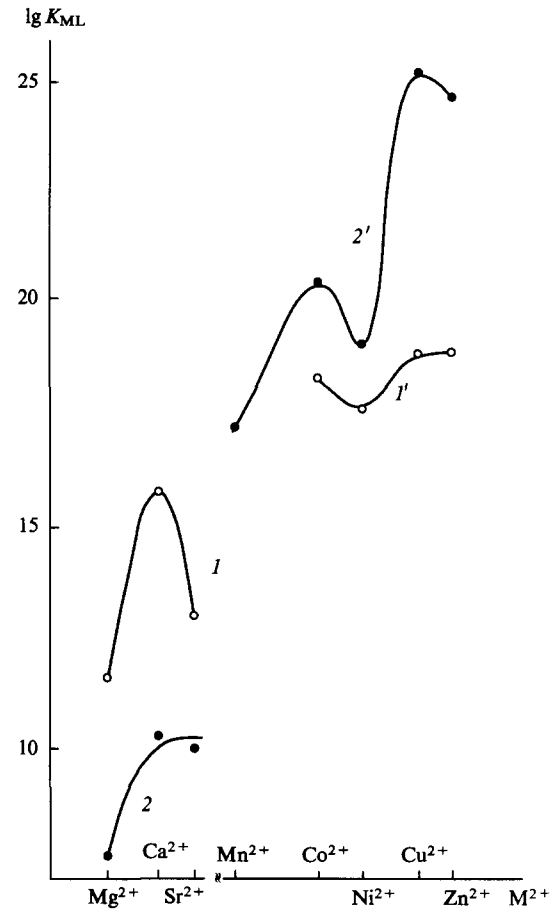


Figure 4. Relative changes in the stability constants in the series of alkaline earth (curves *1* and *2*) and 3*d* cations (curves *1'* and *2'*) for DOTA (curves *1* and *1'*) and its methylenephosphono-analogue (curves *2* and *2'*).[1,89,92,93]

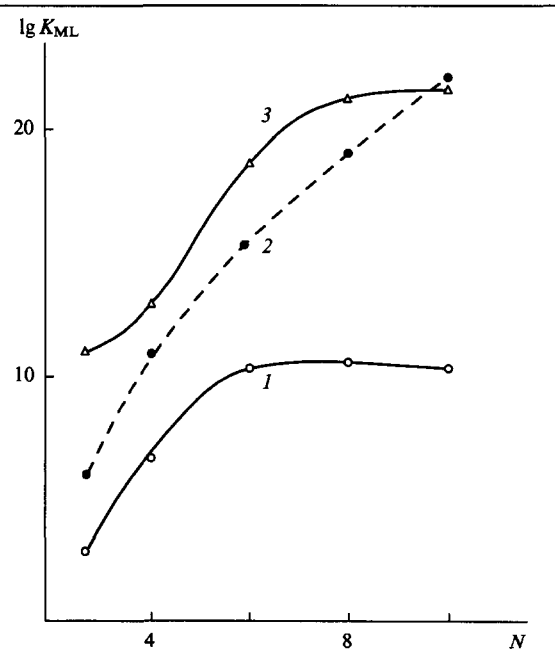


Figure 5. Dependence of the stability constants of the M^{n+} complexonates on the potential denticity of the ligand (*N*); M = Ca (curve *1*), La (curve *2*), or Cu (curve *3*). Data[85] for IDA, NTA (NTA or H_3nta = nitrilotriacetic acid), EDTA, DTPA, and TTHA (TTHA or H_6ttha = triethylenetetraminehexaacetic acid), considered as models of tri-, tetra-, hexa-, octa-, and deca-dentate chelating agents, were employed.

increases under these conditions in the complex formed.[124,125] An increase in the denticity and the charge of the ligand (Figs 5 and 6) as a rule renders this ligand more selective in relation to lanthanides, which have large coordination numbers.[126-129]

At the same time effects which are difficult to explain are also observed. For example, there is no equivalent increase in the stability of the complexes of the barium ion on passing from the hexadentate EDTA to the octadentate DTPA, although the size of the ion is not less than that of the lanthanide ions.

The creation of a chelating agent for a specific cation frequently extends over many decades. As an example, we may consider the development of events in the construction of the molecule of the optimum chelating agent for the iron(III), gallium(III) and indium(III) ions.

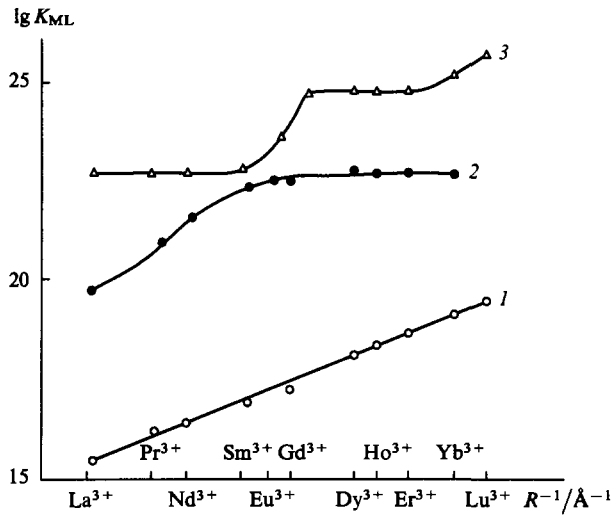
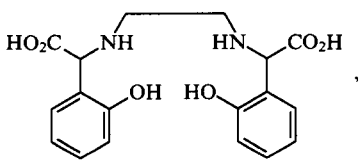
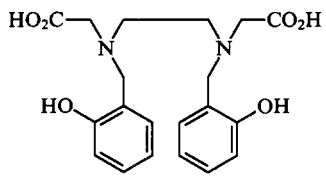


Figure 6. Dependence of the stability constant of the chelating agent on the ionic radius of the lanthanide (R):[85,88,89,93] (*1*) EDTA; (*2*) DTPA; (*3*) DOTA.

At the end of the 1950s and the beginning of the 1960s, it was found that the combination in the complexone molecule of fragments of ethylenediamine-*N,N'*-diaacetic acid and phenol, which happens in *N,N'*-ethylenebis[2-(*o*-hydroxyphenyl)glycine] (H_2ehpg),



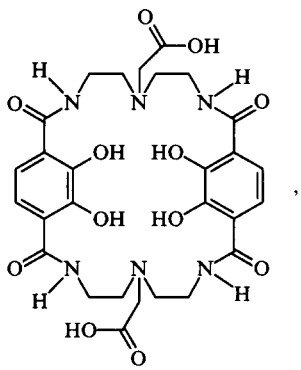
increases sharply the stability of the iron(III) complex ($\lg K_{ML}$ = 33.9) compared with the universal chelating agents such as EDTA ($\lg K_{ML}$ = 25.0).[130,131] The success achieved initiated the synthesis of a series of preparations with contrasting properties.[132-137] However, according to L'Eplattenier et al.,[138] the relative positions of the donor atoms in the ligand considered generated a steric hindrance to their simultaneous involvement in coordination. Later X-ray diffraction studies on the complexes $[Mg(H_2O)_6][Gaehpg]_2 \cdot 3H_2O$, $[Co(H_2O)_6][Coehpg]_2 \cdot 4H_2O$, $Na_2[Cuehpg] \cdot 5.5H_2O$, as well as the iron(III) complex[139-140] showed that these fears were groundless: in all the complexes investigated, the ligand exhibits the maximum possible denticity of six by coordination of both nitrogen atoms, the two oxygen atoms from each carboxylate group, and the two oxygen atoms of the deprotonated hydroxy-groups. Nevertheless, the sterically free complexone ethylenediamine-*N,N'*-di(2-hydroxybenzyl-*N,N'*-diaacetic acid (H_2hbed),



made it possible to achieve the highest attained stability for an iron(III) complex: $\lg K_{ML}$ = 39.68.[138] The corresponding constants for indium(III) and gallium(III) also proved to be some of the highest (39.66 and 39.57).[141] These studies stimulated in their turn the synthesis of a series of bifunctional ligands based on H_2hbed.[68,142]

Subsequent experiments on the modification of similar structures led to the following results. The replacement of the carboxy-groups in H_2hbed by phosphono-groups made it possible to increase the selectivity of the complexone in relation to the copper(II) ions in the series of 3*d* elements.[143] Although another modification of H_2hbed, involving the replacement of the phenol moiety by a pyridine group, led to the formation of iron(III) complexes less stable than the corresponding compound derived from H_2hbed ($\lg K_{ML}$ = 36.91), it made it possible to increase its solubility and also its acceptability to the human organism.[143,144]

Contrary to expectations, attempts to synthesise on the basis of H_2hbed the macrocyclic complexone 4,17-bis(carboxymethyl)-10,11,23,24-tetrahydroxy-8,13,21,26-tetraoxo-9,10,11,12 : 22,23, 24,25-dibenzo-1,4,7,14,17,20-hexaazacyclohexacosane,[145]



did not lead to a further increase in the stability of the iron(III) complexes, although the stability constant proved to be extremely high — $\lg K_{ML}$ = 37.6 (25 °C, I = 0.1).

It is noteworthy that a high stability of the complex is by no means always the main aim. The structure of the chelating agents is frequently dictated by purely biological or methodological features. For example, as a consequence of the low stoichiometric chelate : protein ratios, the cyclic dianhydride of DTPA proved to be entirely effective for the creation of bifunctional conjugates with radioactive cations.[34] However, magnetic-resonance contrasting requires complexes with a high chelating agent : protein ratio. Under these conditions, the given chelating agent is less suitable,[146] since an increase in the relative content of the dianhydride of DTPA entails a sharp increase in the number of intermolecular covalent bonds involving it and in the number of heterogeneous products formed on conjugation; under these conditions, the reproducibility and technological applicability of the synthesis fell.

This obstacle can apparently be overcome by varying the macromolecular component of the conjugate. For example, when albumin was replaced by polysaccharides, it was possible to obtain conjugates with DTPA and gadolinium(III) virtually without intermolecular cross links.[147]

Another problem is the permeability of the cell membrane to the conjugate. Its solution requires the optimisation of a large

number of parameters. It has been shown[148,149] that the membranes are satisfactorily permeable to electrically neutral complexes. Electrical neutrality also reduces the osmotic pressure. However, this is accompanied by a decrease in the solubility of the complexonate itself[1] and also in the effective denticity of the complexone, which leads as a rule to a decrease in the thermodynamic stability of the complex and hence to an increase in its toxicity owing to the removal from the complex of a large amount of the cation-label in a 'free' state.

For example, the gadolinium complex of DTPA proved to be an extremely effective contrasting agent in NMR tomography by virtue of its high stability constant.[150] However, as a consequence of the high negative charge of $[Gddtpa]^{2-}$, this preparation is poorly assimilated through the gastrointestinal track[151] and can be used only in the form of injections. The replacement of DTPA by its dimethylamide derivative made it possible to obtain an electrically neutral gadolinium complex with a significantly higher permeating capacity but a lower thermodynamic stability in relation to dissociation into the 'free' ligand and the metal ion. However, subsequent studies showed that the toxicity of the complex not only did not increase but actually fell (Table 3). This is due to the fact that the stability of the complexes of the dimethylamide of DTPA with ions competing with gadolinium (calcium, zinc) diminishes to an even greater extent and under in vivo conditions the selectivity in the binding of gadolinium and the lethal dose increase.[18]

Table 3. Results of toxicological studies on gadolinium complexes (intravenous administration to mice).[18,151]

Ion investigated, complex	$\Delta \lg K_{ef}$ [a]	LD_{50}/ mmol kg^{-1}
$[Gd^{3+}aq]$	–	0.4 [b]
Na_2Hdtpa - BMA [c]	–	0.16
Na[Cadtpa - BMA]	–	16.6
[Gddtpa - BMA]	9.04	14.8 (0.7)
Na_2[Gddtpa]	7.04	5.6 (0.2)
	–	10.0 [b]
[Gddtpa - BP] [d]	5.32	2.8 (0.1)
Na_2[Gdedta]	4.23	0.3 (0.1)

[a] The difference between the logarithms of the effective stability constants of the gadolinium and zinc complexes with the given ligand at pH 7.4 was adopted as $\Delta \lg K_{ef}$.
[b] Intravenous administration to rats.
[c] dtpa - BMA = DTPA *N,N″*-bis(methylamide).
[d] dtpa - BP = *N,N″*-bis-(2-pyridylmethyl)-DTPA.

It is remarkable that an X-ray diffraction study of the gadolinium(III) complex of the dialkylamide of DTPA[152] did not reveal a decrease in the denticity of the complexone compared with the DTPA itself;[153] a coordination number of 9 in the case of gadolinium is achieved as a result of the presence of the octadentate ligand and one water molecule. Admittedly, the average metal - oxygen distances in the amide fragments proved to be greater than in the acetate fragments. The problem whether this structure is retained on dissolution of the complex still remains open.

* * *

On the whole one may conclude that the predictions of the thermodynamic and kinetic stabilities of the conjugate based on estimates of the properties of simple model chelates have proved to be fairly reliable. In particular, the high stability constants ($\lg K_{ML} > 20$) of the indium(III) complex of EDTA and the gadolinium(III) complex of DTPA make it possible to obtain effective indium- and gadolinium-containing diagnostic and therapeutic preparations, in which the chelating fragment is based on EDTA and DTPA derivatives.[154-157] The approach based on the kinetic stability of CDTA and DOTA complexonates proved no less fruitful. Thus the conjugates based on the CDTA and DOTA ligands retain the kinetic features characteristic of their classical analogues.[158,159]

On the other hand, successful bioconjugates could not be created on the basis of complexones such as IDA and NTA, which form complexes with low and moderate stabilities ($\lg K_{ML} < 17$).

However, one should note that, even in the case of the classical chelating compunds, it is not always possible to predict the optimum effect in vivo. For example, in selecting the ligand for the extraction of plutonium from the human organism it was found that the DTPA-based preparation was just as effective as the tetracarboxycatecholate ligand, which forms with plutonium complexes more stable by a factor of 10^{10} than those formed by DTPA.[160]

Bifunctional complexones constitute a vigorously developing field in the chemistry of chelate compounds. It may be expected that in the immediate future the search for chelating agents and conjugates with a specific tropicity in relation to particular organs and tissues will assume a greater importance.

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Kinetics of the thermal decomposition of alkyl derivatives of Group III and V elements

V A Yablokov, N V Yablokova

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Abstract. The results of kinetic studies on the thermal decomposition of alkyl derivatives of Group III and V elements, used to obtain semiconducting epitaxial structures, are surveyed. Their reaction paths in the gas phase and on the surface of epitaxial layers as well as the factors influencing the mode of decomposition are analysed. The possibility of the formation of complexes between the components of the organoelement mixture during their joint pyrolysis is demonstrated. The bibliography includes 128 references.

I. Introduction

Organometallic compounds (OMC) and hydrides are used as a source of the metal in the formation of epitaxial layers of semiconducting materials.[1–3] The decomposition of the OMC and hydrides on the surface, known as the OMC method or as the metal organic chemical vapour deposition (MOCVD) or the metal organic vapour phase epitaxy (MOVPE) method, is undoubtedly an effective technological process, which makes it possible to achieve the selective growth of epitaxial layers with the required composition and thickness and the necessary set of properties.[4,5] Manasevit was the first to propose the use of the reaction of trimethylgallium with arsine in order to obtain epitaxial gallium arsenide layers.[6,7] This reaction can be formulated by means of the following overall expression:

$$(CH_3)_3Ga + AsH_3 = GaAs + 3CH_4.$$

In subsequent studies,[8,9] the method was used to grow films of organoelement compounds (OEC) of Group III–V elements. This procedure was used to obtain GaP films from $(CH_3)_3Ga$ and PH_3, GaAsP films from $(CH_3)_3Ga$, PH_3, and AsH_3, GaAsSb films from $(CH_3)_3Ga$, SbH_3, and AsH_3, etc. AlAs, GaN, AlN, $GaAs_xP_{1-x}$, $GaAs_xSb_{1-x}$, InAs, GaInAs, InAsP, InP, etc. films, based on the alkyl derivatives of Group III elements and nitrogen, phosphorus, arsenic, and antimony hydrides, have been grown similarly.[8,9]

Initially the investigators were interested exclusively in the technological problems associated with the construction of the reactors, the behaviour of the carrier gas, and the selection of the substances required, problems of mass transfer and hydrodynamic aspects being discussed.[9–11] At the present time, serious attention has been devoted to the fundamental principles of these technological processes: the mechanisms of the chemical reactions occurring in the gas phase and on the surface.[12–14] In his review,[5] Shaw distinguishes the following stages in the MOCVD process: (1) the supply of the reactants to the film growth region; (2) diffusion of the reactants to the surface of the support; (3) adsorption of the reactants on the surface; (4) surface processes involving chemical reactions, surface diffusion, and the binding of deposited materials to the support; (5) desorption of the gaseous chemical reaction products; (6) diffusional transport of the products in the stream of carrier gas; (7) removal of the reaction products from the growth region.

Stages 3–5 generally determine the rate of the deposition process and its principal physicochemical characteristics. In the chain of problems comprising the synthesis, purification, and stabilisation of the OEC, the kinetics, thermodynamics, and mass transfer of the OEC, and the design features of the reactors for the growing of epitaxial layers, each has independent importance. However, it is recognised that the factor inhibiting the development of the chemical gas-phase deposition is primarily the difficulties of understanding the mechanism of the pyrolysis of the OEC.[12–14]

In the present review, attention is concentrated on the consideration of the mechanisms and rates of the thermal decomposition reactions of the OEC of Group III and V elements in the gas phase and under the real conditions in the growth of films as a result of chemical deposition from the gas phase. The study of the kinetics of the thermal decomposition of the above classes of compounds is of theoretical interest for the development of the OEC chemistry and ensures the solution of the technological problems in the preparation of Group III–V semiconducting materials.

The pyrolysis of the OEC to the element and hydrocarbons is a complex chemical process. The multistage nature of the homolytic reactions involving the abstraction of alkyl groups from the initial and intermediate OEC is combined with molecular decomposition reactions (β-elimination). The homogeneous and heterogeneous stages are manifested in different ways

V A Yablokov Department of Chemistry, Nizhnii Novgorod State Academy of Civil Engineering, ul. Il'inskaya 65, 603600 Nizhnii Novgorod, Russian Federation. Fax (7-831) 234 02 01
N V Yablokova Institute of Chemistry, Lobachevskii Nizhnii Novgorod State University, prosp. Gagarina 23, korp. 5, 603600 Nizhnii Novgorod, Russian Federation. Fax (7-831) 235 64 80

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in the pyrolytic reactions. As a consequence of the dual action of the wall, which is involved in the initiation and the destruction of the active centres on the surface, cases are possible where, despite the presence of heterogeneous stages, the rate of the overall process is independent of the ratio of the surface area of the walls (S) to the volume (V) of the reactor.

The homogeneous-heterogeneous character of the pyrolysis of the OEC and the involvement of these compounds in radical and molecular consecutive-parallel elementary reactions is the principal reason why it is impossible to establish a chemical mechanism which corresponds to the experimentally established macrokinetic law. Nevertheless, the knowledge of the macrokinetic laws makes it possible to solve a series of general and specific problems — in the first place, to test the validity of the hypotheses concerning the reaction mechanisms. The postulated mechanism is tested by comparing the experimental and theoretical and kinetic laws. The discrepancy between experiment and theory is a reliable sign that the proposed mechanism is erroneous. On the other hand, consistency between theory and experiment is not a sufficient basis for the adoption of the postulated mechanism.

Furthermore, the knowledge of the macrokinetics makes it possible to distinguish certain characteristic features of the reaction investigated. Thus a fractional order with respect to the OEC concentration and the independence of the rate of reaction of the concentration of one of the reactants yield reliable information about the involvement of free radicals in the reaction and about the role of the reactants in the rate-limiting stage of the process. Here one should also include the determination of the heterogeneity factor (S/V). The variation of the rate of the overall reaction as a function of S/V indicates an appreciable contribution of the desorption process (the fifth stage) and of the reactions at the interface.

There have been fairly numerous kinetic measurements on the pyrolysis of OEC of Group III and V elements, but they are frequently contradictory. Systematic treatment and discovery of the general features of the variation of the reactivity of individual OEC and their mixtures in the gas state and under the conditions of the growth of epitaxial layers will make it possible to select keys to the regulation of these processes.

II. Kinetics of the thermal decomposition of alkyl derivatives of Group III elements

The most 'puzzling' OEC among the compounds of Group III elements are probably organoaluminium compounds and particularly $(CH_3)_3Al$. The formal kinetics of its thermal decomposition were investigated for the first time by Yeddanapalli et al.[15] In the temperature range 570–610 K, the rate of thermal decomposition of $(CH_3)_3Al$ is described by the equation for a reaction the order of which is 3/2. The rate constant can be expressed as follows:

$$k = 8.1 \times 10^{15} \exp\left(-\frac{188.3}{RT}\right).$$

It is independent of the initial pressure of the gaseous $(CH_3)_3Al$ in the pressure range $(0.2-1.14) \times 10^4$ Pa. The variation of S/V hardly affects the constant k. The principal gaseous reaction product is methane (91 vol.%–98 vol.%). In the presence of hydrogen, the activation energy (here and henceforth E is expressed in kJ mol^{-1}) for the $(CH_3)_3Al$ decomposition reaction decreases from 188.3 to 127.6 kJ mol^{-1}. The numerical values of the rate constants decrease under these conditions, while the reaction order remains 3/2.

In later studies,[12,16] it was reported that the pyrolysis of $(CH_3)_3Al$ is first order with respect to the organoaluminium compound.

The reaction was carried out under a hydrogen atmosphere (10^5 Pa), where the partial pressure of $(CH_3)_3Al$ was ~200 Pa. The pressure was sufficiently low to allow the virtual exclusion of the sensitised decomposition of the OEC.

$$(CH_3)_3Al + \dot{C}H_3 \longrightarrow (CH_3)_2Al\dot{C}H_2 + CH_4$$

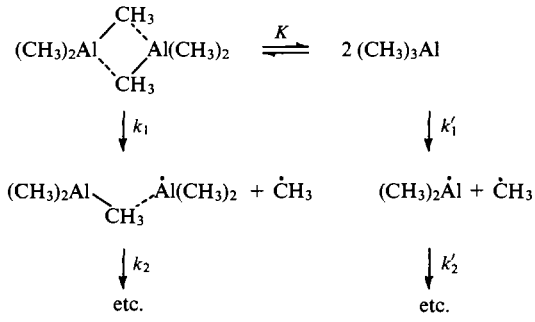
A distinctive feature of the pyrolysis of $(CH_3)_3Al$ at 200 Pa is the existence of 'high-temperature' (450–550 K)[12] and 'low-temperature' (290–320 K)[16] reaction regions. Activation energies for pyrolysis of 158.6 and 37.6 kJ mol^{-1} correspond respectively to these regions. In a general form, the 'low-temperature' pyrolysis is considered as a system of consecutive parallel reactions, where the first stage is the thermal decomposition of the trimethylaluminium dimer.[16]

$$[(CH_3)_3Al]_2 \xrightarrow{k_1} 2\,\dot{C}H_3 + [(CH_3)_2Al]_2$$

The low activation energy for the 'low-temperature' pyrolysis can be explained[16] by the fact that the bonds between the bridging methyl groups of the dimeric compound and the aluminium atom are weaker than the bonds in the monomeric molecule: the bond strength in the latter has been estimated, according to the data in Tel'noi's book,[17] as 278 ± 4 kJ mol^{-1}. The concentration of dimeric trimethylaluminium at 290–425 K is known[18] to exceed or be comparable to the concentration of the monomer, so that the dimers may play a significant role in the 'low-temperature' macrokinetics. However, this is not the only possible explanation of the characteristic features of the 'low-temperature' pyrolysis. Studies on the kinetics of the decomposition of trimethylaluminium on hot solid surfaces of copper and aluminium at 295–880 K demonstrated that methyl radicals are predominantly formed during the reaction.[19] The energy for the generation of methyl radicals in the interaction of $(CH_3)_3Al$ with the aluminium surface is 46 ± 8 kJ mol^{-1}. Within the limits of the error of the measurement, this quantity agrees with the activation energy for the 'low-temperature' pyrolysis (37.6 kJ mol^{-1}) quoted by Suzuki et al.[16] It is entirely probable that at 290–425 K the source of methyl radicals may be the dimeric trimethylaluminium, which decomposes heterogeneously at the surface.

With increase in temperature, the fraction of trimethylaluminium dimers diminishes as a result of dissociation. Therefore, over a wide temperature range it is necessary to take into account the contributions to the overall process by both the dimeric and monomeric forms (Scheme 1).

Scheme 1



T/K	E/kJ mol^{-1}	Ref.
290–450	37.6	16
450–565	158.6	12
570–610	188.3	15

The role of each of the competing paths in the pyrolysis is determined by two temperature-dependent factors: the shift of the dimer ⇌ monomer equilibrium (K) and the change in the rate constants for the abstraction of the methyl groups from the dimer (k_1) and the monomer (k_1'). The higher the reaction temperature, the higher the activation energy for the pyrolysis of $(CH_3)_3Al$.

This type of variation of E is consistent with the concept of competing reactions occurring with rate constants k_i and k_i', where $i = 1, 2$ (see Scheme 1).

The monomer concentration increases with increasing temperature. The rate constant for the decomposition of the monomer (k_1') increases with temperature faster than the rate constant for the composition of the dimer (k_1). In the ideal case, the complete conversion of the dimer into the monomer can be achieved by raising the temperature. If the rate-limiting stage is the abstraction of the first methyl group from the $(CH_3)_3Al$ molecule, then the value of E at temperatures above 600 K should approach the average bond dissociation energy $D_{Al-CH_3} = 278$ kJ mol^{-1}. An increase in the length of the hydrocarbon group virtually rules out the possibility of the existence of the dimeric form of the organoaluminium compound in the gas phase.[18,20] The nature of the pyrolysis products then changes. The contribution of the molecular β-elimination reaction increases. With increase in the length of the hydrocarbon group R, the thermal stability of the organoaluminium compounds falls.

$$R_3Al \begin{cases} \longrightarrow R_2AlH + R'CH{=}CH_2 & (1) \\ \longrightarrow R_2\dot{A}l + \dot{R} & (2) \end{cases}$$

For example, the rate of the gas-phase decomposition of $(C_2H_5)_3Al$ ($P_0 = 6.7 \times 10^3$ Pa, T = 435 – 465 K) is appreciably higher than the rate of decomposition of $(CH_3)_3Al$.[21] The temperature dependence of the effective rate constant for the overall $(C_2H_5)_3Al$ reaction is given by the equation[21]

$$k = 10^{8.2} \exp\left(-\frac{121.3}{RT}\right).$$

The attainment of a limiting value of the rate constant for the gas-phase decomposition of the organoaluminium compounds R_3Al on passing from $R = C_2H_5$ to $R = n-C_8H_{17}$ is indicated indirectly by data on the liquid-phase thermal decomposition of R_3Al.[22] The rate constants for the liquid-phase thermal decomposition of $(n\text{-}C_4H_9)_3Al$ and $(n\text{-}C_8H_{17})_3Al$ differ only slightly (1.5×10^{-4} s^{-1} and 1.7×10^{-4} s^{-1} respectively).

The thermal decomposition of the gaseous alkylgallium compound R_3Ga ($R = CH_3$, C_2H_5, $n\text{-}C_3H_7$, $n\text{-}C_4H_9$) obeys the kinetic equation for a first-order reaction.[13,14,23–32] Trimethylgallium exhibits the highest thermal stability. The homolysis of the Ga–C bond with a fairly ready loss of two methyl groups is characteristic of this compound.[23,26,28] The rate-limiting stage of the process is the abstraction of the first methyl group.

$$(CH_3)_3Ga \longrightarrow (CH_3)_2\dot{G}a + \dot{C}H_3$$

The subsequent fate of the methyl radicals depends on the composition of the gas phase. The reaction

$$C_6H_5CH_3 + \dot{C}H_3 \longrightarrow C_6H_5\dot{C}H_2 + CH_4,$$

is observed in a stream of toluene. The bibenzyl formed confirms the radical mechanism of the decomposition of $(CH_3)_3Ga$ in a toluene atmosphere.[23]

Mass-spectrometric analysis of the gas phase[14] confirms the occurrence of the following reactions of the methyl radicals:[14]

$$\dot{C}H_3 + \dot{C}H_3 + M \longrightarrow C_2H_6 + M^*$$

$$\dot{C}H_3 + H_2(D_2) \longrightarrow CH_4(CH_3D) + \dot{H}(\dot{D})$$

$$\dot{C}H_3 + (CH_3)_3Ga \longrightarrow CH_4 + (CH_3)_2Ga\dot{C}H_2$$

M= reactor wall or any molecule.

In a stream of hydrogen, the decomposition is faster than in a stream of helium, which suggests the possibility of the occurrence of the reaction

$$(CH_3)_3Ga + \dot{H} \longrightarrow (CH_3)_2\dot{G}a + CH_4.$$

At a temperature below 720 K, the polymer $(GaCH_x)_n$ is formed.[26] Above 770 K, it decomposes with liberation of metallic gallium.

One may agree with the claim that hydrogen reduces the activation energy by the abstraction of the last methyl group in the final stage of the pyrolysis.[13] The dissociation of the bond in monomethylgallium requires an energy of approximately 343 kJ mol^{-1}.[33] The overall activation energy for the decomposition of $(CH_3)_3Ga$ in a stream of hydrogen is in the range 184–260 kJ mol^{-1} according to the data of different workers.[25,26] The concluding stage of the decomposition of $(CH_3)_3Ga$ in the gas phase should therefore be a reaction favoured energetically.[34]

$$CH_3Ga{:} + H_2 (\text{or } \dot{H}) \longrightarrow Ga + CH_4 + \dot{H}$$

An attempt to detect the presence of gallium atoms in the vapour-phase decomposition of $(CH_3)_3Ga$ by IR spectroscopy was unsuccessful.[35] At any rate the pyrolytic reactions catalysed by the surface or occurring on the surface do not limit the rate of the process,[26,36] since an increase in the surface area does not accelerate the pyrolysis of $(CH_3)_3Ga$.

The homogeneous-heterogeneous mechanism of the decomposition of $(CH_3)_3Ga$, examined in detail by Masi et al.,[36] has been proposed on the basis of studies of the decomposition of this compound under the conditions of the formation of epitaxial layer by the MOCVD method,[23,28–30] while a model mechanism has been proposed on the basis of data on the pyrolysis of $(CH_3)_3Ga$ at different temperatures and the involvement of H_2 in the decomposition processes and in the processes leading to the formation of the decomposition products in the gas phase and on the GaAs surface. It was established that, in the gas-phase decomposition of $(CH_3)_3Ga$ in a stream of hydrogen, the gallium hydrides $[H_xGa(CH_3)_{3-x}]$ are not formed, especially under the conditions for the growth of GaAs films. The absence of the dissociation of $(CH_3)_3Ga$ in the gas phase to metallic gallium has been confirmed by spectroscopic data, according to which the concentration of gallium atoms in the gas phase is several orders of magnitude lower than the concentration of the intermediate species $CH_3Ga{:}$. Spectroscopic studies[37,38] made it possible to consider in detail the surface reactions of $(CH_3)_3Ga$, which include the dissociation of $(CH_3)_3Ga$ and of the intermediate species $(CH_3)_2Ga^*$ and $CH_3Ga{:}$ on the surface adsorption centres (s).[36] The activation parameters were estimated for each of the reactions presented below, which makes it possible to predict their occurrence in the real MOCVD process (Scheme 2).

Reactions (3)–(6) take place in the gas phase, whilst reactions (7)–(13) occur on the surface. The activation energies E are given in kJ mol^{-1} and the rate constants k in (mol cm^{-3})$^{1-n}$s^{-1}, where n is the reaction order.

The epitaxial GaAs layers were grown by the MOCVD method on a base comprising $(CH_3)_3Ga$ and metallic arsenic using hydrogen as the carrier gas.[39] Methane molecules are obtained in this process via two paths: via the direct gas-phase interaction of two methyl radicals [see Eqn (44) below], formed on decomposition of $(CH_3)_3Ga$, and via the reaction of the $\dot{C}H_3$ radical with the carrier gas. The activation energies for these processes were estimated as 23 and 39 kJ mol^{-1} respectively.

The reaction involving the abstraction of alkyl radicals, typical for $(CH_3)_3Ga$, is also characteristic of $(C_2H_5)_3Ga$ with the sole difference that in the case of the latter β-elimination takes place as a parallel reaction. The probable mechanism of

Scheme 2

$$(CH_3)_3Ga \longrightarrow (CH_3)_2\dot{G}a + \dot{C}H_3, \qquad k = 3.5 \times 10^5 \exp\left(-\frac{249}{RT}\right); \tag{3}$$

$$(CH_3)_2\dot{G}a \longrightarrow CH_3Ga{:} + \dot{C}H_3, \qquad k = 8.7 \times 10^7 \exp\left(-\frac{148}{RT}\right); \tag{4}$$

$$(CH_3)_3Ga + \dot{H} \longrightarrow (CH_3)_2\dot{G}a + CH_4, \qquad k = 5 \times 10^{13} \exp\left(-\frac{41.9}{RT}\right); \tag{5}$$

$$(CH_3)_2\dot{G}a + \dot{H} \longrightarrow CH_3Ga{:} + CH_4, \qquad k = 5 \times 10^{13} \exp\left(-\frac{41.9}{RT}\right); \tag{6}$$

$$CH_3Ga{:} + Ga\,(s) \longrightarrow CH_3Ga\,(s), \qquad k = 5.4 \times 10^{11} T^{0.5}; \tag{7}$$

$$CH_3Ga\,(s) \longrightarrow CH_3Ga{:} + Ga\,(s), \qquad k = 10^{14} \exp\left(-\frac{188}{RT}\right); \tag{8}$$

$$CH_3Ga\,(s) \longrightarrow Ga\,(s) + \dot{C}H_3, \qquad k = 2.6 \times 10^{13} \exp\left(-\frac{159}{RT}\right); \tag{9}$$

$$Ga\,(s) + \dot{C}H_3 \longrightarrow CH_3Ga\,(s), \qquad k = 1.3 \times 10^{12} T^{0.5} \tag{10}$$

$$Ga\,(s) + \dot{C}H_3\,(s) \longrightarrow GaCH_3\,(s) + s, \qquad k = 10^{17} \exp\left(-\frac{41.9}{RT}\right); \tag{11}$$

$$(CH_3)_2\dot{G}a + s \longrightarrow CH_3Ga\,(s) + \dot{C}H_3, \qquad k = 5 \times 10^{11} T^{0.5}; \tag{12}$$

$$(CH_3)_3Ga + s \longrightarrow CH_3Ga\,(s) + 2\dot{C}H_3 \qquad k = 4.6 \times 10^{11} T^{0.5} \exp\left(-\frac{41.9}{RT}\right). \tag{13}$$

the decomposition of $(C_2H_5)_3Ga$, investigated by the mass-spectrometric method in a stream of He and H_2,[14] may be represented by the reactions

$$(C_2H_5)_3Ga \longrightarrow (C_2H_5)_2\dot{G}a + CH_3\dot{C}H_2 \tag{14}$$

$$(C_2H_5)_3Ga \longrightarrow (C_2H_5)_2GaH + C_2H_4 \tag{15}$$

$$2CH_3\dot{C}H_2 + M \longrightarrow C_4H_{10} + M^*, \tag{16}$$

$$CH_3\dot{C}H_2 + H_2 \longrightarrow C_2H_6 + \dot{H}, \tag{17}$$

$$CH_3\dot{C}H_2 + (C_2H_5)_3Ga \longrightarrow C_2H_6 + (C_2H_5)_2Ga\dot{C}HCH_3 \tag{18}$$

M = reactor wall or any molecule.

The radical recombination reaction (16) proceeds virtually with zero activation energy. Reaction (17) has an activation energy of 55 kJ mol^{-1}.[40] With increase in temperature, the fraction of ethene in the reaction products increases and above 600 K the elimination reaction (15) becomes the dominant path.

Quantum-mechanical calculations[41] demonstrated that the β-elimination reaction is favoured energetically for $(C_2H_5)_3Ga$ compared with the homolysis of the Ga–C bond, which agrees with the results of experimental measurements at temperatures above 600 K.

The kinetics of the pyrolysis of the alkylindium derivatives R_3In, where $R = C_2H_5$, n-C_4H_9, n-C_5H_{11}, or n-C_6H_{13}, have been investigated.[42–45] Analysis of the literature data permits the conclusion that the pyrolysis of the alkylindium derivatives in the gas phase in the temperature range 473–780 K is described by the kinetic equation for a first-order reaction. The apparent activation energy for the process decreases on passing from the methyl derivative (197.5 kJ mol^{-1}) to the hexyl derivative (63.2 kJ mol^{-1}). It was established that the pyrolysis of trialkylindium is a complex homogeneous-heterogeneous process, which proceeds simultaneously via radical and olefinic-hydride mechanisms, the radical reaction paths predominating. The formal process mechanism can be represented as follows:

$$R_3In \longrightarrow R_2\dot{I}n + \dot{R}$$

$$\downarrow$$

$$In + 2\dot{R}$$

$$2\dot{R} \longrightarrow RH + R_{(-H)}$$

$$2\dot{R} \longrightarrow R_2$$

$$\dot{R} + R_3In \longrightarrow RH + RIn\dot{R}_{(-H)}$$

$$\dot{R} \xrightarrow{In} R_{(-H)} + \dot{H}$$

$$R_3In \longrightarrow R_2InH + R_{(-H)}$$

$$2R_2\dot{I}n \longrightarrow R_2InInR_2 \longrightarrow R_2In\dot{I}nR + \dot{R}.$$

The pyrolysis $(CH_3)_3In$ at atmospheric pressure in a stream of helium or hydrogen (deuterium) has been studied in detail by the mass-spectrometric method.[45] The rate constant for the pyrolysis of $(CH_3)_3In$ in a stream of helium is comparable to the rate constants published recently and obtained in the presence of a radical trapping agent (toluene).[44]

$$\lg k = 17.9 - \frac{226}{2.3RT}$$

Trimethylindium decomposes predominantly homolytically in a stream of helium and does not undergo radical attack by methyl radicals. The pyrolysis is accelerated slightly in a stream of H_2 or D_2.

$$\lg k = 13.4 - \frac{167}{2.3RT} \qquad \text{(in a stream of } D_2\text{)},$$

$$\lg k = 15.0 - \frac{178}{2.3RT} \qquad \text{(in a stream of } H_2\text{)}.$$

The principal pyrolysis products are CH_3D and C_2H_6 in a stream of D_2 and CH_4 and C_2H_6 in a stream of H_2. The ratio CH_3D/C_2H_6 decreases monotonically with increase in temperature. In the study of the mechanism of the decomposition of $(CH_3)_3In$ in a stream of D_2, the authors[45] used a modelling procedure. It was postulated that the hypervalent short-lived

intermediate $[D(CH_3)_3In]^*$ is formed initially.

$$\dot{D} + (CH_3)_3In \longrightarrow [D(CH_3)_3In]^*$$

$$\dot{C}H_3 + [D(CH_3)_3In]^* \longrightarrow CH_3D + (CH_3)_3In$$

$$\dot{D} + [D(CH_3)_3In]^* \longrightarrow D_2 + (CH_3)_3In$$

$$[D(CH_3)_3In]^* \longrightarrow CH_3D + 2\dot{C}H_3 + In$$

This model explains the increase in the rate of pyrolysis of $(CH_3)_3In$ in a D_2 atmosphere. A similar decomposition mechanism has also been proposed for a H_2 atmosphere.

New organometallic sources of metallic indium have been investigated—$C_2H_5(CH_3)_2In$ and $(CH_3)_2N(CH_2)_3In(CH_3)_2$. These are potential substitutes for $(CH_3)_3In$.[46,47] In contrast to $(CH_3)_3In$, these compounds are liquid at room temperature with relatively high vapour pressures. It is particularly effective to employ them in combination with *tert*-$C_4H_9PH_2$ for the preparation of high-quality InP films. $(C_2H_5)_2InCl$, which is converted into InCl on decomposition, is very effective in organometallic gas-phase epitaxy. When PH_3 and *tert*-$C_4H_9PH_2$ are used, phosphorus is incorporated during the growth of InP films.

The pyrolysis of $(CH_3)_3Tl$ has been investigated in a flow system in a stream of toluene in the temperature range 452–536 K.[48] The CH_4, C_2H_6, and $C_6H_5C_2H_5$ found in the reaction products are formed from the methyl radicals abstracted from $(CH_3)_3Tl$.

$$(CH_3)_3Tl \longrightarrow (CH_3)_2\dot{T}l + \dot{C}H_3$$

$$\downarrow$$

$$Tl + 2\dot{C}H_3$$

The apparent activation energy of 152.3 kJ mol^{-1} corresponds to the Tl–C bond dissociation energy.[48]

The kinetic parameters of the thermal decomposition of the alkyl derivatives of Group III elements are presented in Table 1. There is no unanimity as regards the estimation of the effective rate constants for the overall reactions. The constants k based on the data of different workers differ significantly for the same compound. The studies of Price and coworkers,[23,44,48,49] where the thermal stabilities of the compounds $(CH_3)_3E$ (E = Ga, In, Tl) were investigated under comparable conditions, merit special attention. The reactivities of such organometallic compounds increase in the sequence $(CH_3)_3Ga < (CH_3)_3In < (CH_3)_3Tl$. $(CH_3)_3Al$ 'deviates' from this series. Relatively low activation energies[12,15,16] and a low thermal stability, consistent with the hypothesis that its dimeric form is involved in the process kinetics, are characteristic of this compound.

The causes of the variation of the reactivity of the compounds R_3Ga in the sequence $CH_3 < C_2H_5 <$ n-$C_4H_9 <$ n-C_3H_7 [13,24,49] and of R_3In in the sequence $CH_3 <$ n-$C_4H_9 < C_2H_5 \approx$ n-$C_5H_{11} \ll$ n-C_6H_{13} [43,44] so far remain unelucidated.

It has been shown comparatively recently[50–54,55] that high-quality thin aluminium and gallium films may be obtained when complexes of aluminium and gallium hydrides with the tertiary amines $EH_3 \cdot NR_3$, where E = Al or Ga and R = CH_3 or C_2H_5, are used as the organometallic sources.[55] Such adducts do not contain an E–C bond, are less combustible and toxic than the compounds R_3E, and their vapour pressures are sufficient to employ them in the MOCVD processes at relatively low temperatures.

The thermal decomposition of the complexes $AlH_3 \cdot NR_3$, where R = CH_3 or C_2H_5, has been investigated.[56] The gas-phase decomposition leads to the formation of hydrogen, metallic aluminium, and the corresponding amine. In the condensed phase, the thermal decomposition in the temperature range 353–393 K is accompanied by the formation of the amine and a solvated polymeric form of aluminium hydride. The decomposition mechanism can be expressed as follows:

$$AlH_3 \cdot NR_3\,(g) \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} AlH_3\,(g) + NR_3\,(g), \qquad (19)$$

$$AlH_3\,(g) \xrightarrow{k_2} Al\,(s) + 1\tfrac{1}{2}H_2\,(g), \qquad (20)$$

$$AlH_3 \cdot NR_3\,(l) \longrightarrow \frac{n-1}{n} NR_3\,(g) + \frac{1}{n}[(AlH_3)_n \cdot NR_3]\,(s), \qquad (21)$$

$$\frac{1}{n}[(AlH_3)_n \cdot NR_3]\,(s) \longrightarrow Al\,(s) + 1\tfrac{1}{2}H_2\,(g) + \frac{1}{n}NR_3\,(g). \qquad (22)$$

The abbreviations g, l, and s correspond to the gas, liquid, and solid phases.

The following expressions were obtained for k_1 and k_2 (s^{-1}):

$$k_1 = 1.6 \times 10^{12} \exp\left(-\frac{117.2}{RT}\right) \quad \text{for } AlH_3 \cdot N(CH_3)_3,$$

$$k_1 = 5.3 \times 10^{12} \exp\left(-\frac{113}{RT}\right) \quad \text{for } AlH_3 \cdot N(C_2H_5)_3,$$

$$k_2 = 4.2 \times 10^{20} \exp\left(-\frac{175.8}{RT}\right).$$

Table 1. Parameters of the thermal decomposition of the alkyl derivatives of Group III elements.

Compound	T/K	$\ln k_0$	E/kJ mol^{-1}	Experimental conditions	Ref.
$(CH_3)_3Al$	571–607	36.63	188.3	Static system	15
$(C_2H_5)_3Al$	435–465	18.88	121.3	"	21
$(CH_3)_3Ga$	686–983	35.7	249	Flow system, toluene carrier	23
	683–703	29.3	184	Flow system, hydrogen atmosphere	25
$(C_2H_5)_3Ga$	610–749	36.1	197.5	Flow system, toluene carrier	49
	543–1023	18.2	95	Flow system, hydrogen atmosphere	24
	573–653	11.3	95.8	Static system	27
(n-$C_3H_7)_3Ga$	473–553	13.1	76.5	"	27
(n-$C_4H_9)_3Ga$	473–553	5.8	49.8	"	27
$(CH_3)_3In$	550–781	36.2	197.5	Flow system, toluene carrier	44
$(C_2H_5)_3In$	453–523	28.3	144	Static system	42
(n-$C_4H_9)_3In$	473–553	17.7	110.8	"	43
(n-$C_5H_{11})_3In$	473–553	14.5	86.2	"	43
(n-$C_6H_{13})_3In$	473–553	13.8	63.2	"	43
$(CH_3)_3Tl$	452–536	34.7	152.3	Flow system, toluene carrier	48

Note. The parameters of the Arrhenius equation which correspond to a first-order rate constant are quoted with the exception of the parameters for $(CH_3)_3Al$, the order of the reaction of which is 3/2 and the dimensions of k are s^{-1} mol$^{-0.5}$ litre$^{0.5}$.

The enthalpy of reaction (19) is 113 ± 4 kJ mol^{-1}, which virtually agrees with the activation energy for this process and is close to the Al–N bond dissociation energy. The constant k_2 is the effective rate constant for the decomposition of AlH_3 in the gas phase.

The mechanism of the growth of a thin aluminium film on the crystalline surface of aluminium (111) has been investigated by a method involving the decomposition of the complexes of aluminium hydride with trimethylamine[52] and triethylamine.[57] The process occurring on the surface can be represented in a simplified form by the following reactions:

$$AlH_3 \cdot NR_3\,(g) \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} AlH_3 \cdot NR_3\,(s), \quad (23)$$

$$AlH_3 \cdot NR_3\,(s) \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} AlH_3\,(s) + NR_3\,(s), \quad (24)$$

$$AlH_3\,(s) \xrightarrow{k_3} Al\,(s) + 3H\,(s), \quad (25)$$

$$NR_3\,(s) \xrightarrow{k_4} NR_3\,(g), \quad (26)$$

$$3H\,(s) \xrightarrow{k_5} \tfrac{3}{2}H\,(g, s). \quad (27)$$

It was shown[52] that reaction (24)—the dissociation of the Al–N bond in the complex adsorbed on the surface—is the rate-limiting stage in the deposition of the aluminium film in the aluminium hydride–trimethylamine system, while in the aluminium hydride–triethylamine system the rate-limiting stage in the growth of the film is reaction (27)—the desorption of hydrogen atoms from the surface.[57] The activation energy for bond dissociation in $AlH_3 \cdot N(C_2H_5)_3$ on the surface has been estimated as 65–80 kJ mol^{-1}, which is less than the activation energy for the desorption of hydrogen from the surface. Epitaxial aluminium layers without an admixture of carbon were obtained at 310 K and above.[52, 57]

The complexes between aluminium hydride and tertiary amines, such as $AlH_3 \cdot N(C_2H_5)_3$, $AlH_3 \cdot N(n\text{-}C_3H_7)_3$, and $AlH_3 \cdot N(n\text{-}C_4H_9)_3$, are liquids at room temperature, but their thermal stability diminishes with increase in the bulk of the substituents in the amine. Among the liquid aluminium hydride complexes, the most stable is that with ethyldimethylamine,[54] which has been used to obtain ultrapure aluminium in the construction of lasers. It has been suggested that the adduct decomposes via reactions (23)–(27).[54]

The gallium complexes $GaH_3 \cdot NR_3$ are hardly used in the formation of epitaxial layers, since, for example, $GaH_3 \cdot N(CH_3)_3$ is unstable and decomposes even at room temperature. The more stable adduct $GaH_3 \cdot NH(CH_3)_2$ has been described. It has been used in combination with AlH_3 and *tert*-$C_4H_9AsH_2$ for the formation of (AlGa)As/GaAs heterostructures.[58]

The adduct $(CH_3)_3In \cdot N(CH_3)_3$ has been synthesised in a satisfactory yield and with adequate purity from metallic indium, NMe_3, and methyl iodide in the presence of magnesium and diethyl ether.[59] The vapour pressure of the adduct was determined: 7.42 × 10^6 Pa at 323 K and 0.97 × 10^6 Pa at 293 K. For comparison, we may note that the vapour pressure of $(CH_3)_3In$ at 293 K is 1.41 × 10^6 Pa. The complex $(CH_3)_3In \cdot N(CH_3)_3$ and PH_3 have been used to prepare InP films.

III. Kinetics of the thermal decomposition of alkyl derivatives of Group V elements

The rate of thermal decomposition of gaseous alkyl derivatives of Group V elements is described by the equation for a first-order reaction regardless of the nature of the heteroatom or the alkyl group R in R_3E^V, where E^V = P, As, Sb, or Bi and R = CH_3, C_2H_5, or n-C_3H_7 (Table 2).

The kinetic parameters of the thermal decomposition of $(CH_3)_3As$ have been published[60–62] for both dynamic and static conditions. The decomposition in a closed quartz reactor[60] at 673–733 K leads to the formation of methane (~90 vol.%), ethane (4%), ethene (2.5%), hydrogen (1%), and higher hydrocarbons. Approximately the same proportions of the gaseous products have been observed in a flow reactor.[61] The solid phase contains 98.4% of metallic arsenic. An increase in the length of the hydrocarbon group diminishes the thermal stability of alkylarsines.[62, 63] The reactivities of trialkylarsines increase in the sequence $(CH_3)_3As < (C_2H_5)_3As < (n\text{-}C_3H_7)_3As$. Thus, at 679 K the rate constants for the decomposition of trimethyl-, triethyl- and tri-n-propyl-arsines are 9 × 10^{-5}, 193 × 10^{-5}, and 257 × 10^{-5} s^{-1} respectively. The composition of the gaseous products indicates an increase in the contribution of the β-elimination to the overall process on passing from the ethyl to the propyl derivatives.

Systematic studies of the influence of the central heteroatom on the rate of thermal decomposition of the methyl[61, 64–66] and ethyl,[62, 67–70] derivatives of Group V elements showed that the reactivities of $(CH_3)_3E^V$ and $(C_2H_5)_3E^V$ increase from phosphorus to bismuth: P < As < Sb < Bi.

Comparison of the temperatures at which the effective rate constants for the pyrolysis of the ethyl derivatives of Group V elements are the same and equal to 10^{-5} s^{-1} shows that this temperature is 653 K for $(C_2H_5)_3P$, whereas the significantly lower temperature of 433 K corresponds to $(C_2H_5)_3Bi$.[67, 69–71]

The composition of the products of the decomposition reaction (Table 3) indicates a radical mechanism for the decomposition of $(CH_3)_3E^V$ and the occurrence of the competing radical and molecular reactions of the corresponding ethyl derivatives $(C_2H_5)_3E^V$. Unsaturated compounds are formed via the β-elimination reactions and also as a result of the disproportionation of the alkyl radicals.

Table 2. Kinetic parameters of the decomposition of the alkyl derivatives of Group V elements.

Compound	T/K	$\ln k_0$	E/kJ mol^{-1}	Experimental conditions	Ref.
$(C_2H_5)_3P$	693–753	34.7	251.8	Static system	69, 70
	850–1050	36.8	263.6	Flow system	71
$(CH_3)_3As$	673–733	29.4	228.4	Static system	60
	764–858	36.4	262.8	Flow system, toluene carrier	61
	687–736	33.1	240	Static system	62
$(C_2H_5)_3As$	653–693	31.1	210.8	"	62, 67
	650–690	29.9	167.3	"	64
$(n\text{-}C_3H_7)_3As$	661–693	30.2	204	"	63
$(CH_3)_3Sb$	705–767	35.2	233.8	Flow system, toluene carrier	65
$(C_2H_5)_3Sb$	578–613	31.1	189.5	Static system	67
$(CH_3)_3Bi$	655–680	32.2	184	Flow system, toluene carrier	66
$(C_2H_5)_3Bi$	465–497	19.6	110.8	Static system	67

Table 3. Composition of the gaseous products of the decomposition of the methyl and ethyl derivatives of Group V elements.[62,67]

Compound	T/K	Composition (mol.%)								
		H_2	CH_4	C_2H_6	C_2H_4	C_3H_8	C_3H_6	C_4H_{10}	C_4H_8	Unidentified compounds
$(CH_3)_3As$	688–731	0.4–0.27	88.1–90.4	4.9–1.5	1.1	1.9–3.5	3.6–1.3	–	–	–
$(C_2H_5)_3As$	642–693	–	5.1	77.0	8.4	2.5	5.0	2.0	–	–
$(C_2H_5)_3Sb$	578–613	–	0.5	65.3	3.3	1.9	4.0	16.4	8.3	0.7
$(C_2H_5)_3Bi$	465–497	–	–	45.5	7.3	–	–	28.8	6.3	12.0

The consecutive-parallel thermal decomposition reactions of the ethyl derivatives of Group V elements can be represented in the following way in a general form (Scheme 3):

Scheme 3

$$(C_2H_5)_3E \longrightarrow \begin{cases} (C_2H_5)_2\dot{E} + CH_3\dot{C}H_2, \\ (C_2H_5)_2EH + C_2H_4, \end{cases}$$

$$(C_2H_5)_2\dot{E} \longrightarrow C_2H_5E: + CH_3\dot{C}H_2,$$

$$(C_2H_5)_2EH \longrightarrow C_2H_5E: + C_2H_6,$$

$$C_2H_5E: \longrightarrow E + CH_3\dot{C}H_2,$$

$$2CH_3\dot{C}H_2 \longrightarrow \begin{cases} C_2H_6 + C_2H_4, \\ C_4H_{10}. \end{cases}$$

The decomposition mechanism was devised on the basis of the analysis of the composition of the stable gaseous products and does not provide, for example, for the successive transformation of $(C_2H_5)_3E^V$ into E^VH_3, because molecular hydrogen, the formation of which would have been expected in the pyrolysis of E^VH_3, is not detected in the products at fairly low temperatures. At high temperatures, the role of secondary processes involving the reactions of the ethyl radicals increases. This is the reason for the presence of methane and higher hydrocarbons in the products of the thermal decomposition of $(C_2H_5)_3As$ and $(C_2H_5)_3Sb$.[72]

The radical reactions in the pyrolysis of $(C_2H_5)_3As$ and $(C_2H_5)_2AsH$ in a stream of hydrogen and deuterium have been investigated in detail by the mass-spectrometric method.[73] Tetraethylhydrazine was used as the source of ethyl radicals. Ethyl radicals accelerated the pyrolysis of $(C_2H_5)_2AsH$ but did not affect the pyrolysis of $(C_2H_5)_3As$. Isotopic analysis of the reaction products showed that β-elimination hardly occurs in the pyrolysis of these compounds under the conditions of the given experiment and that the radical reactions predominate. It has been established by computer modelling that the proposed reaction mechanism is consistent with experimental data.

Since the hydrides of Group V elements (PH_3, AsH_3, SbH_3) are toxic, it has been suggested in recent years that somewhat less toxic compounds such as *tert*-$C_4H_9PH_2$ or *tert*-$C_4H_9AsH_2$ be used for the MOCVD processes.[74–76]

The mechanisms of the thermal decomposition of *tert*-$C_4H_9PH_2$ and *tert*-$C_4H_9AsH_2$ have been discussed.[77–83] It was shown that the molecular processes leading to the formation of $\dot{A}sH_2$ and isobutane should be regarded as dominant in the decomposition of *tert*-$C_4H_9AsH_2$ in a D_2 atmosphere when the gas phase comes into contact with a SiO_2 or GaP surface.[78] β-Elimination, accompanied by the formation of AsH_3 and isobutene, becomes appreciable at high temperatures.

In contrast to *tert*-$C_4H_9AsH_2$, the decomposition of *tert*-$C_4H_9PH_2$ is a multistage process where free-radical reactions predominate according to Li and coworkers[81,82] and Fan et al.[83]

$$tert\text{-}C_4H_9PH_2 \longrightarrow (CH_3)_3\dot{C} + H_2\dot{P} \quad (28)$$

$$tert\text{-}C_4H_9PH_2 + (CH_3)_3\dot{C} \longrightarrow (CH_3)_3CH + tert\text{-}C_4H_9\dot{P}H \quad (29)$$

$$tert\text{-}C_4H_9\dot{P}H \longrightarrow (CH_3)_3\dot{C} + HP: \quad (30)$$

$$(CH_3)_3\dot{C} \longrightarrow (CH_3)_2C{=}CH_2 + \dot{H} \quad (31)$$

The *tert*-butyl radicals are destroyed by reactions (29) and (31), while the :PH and $\dot{P}H_2$ radicals are adsorbed on the surface and interact with one another. A change in the SiO_2 surface area does not influence significantly the rate of thermal decomposition of *tert*-$C_4H_9PH_2$, whereas the GaP surface has a catalytic effect on the decomposition of phosphine.[81] Gallium atoms play the role of catalytic centres. The adsorbed species located on the neighbouring Ga atoms participate in the reaction

$$tert\text{-}C_4H_9PH_2\,(s) + PH\,(s) \longrightarrow \quad (32)$$

$$\longrightarrow (CH_3)_3CH\,(g) + PH_{x-1}\,(s) + PH_2\,(s);$$

$x = 1–2$.

At high temperatures, the intramolecular β-elimination reaction cannot be ruled out for *tert*-$C_4H_9PH_2$.[83]

$$tert\text{-}C_4H_9PH_2 \longrightarrow (CH_3)_2C{=}CH_2 + PH_3 \quad (33)$$

In contrast to *tert*-$C_4H_9PH_2$, PH_3 decomposes under the conditions of the MOCVD process at temperatures higher by ~300 °C. The mechanism of the pyrolysis of PH_3 on the surface includes the following reactions:[84]

$$PH_3\,(g) \rightleftharpoons PH_3\,(s) \quad (34)$$

$$PH_3\,(s) \rightleftharpoons PH\,(s) + H_2\,(s) \quad (35)$$

$$2PH\,(s) \longrightarrow P_2\,(s) + H_2\,(g) \quad (36)$$

$$PH_3\,(s) + PH\,(s) \longrightarrow P_2\,(s) + 2H_2\,(g) \quad (37)$$

$$2P_2\,(s) \longrightarrow 2P_2\,(g) \quad (38)$$

$$PH_3\,(s) + PH\,(s) \longrightarrow 2PH_2\,(s) \quad (39)$$

Comparison of the mechanisms of the decomposition of *tert*-$C_4H_9PH_2$ and PH_3 shows that the reactions of the radicals: PH and $\dot{P}H_2$, which generally occur on the surface, are common to them. The difference is determined by the nature of the rate-limiting stages for the processes: reaction (28) or (32) is such a stage for *tert*-$C_4H_9PH_2$, while for PH_3 it is reaction (35), which can occur both homogeneously and heterogeneously.

The study of the kinetics of the thermal decomposition of *tert*-$C_4H_9PH_2$ (22 experiments)[85] showed that the reaction is pseudo-first-order with respect to the substrate. The kinetic parameters of the pyrolytic reaction were determined in the temperature range 593–626 K at an initial pressure $P_0 = (2.2 - 2.7) \times 10^4$ Pa. The rate constant varies from 2.39 [2.39×10^{-4}? (translator)] to 12.5×10^{-4} s^{-1} and the process activation energy is 159 ± 5 kJ mol^{-1}. The composition of the gaseous decomposition products (in mol.%), determined by gas–liquid chromatography, is as follows: CH_4 (0.2), iso-C_4H_{10} (99.3), and iso-C_4H_8 (0.5). At temperatures above 780 K, the gaseous products of the

hydrolysis of *tert*-$C_4H_9PH_2$ undergo further decomposition.[85] According to the data of Li et al.,[81] further decomposition does not occur in a flow system in a D_2 atmosphere. Under static conditions in the temperature range 780–840 K, the thermal decomposition of isobutane takes place at an appreciable rate with formation of CH_4, C_2H_6, C_2H_4, C_3H_8, C_3H_6, and iso-C_4H_8.

The high pyrolysis temperature and the toxicity of the hydrides of Group V elements forced investigators to turn to the alkyl derivatives of Group V elements capable of generating hydrides at fairly low temperatures directly in the hot zone of the reactor. The possibility of using the compounds $As(R_r)(R_\beta)_{3-n}$ for the preparation of semiconducting layers, where R_r is the alkyl group participating in the free-radical decomposition at the $As-R_r$ bond, and R_β is the alkyl group (usually iso-C_3H_7 or *tert*-C_4H_9) undergoing β-elimination with formation of $As(R_r)_nH_{3-n}$, has been analysed.[86] A model compound of this kind is *tert*-$C_4H_9(C_2H_5)_2As$.[86] The decomposition of this compound in the temperature range 373–725 K was investigated by the mass-spectrometric method. It was established that at 373–573 K the free-radical decomposition of this compound predominates over β-elimination (in proportions of 2:1). At a temperature above 620 K, β-elimination is the main process leading to the formation of $(C_2H_5)_2AsH$.

$$tert\text{-}C_4H_9(C_2H_5)_2As \longrightarrow (C_2H_5)_2AsH + \text{iso-}C_4H_8$$

The hydride $(C_2H_5)_2AsH$ is a source of arsenic in the preparation of epitaxial III–V layers.

Similarly it has been suggested that *tert*-$C_4H_9(CH_3)_2Sb$ be employed to prepare InSb layers. The temperature at which the epitaxial layers are grown is then reduced by about 100 °C compared with the process employing $(CH_3)_3Sb$ and by about 50 °C compared with (iso-$C_3H_7)_3Sb$.[87,88]

Comparison of the reactivities of alkyl derivatives of Group III and V elements (Tables 1 and 2) indicates a higher thermal stability of $(CH_3)_3E^V$ compared with $(CH_3)_3E^{III}$ (E^{III} and E^V are Group III and V elements in the same Period). Price and coworkers[23,44,48,49,61,65,66] carried out systematic studies on the kinetics of the thermal decomposition of the methyl derivatives of the above elements in a flow system, using toluene as the carrier gas. We used these data to compare the reactivities of the alkyl derivatives of Group III and V elements. The linear plots of $\ln k_{R_3E^{III}}$ against $\ln k_{R_3E^V}$ presented in Fig. 1 (lines *1* and *2*) confirm the existence of a correlation between the rate constants for the pyrolysis of the methyl derivatives of Group III elements and the rate constants for the pyrolysis of the methyl derivatives (line *1*) and ethyl derivatives (line *2*) of Group V elements. This finding confirms that the mechanisms of the pyrolysis of the compounds R_3E of Group III and V elements are of the same type. A certain scatter of the points about line *1* is associated with the fact that constants obtained by extrapolation were compared. The relations presented permit an estimate of the rate constant for the thermal decomposition of the monomeric compound $(CH_3)_3Al$, which proved to be 10^{-8} s^{-1} at 688 K. Hence it follows that the monomeric trimethylaluminium is a very stable compound. The rate constant for the pyrolysis of $(CH_3)_3Al$ obtained experimentally[15] at this temperature proved to be significantly higher than the value quoted. This is associated with the fact that the kinetically active species in the thermolysis is the dimer, its presence in the vapour phase reducing the thermal stability of the monomer in equilibrium with it.

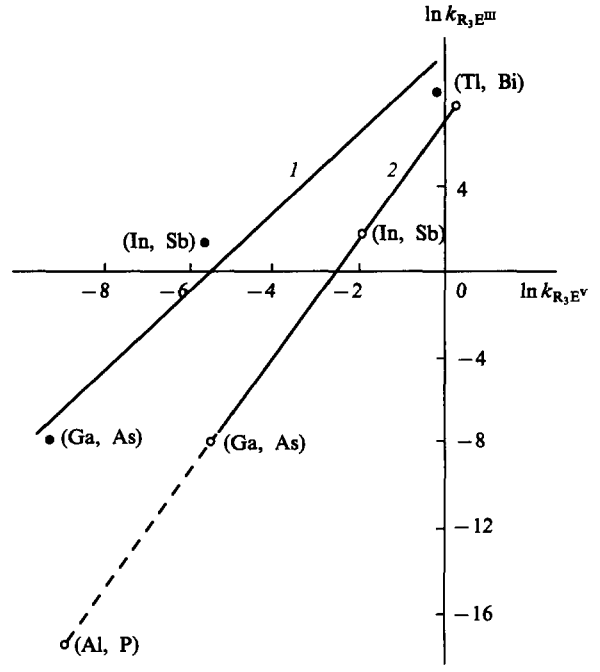


Figure 1. Relation between the rate constants for the pyrolysis of the methyl derivatives of Group III elements and the rate constants for the pyrolysis of the methyl (line *1*) and ethyl (line *2*) derivatives of Group V elements ($T = 488$ K).

IV. Joint decomposition of the organoelement compounds and hydrides of Group III and V elements in the gas phase and under the conditions for the formation of epitaxial layers

It follows from the data presented in Tables 1 and 2 that the majority of organometallic alkyl derivatives of Group III elements decompose in the temperature range 450–650 K, whereas the analogous compounds of Group V elements decompose at higher temperatures (600–850 K). The 'gap' between the temperature ranges of the decomposition reactions complicates the preparation of high-quality epitaxial III–V layers and heterostructures. As a rule, it is necessary to introduce the Group V compound into the reaction system in a large excess (by a factor of 10–100). However, the 'gap' is only apparent, since during their joint decomposition the compounds of Group III and V elements influence one another and the difference between their thermal stabilities is eliminated. The change in thermal stability may be associated with the possibility of the formation of adducts between the mixture components.

$$R_3M^{III} + R_3E^V = R_3M^{III} \cdot E^VR_3$$

The formation of such complexes follows from the acid–base properties of the reactants, since the organoelement compounds of Group III elements, having an unoccupied orbital, behave as Lewis acids, while the compounds of Group V elements, containing a lone pair, behave as Lewis bases.

The formation of adducts promotes the polarisation of the M–C bonds and changes in the steric configuration of the molecules, in the interatomic distances, and in the bond angles.[89] For example, the study of the NMR spectra of $(C_2H_5)_3Al$, $(C_2H_5)_3Ga$, and their etherates led to the conclusion that the element–carbon bonds in the complexes with ether are 'loosened' to a greater extent than the E–C bonds in the initial alkyl complexes.[90]

In the series of alkyl derivatives of Group V elements, the electron-donating properties are weakened in the following

sequence: N > P > As > Sb > Bi.[91-93] Among the compounds of Group III elements, the most pronounced electron-accepting properties are those of R_3Al.[91]

The thermal stability of the mixture of organoelement compounds is determined by the stabilities of kinetically independent species of different types: the molecules of individual compounds, their adducts, dimers, and the intermediates of the decomposition reaction formed in the mixture. The alkyl derivatives of Group III and V elements are known[91] to form fairly stable complexes $R_3M^{III}.E^VR_3$. The possibility of the existence of these complexes under the conditions of the thermal decomposition of the $(CH_3)_3Ga$ + $(CH_3)_3As$ and $(CH_3)_3Al$ + $(CH_3)_3As$ mixtures has been investigated.[94-97] The vapour pressure of the complex $(CH_3)_3Ga\cdot As(CH_3)_3$ was investigated at different temperatures and it was shown that the complex is fully dissociated in the gas phase at 470 K.[94] Under the severe conditions of the thermal decomposition of $(CH_3)_3Ga$ and $(CH_3)_3As$, one can therefore consider only the probability of the existence of the adduct $(CH_3)_3Ga\cdot As(CH_3)_3$,[96] which could not be detected with the aid of Raman spectroscopy.[98]

The rates and mechanisms of the thermochemical, photochemical, and plasmochemical decomposition of the mixture of organoelement compounds depend on the contribution by the decomposition of the complex to the effective pyrolysis rate constant. Thus, when $(CH_3)_3Ga$ and $(CH_3)_3As$ are mixed, the rate of their joint thermal decomposition increases by a factor of ~1.5–2 compared with the individual organoelement compounds.[95] Therefore knowledge of the thermodynamic and kinetic characteristics of the complexes formed becomes useful for the understanding of the kinetics of the joint decomposition of the organoelement compounds. The complexes $(CH_3)_3E\cdot As(CH_3)_3$ (E = Al, Ga, In) were synthesised in vacuo (P = 1–2 Pa) by mixing the initial organoelement compounds. $(CH_3)_3As$ was taken in excess and was then removed from the reactor by freezing out in a trap cooled with liquid nitrogen. By repeated sublimation, the complexes may be freed from the possible impurities comprising the individual organoelement compounds. The melting points (T_m) of the complexes $(CH_3)_3E\cdot As(CH_3)_3$ are given below.

E	T_m/K	Ref.
Al	304.2	96
Ga	296.6	91
	296.4–296.7	91
In	297.6	96
	297.2–297.8	91

The change in the Gibbs free energy or the dissociation constant K_e serves as a measure of the thermal dissociation of the complexes. The capacity of the test complexes[96,97] for thermal dissociation increases in the sequence

$$(CH_3)_3Al\cdot As(CH_3)_3 < (CH_3)_3In\cdot As(CH_3)_3 < (CH_3)_3Ga\cdot As(CH_3)_3.$$

For example, at 430 K the dissociation constants K_e for the above series of compounds are respectively 0.21, 1.005, and 3.51 atm.[97]

The temperature dependence of K_e suggests that the concentrations of the complexes are very low in the processes involving the high-temperature (~800 K) deposition of epitaxial layers. However, one cannot rule out the possibility that the role of such complexes in the kinetics of the pyrolysis is the same as that of free radicals and other active intermediate species. At lower temperatures (~350 K), the saturated vapour is a mixture of the gaseous complex and its dissociation products. The degree of dissociation of the complexes in equilibrium with the liquid phase at any temperature can be readily determined from K_e and the pressure P.

The rate of thermal decomposition of a mixture of $(CH_3)_3Al$ and $(CH_3)_3As$ has been investigated and the kinetic data obtained have been compared with the results for the thermal decomposition of the individual aluminium and arsenic compounds.[96] When gaseous $(CH_3)_3Al$ and $(CH_3)_3As$ are mixed at room temperature, the crystalline complex $(CH_3)_3Al\cdot As(CH_3)_3$ is formed. It was established that the arsine decomposes in the mixture independently of $(CH_3)_3Al$. On the other hand, the presence of $(CH_3)_3As$ influences the nature of the thermal decomposition of $(CH_3)_3Al$: firstly, its thermal stability increases (the temperature range of the decomposition reaction shifts from 590–650 K to 670–720 K) and, secondly, its decomposition is described by the kinetic equation for a first-order reaction. The results led to the following hypothesis concerning the mechanism of the joint decomposition of the above organoelement compounds: at 420–470 K, the saturated vapour obtained on evaporation of the complex $(CH_3)_3Al\cdot As(CH_3)_3$ is an equilibrium mixture of the individual OEC, the complex, and dimeric trimethylaluminium.

$$(CH_3)_3Al\cdot As(CH_3)_3 \rightleftharpoons (CH_3)_3Al + (CH_3)_3As$$
$$\Downarrow\Uparrow$$
$$[(CH_3)_3Al]_2$$

With increase in temperature, the complex and the dimer dissociate. Under the conditions of the thermal decomposition (670–720 K), the equilibrium concentrations of the dimer and the complex become insignificant. This may be inferred from results on the thermodynamic measurements of the degree of dissociation of dimeric trimethylaluminium.[18] However, even small amounts of the dimer and the complex may prove to be kinetically active in the thermal decomposition process. Therefore, under the pyrolysis conditions, it is essential to take into account the following paths in the reaction of the OEC:

$$\dot{C}H_3 + (CH_3)_2\dot{A}l + As(CH_3)_3 \qquad \dot{C}H_3 + (CH_3)_2\dot{A}s$$
$$\uparrow k_1' \qquad \uparrow k_2$$
$$(CH_3)_3Al\cdot As(CH_3)_3 \rightleftharpoons (CH_3)_3Al + As(CH_3)_3$$
$$\swarrow \quad \searrow k_1''$$
$$[(CH_3)_2Al]_2 \qquad \dot{C}H_3 + (CH_3)_2\dot{A}l$$
$$\downarrow k_1'''$$
$$2\dot{C}H_3 + \text{polymer}.$$

The experimentally determined constant k_1 (see below) is an effective quantity and includes the constants for the primary elementary stages k_1', k_1'', and k_1'''.

The Arrhenius relations for the temperature variation of the rate constants for the decomposition of $(CH_3)_3Al$ and $(CH_3)_3As$ in the mixture can be represented by the equations

$$\ln k_1 = (14.8 \pm 4.4) - \frac{123 \pm 10}{RT} \quad \text{for } (CH_3)_3Al,$$

$$\ln k_2 = (33.1 \pm 1.5) - \frac{240 \pm 9}{RT} \quad \text{for } (CH_3)_3As.$$

The formation of a 1 : 1 adduct of trimethylgallium and arsine has been demonstrated by the matrix isolation method in an argon matrix at 77 K.[99] Its spectroscopic characteristics have been published. The thermal stability of $(CH_3)_3Ga$ decreases on mixing with the arsine. The decomposition is observed already at 476 K.[92] The degree of decomposition increases with increase in temperature.[100]

$$Me_3Ga \cdot AsH_3 \longrightarrow Me_2Ga{-}AsH_2 + CH_4$$
$$Me_2Ga{-}AsH_2 \longrightarrow \text{-[MeGa-AsH]-}_n + CH_4$$
$$\text{-[MeGa-AsH]-}_n \longrightarrow GaAs + CH_4$$

The indium-containing adducts $R_3In \cdot AsH_3$, which are formed even at room temperature, are still more reactive.[101,102]

The formation of the adducts $R_3M^{III} \cdot E^V R'_3$ or the dimers $(R_3M)_2$ must be taken into account in describing the kinetics and mechanism of their decomposition. They influence significantly the mass transfer conditions in the chemical gas-phase deposition. The rate of thermal decomposition of arsine[26,104,106] increases significantly in the presence of $(CH_3)_3Ga$ and arsine itself reduces the thermal stability of $(C_2H_5)_3Ga$.[100,106-108]

An important factor in the variation of the thermal stability of the mixture of OMC is the exchange interaction between them. The exchange of radicals between $(CH_3)_3Ga$ and $(CH_3)_3Al$ [109] and also between $(iso\text{-}C_4H_9)_3Al$ and $(CH_3)_3Al$ [110] has been established by NMR spectroscopy. Such exchange alters the reactivities of the mixture components as a consequence of the change in the composition of the OEC.

The pyrolysis of $(C_2H_5)_3Ga$ in the presence of AsH_3 and $(CH_3)_3Al$ in a stream of H_2 has been investigated mass-spectrometrically.[107] It was established that the decomposition of $(C_2H_5)_3Ga$ is influenced by the components of the gas mixture: arsine diminishes the temperature of the pyrolysis of $(C_2H_5)_3Ga$ approximately by 20 °C, while $(CH_3)_3Al$ increases it by 25 °C. This is associated with the different mechanisms of the decomposition of $(C_2H_5)_3Ga$ in the presence of the above components. The rate-limiting stages of the processes differ significantly.

In a mixture of $(C_2H_5)_3Ga$ and AsH_3 in a stream of hydrogen, the main reactions are

$$(C_2H_5)_3Ga \longrightarrow CH_3\dot{C}H_2 + (C_2H_5)_2\dot{G}a,$$
$$CH_3\dot{C}H_2 + AsH_3 \longrightarrow C_2H_6 + \dot{A}sH_2,$$
$$CH_3\dot{C}H_2 + \dot{A}sH_2 \longrightarrow C_2H_5AsH_2,$$

while in a mixture of $(C_2H_5)_3Ga$ and $(CH_3)_3Al$ exchange reactions take place and mixed alkyl derivatives are formed.

$$2(CH_3)_3Al \rightleftharpoons (CH_3)_2Al(\mu\text{-}CH_3)_2Al(CH_3)_2$$

$$(C_2H_5)_3Ga + (CH_3)_2Al(\mu\text{-}CH_3)_2Al(CH_3)_2 \rightleftharpoons \quad (40)$$

$$\rightleftharpoons (CH_3)_2Al(\mu\text{-}CH_3)(\mu\text{-}C_2H_5)Ga(C_2H_5)_2 + (CH_3)_3Al$$
$$\Downarrow$$
$$(CH_3)_2C_2H_5Al + CH_3(C_2H_5)_2Ga$$

$$(CH_3)_3Al + CH_3(C_2H_5)_2Ga \longrightarrow \quad (41)$$
$$\longrightarrow (CH_3)_2C_2H_5Al + (CH_3)_2C_2H_5Ga$$

The compounds $CH_3(C_2H_5)_2Ga$ and $(CH_3)_2C_2H_5Ga$ formed in the exchange reactions (40) and (41) are thermally more stable than $(C_2H_5)_3Ga$. This explains the increase in the temperature of the pyrolysis of the mixture of $(C_2H_5)_3Ga$, $(CH_3)_3Al$, and H_2. As a result of the occurrence of the equilibrium reactions (40) and (41), the pyrolysis is undergone virtually not by the two individual OEC but by a mixture with a complex chemical composition.

It has been noted that the bimolecular reaction between $(CH_3)_3Ga$ and arsine alters the thermal stability of this mixture.[111-114]

Direct measurements of the concentration of the methyl radicals by means of laser IR spectroscopy made it possible to estimate the relative contributions of certain reactions to the joint decomposition of AsH_3 with $(CH_3)_3Ga$ or $(CH_3)_3In$ in a hydrogen atmosphere.[115]

$$\dot{C}H_3 + H_2 \longrightarrow CH_4 + \dot{H} \quad (42)$$
$$\dot{C}H_3 + \dot{C}H_3 \longrightarrow C_2H_6 \quad (43)$$
$$\longrightarrow CH_4 + {:}CH_2 \quad (44)$$
$$\longrightarrow C_2H_4 + H_2 \quad (45)$$
$$\dot{C}H_3 + AsH_m \longrightarrow CH_4 + \dot{A}sH_{m-1} \quad (46)$$
$$\dot{C}H_3 + (CH_3)_nM \longrightarrow CH_4 + (CH_3)_{n-1}M\dot{C}H_2 \quad (47)$$
$$\longrightarrow C_2H_6 + (CH_3)_{n-1}\dot{M} \quad (48)$$
$$(CH_3)_nM \longrightarrow \dot{C}H_3 + (CH_3)_{n-1}\dot{M} \quad (49)$$
$$(CH_3)_nM + AsH_m \longrightarrow (CH_3)_nM \cdot AsH_m \quad (50)$$

$n, m = 1-3$; M = Ga, In.

One cannot exclude from consideration reactions (42), (44), and (47) as potential sources of methane. The main supplier of methyl radicals in these processes is reaction (49). Reactions (43) and (48) are insignificant at low concentrations of the OEC, so that ethane is virtually absent from the reaction products. The formation of ethene has been observed only at temperatures above 870 K [reaction (45)]. The concerted variation of the concentrations of methyl radicals and methane has been noted when AsH_3 was introduced into the $(CH_3)_3M$ undergoing decomposition, which confirms the important role of reaction (46) in the chemical gas-phase deposition of epitaxial GaAs or InAs layers.

Within the framework of the classical Langmuir–Hinshelwood theory of the growth of layers, it has been possible to differentiate the kinetic and diffusional temperature ranges corresponding to the development of the MOCVD process.[116-120] For example, in a stream of hydrogen the kinetic region corresponding to the growth of the GaAs layer from $(CH_3)_3Ga$ and AsH_3 occurs in the temperature range 720–870 K. According to the results of Reep and Chandhi,[117] the effective process activation energy is 92 kJ mol^{-1}, which differs little from the activation energy for the heterogeneous decomposition of AsH_3.[108] It has been suggested that the adsorption of AsH_3 and its subsequent decomposition are the rate-limiting stages in the deposition of GaAs. The temperature range 870–1120 K corresponds to the diffusional region of the growth of the GaAs film. In this range, the rate of growth is almost independent of temperature. The apparent activation energy is only ~8.4 kJ mol^{-1}. A further increase in temperature leads to the 'etching' of the epitaxial layer.

Evidence for the formation of the intermediates CH_3AsH_2 and $(CH_3)_2AsH$ in the pyrolysis of a mixture of $(CH_3)_3Ga$ and AsH_3 and also of $C_2H_5AsH_2$ in the decomposition of $(C_2H_5)_3Ga$ in the presence of AsH_3 has been obtained by IR spectroscopy.[121] The formation of a complex between R_3Ga and AsH_3 and the surface reactions are not then taken into account, the radical gas-phase reactions being considered in detail (Scheme 4). A characteristic feature of this scheme is the hypothesis of the formation as intermediates of complexes of the alkyl radicals produced on decomposition of R_3Ga in the presence of arsenic hydrides with different degrees of substitution, i.e. $R_{4-m}\dot{A}sH_m$, where $m = 1-3$.

Scheme 4

$R_3Ga \longrightarrow \dot{R} + R_2\dot{G}a$

$R_2\dot{G}a \longrightarrow \dot{R} + RGa$

$RGa \longrightarrow \dot{R} + Ga$

$\dot{R} + AsH_3 \longrightarrow RH + \dot{A}sH_2$

$\dot{R} + \dot{A}sH_2 \longrightarrow RAsH_2$

$\dot{R} + AsH_3 \longrightarrow R\dot{A}sH_3 \longrightarrow RAsH_2 + \dot{H}$

$\dot{R} + RAsH_2 \longrightarrow RH + R\dot{A}sH$

$\dot{R} + R\dot{A}sH \longrightarrow R_2AsH$

$\dot{R} + RAsH_2 \longrightarrow R_2\dot{A}sH_2 \longrightarrow R_2AsH + \dot{H}$

$\dot{R} + R_2AsH \longrightarrow RH + R_2\dot{A}s$

$\dot{R} + R_2\dot{A}s \longrightarrow R_3As$

$\dot{R} + R_2AsH \longrightarrow R_3\dot{A}sH \longrightarrow R_3As + \dot{H}$

The decomposition of $(CH_3)_3As$ and $(C_2H_5)_3Ga$ on the GaAs surface has been investigated mass-spectrometrically.[122] The rate constant found for the decomposition of $(CH_3)_3As$ (231.5) is much higher than the values obtained in a toluene atmosphere[61] and in the absence of a carrier gas.[60] The difference is associated not only with the influence of the carrier gas and with the catalysis by the GaAs surface, but apparently also with the formation of an adduct between the mixture components. The simplified model of the decomposition process then assumes the following form:

$(C_2H_5)_3\dot{G}a \longrightarrow (C_2H_5)_{3-x}Ga + x\,CH_3\dot{C}H_2,$

$(C_2H_5)_{3-x}Ga + (CH_3)_3As \longrightarrow (C_2H_5)_{3-x}Ga\cdot As(CH_3)_3,$

$(C_2H_5)_{3-x}Ga\cdot As(CH_3)_3 \longrightarrow GaAs(CH_3)_3 + (3-x)CH_3\dot{C}H_2,$

$(C_2H_5)_3Ga + (CH_3)_3As \rightleftharpoons (C_2H_5)_3Ga\cdot As(CH_3)_3,$

$(C_2H_5)_3Ga\cdot As(CH_3)_3 \rightleftharpoons GaAs(CH_3)_3 + 3CH_3\dot{C}H_2,$

$x = 1-3.$

The kinetics and mechanism of the joint pyrolysis of $(CH_3)_3Ga$ and AsH_3 on the growing GaAs surface have been investigated at low pressures of the initial reactants (1.3×10^{-2} Pa).[31] The primary stages in this case are the adsorption of $(CH_3)_3Ga$ on the surface (on Ga or As centres) and the subsequent removal of the methyl group from the surface [reactions (51) and (52)].

$(CH_3)_3Ga\,(g) \rightleftharpoons (CH_3)_3Ga\,(s)$ (51)

$(CH_3)_3Ga\,(s) \longrightarrow (CH_3)_xGa\,(s) + (3-x)CH_3\,(s)$ (52)

$x = 0-2.$

Methyl radicals are adsorbed on the Ga and As centres and are then desorbed into the gas phase.

$CH_3E\,(s) \longrightarrow \dot{C}H_3\,(g) + E\,(s)$ (53)

E = Ga, As.

Reactions (54) and (55) reflect the different paths to the formation of ethane.

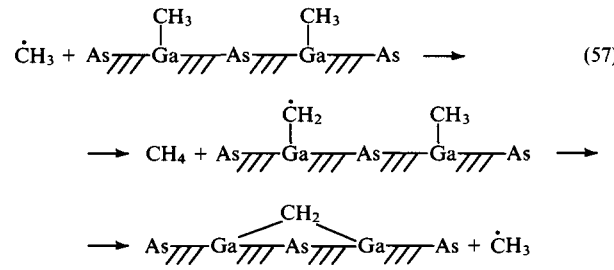
$\dot{C}H_3\,(g) + CH_3Ga\,(s) \longrightarrow C_2H_6 + Ga\,(s)$ (54)

$\dot{C}H_3\,(s) + \dot{C}H_3\,(s) \longrightarrow C_2H_6\,(g)$ (55)

The process becomes important only at temperatures above 850 K.

$(CH_3)_xGa\,(s) \rightleftharpoons (CH_3)_xGa\,(g)$ (56)

Reaction (57) demonstrates the possible ways in which carbon can be inserted in the growing epitaxial layer.



(57)

A methyl radical from the gas phase attacks the methyl group of the CH_3Ga fragment on the surface and abstracts a hydrogen atom. The resulting $\dot{C}H_2Ga$ fragment displaces a methyl radical from a neighbouring surface centre, forming a CH_2 bridge.

The products of the decomposition of AsH_3 were not detected in the gas phase (low pressure of the initial reactants). Reactions (58) and (60) reflect the AsH_3 decomposition processes on the surface.

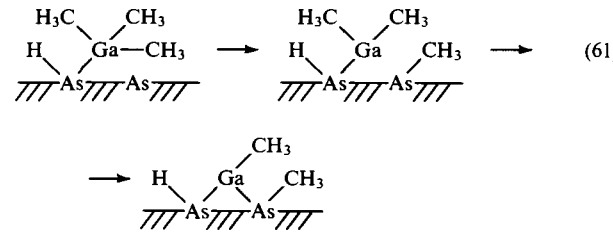
$AsH_3\,(g) \rightleftharpoons AsH_3\,(s)$ (58)

$AsH_3\,(s) \longrightarrow AsH_y\,(s) + (3-y)\dot{H}\,(s)$ (59)

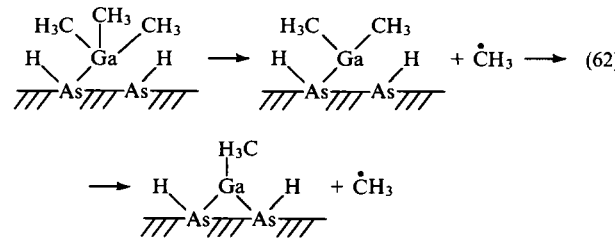
$H_yAsGa(CH_3)_x\,(s) \longrightarrow GaAs\,(s) + y\dot{H}\,(g) + x\dot{C}H_3\,(g)$ (60)

$y = 0-2.$

At low pressures of the reactants, the reactions occurring on the surface can probably be represented in the following way:



(61)



(62)

Reactions (61) and (62) correspond to the concerted processes occurring on the growing GaAs surface. The activation energy for the pyrolysis of $(CH_3)_3Ga$ on the surface is 108.8 kJ mol^{-1} and the pre-exponential factor is $10^{13.3}$ s^{-1}. The presence of arsine increases the rate of decomposition of $(CH_3)_3Ga$, whereupon E diminishes to ~84 kJ mol^{-1}.

A complex of the donor–acceptor type has been obtained in the reaction of $(CH_3)_3Ga$ with *tert*-$C_4H_9PH_2$. When the components are mixed in 1 : 1 molar proportions at room temperature, a liquid with a low vapour pressure is produced.[85]

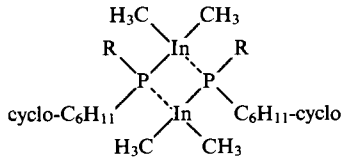
On the basis of the results of a study[81] in which it had been established that *tert*-$C_4H_9PH_2$ accelerates the decomposition of $(CH_3)_3Ga$, remaining insensitive to its presence, Yablokov et al.[85] expected to observe two different temperature ranges for the decomposition of this mixture. One should have corresponded to the decomposition of *tert*-$C_4H_9PH_2$ and the other to the

decomposition of $(CH_3)_3Ga$. In reality, the process proved to be more complex. In the temperature range 513–520 K, the rate of thermal decomposition of the mixture is described by the kinetic equation for a first order reaction and assumes the following numerical form for the rate constant (in s^{-1}):

$$\lg k = (17.2 \pm 0.8) - \frac{(125 \pm 6)}{8.314T} .$$

The mixture of gaseous decomposition products consists of CH_4 (73.4 mol.%), C_2H_6 (0.21 mol.%), iso-C_4H_{10} (17.4 mol.%), and iso-C_4H_8 (9 mol.%). This product composition differs from that in the decomposition of the individual *tert*-$C_4H_9PH_2$ (where the amount of isobutane is 99.3 mol.%) and the authors[85] therefore postulated that the complex $(CH_3)_3Ga.$*tert*-$C_4H_9PH_2$ decomposes in the temperature range 513–520 K. CH_4 and the condensation products $[(CH_3)_2Ga-PHC_4H_9$-*tert*$]$ and $[CH_3Ga-PC_4H_9$-*tert*$]_n$ are formed. Their decomposition temperature is above 680 K. The probable mechanism of the joint decomposition of *tert*-$C_4H_9PH_2$ and $(CH_3)_3Ga$ has been put forward,[85] but it requires further confirmation.

Similar phenomena have been observed on mixing *tert*-$C_4H_9PH_2$ or $C_6H_{11}PH_2$ with $(CH_3)_3In$.[83] The adduct obtained on interaction of $C_6H_{11}PH_2$ with $(CH_3)_3In$ and deposited at room temperature on the walls of the reactor and of the measuring spectroscopic cell has the following structure:



The processes involving the pyrolysis of $(CH_3)_3Ga$ and R_3As on the GaAs(001) surface have been investigated[123] by the surface photoabsorption method[124] under the conditions of the MOCVD process. In the pyrolysis of $(CH_3)_3Ga$ on the GaAs surface, the rate-determining stage in the growth of the film is the desorption of methyl radicals from the surface. In the study of the pyrolysis of $(CH_3)_3As$, $(C_2H_5)_3As$, $(C_2H_5)_2AsH$, and *tert*-$C_4H_9AsH_2$, process activation energies of 2.93, 1.58, 0.82, and 0.82 eV respectively were determined (for comparison, we may note that the activation energy for the pyrolysis of AsH_3 is 0.74 eV). The authors postulate that $(C_2H_5)_2AsH$ and *tert*-$C_4H_9AsH_2$ are possible sources of hydrogen, alternative to AsH_3, in the MOCVD processes, since the activation energy for their pyrolysis is relatively low.

Fundamental advances have been made in the modelling of processes occurring in the complex $(CH_3)_3Ga-(CH_3)_3As-AsH_3-H_2$ multicomponent system in the gas phase and on the surface of GaAs epitaxial layers.[36] The authors were interested in the mechanism of the incorporation of carbon atoms in the epitaxial layers. The proposed mechanisms of the formation of such layers include 23 gas-phase and 64 surface reactions, in which 20 gaseous compounds and 14 compounds adsorbed on the surface participate. Fig. 2 illustrates schematically the principal reaction paths of these compounds in the MOCVD process. The communication cited[36] presents the kinetic and activation parameters for all the gas-phase and surface reactions calculated from literature sources and the author's own data.

Preliminary analysis of the kinetic model showed that contamination of the epitaxial layers by carbon takes place as a result of surface reactions in which the $GaCH_3$ intermediate species is most important. The gas-phase reactions do not affect the contamination of the surface layers by carbon.

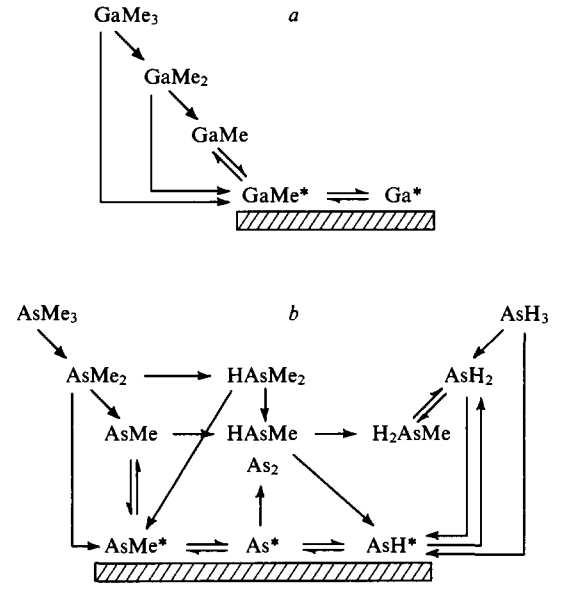


Figure 2. Schematic representation of gas-phase and surface paths of decomposition of OEC in the system $(CH_3)_3Ga-(CH_3)_3As-AsH_3$ in a stream of hydrogen (after Masi et al.[36]): (*a*) decomposition of $(CH_3)_3Ga$; (*b*) decomposition of $(CH_3)_3As$ and AsH_3.

V. Conclusion

Investigators have now come closer to understanding the detailed mechanism of the pyrolysis of the OEC of Group III and V elements in the gas phase and on the surface to such an extent that they are able to obtain excellent epitaxial layers, finding their way successfully through the labyrinth of incompatible, as regards thermal stability, explosive and toxic OEC.

The set of alternative organoelement sources in the MOCVD technology has expanded. The causes of the decrease in the rate of pyrolysis of both individual OEC and their mixtures have become understood. Ideas have been formulated concerning the combined study of the stability of OEC from the standpoint of the stability of an isolated molecule, the thermodynamic and kinetic stabilities, and also the dynamic stability of thermodynamically irreversible systems consisting of the OEC and the products of their decomposition in specific states of aggregation in the presence of mass and energy fluxes under conditions close to and remote from thermodynamic equilibrium.[125–128]

It is likely that these aspects of the investigations will in fact permit the development not only of the MOCVD technology for optoelectronics and semiconductor techniques but also for the solution of theoretical problems concerning the reactivity in the macro- and micro-processes occurring with participation of the OEC.

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Dehydrogenating properties of supported low-percentage palladium-containing catalysts

M A Ryashentseva

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Abstract. The catalytic and certain physicochemical properties of low-percentage palladium and bimetallic (Pd–Re, Pd–Co, and Pd–lanthanide oxides) supported catalysts have been examined in the dehydrogenation reactions of cyclanes, cyclenes, cyclohexadienes, their functional derivatives, and heterocyclic compounds and also in the aromatisation of petrol fractions at elevated temperatures and at hydrogen pressures ranging from atmospheric upwards. The influence of thermodynamic factors on the dehydrogenation reaction is discussed and the mechanism of this reaction is considered. The bibliography includes 160 references.

I. Introduction

During the 1950s–1960s, the catalytic reactions of C_6–C_8 hydrocarbons designed to obtain aromatic hydrocarbons were vigorously investigated both in our country and abroad. In particular, the dehydrogenation reaction of cyclanes served as a model for the selection of active metal oxide catalysts. This reaction is also of practical interest, since the aromatisation of cyclanes makes it possible to increase the octane number of the petrols obtained in the catalytic reforming process.

Mainly platinum is mentioned in the extensive patent literature of those years devoted to catalytic aromatisation in the presence of Group VIII metals. Active studies in this field were performed in the USA.[1,2] Together with the platinum catalysts, certain patents mentioned palladium catalysts on various carriers.[3–9] However, there is no information in these patents about the methods for the preparation of the catalysts, their activation, stability, etc.

M A Ryashentseva Laboratory for Catalysis on Rare and Scarce Elements, Zelinskii Institute of Organic Chemistry, Russian Academy of Sciences, Leninskii prosp. 47, 117913 Moscow, Russian Federation. Fax (7-095) 135 53 28. Tel. (7-095) 137 65 18

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Studies on the selection of effective low-percentage supported metal oxide catalysts, including those containing palladium, for the dehydrogenation of cyclanes and the aromatisation of petrol fractions under reforming conditions at elevated temperatures and hydrogen pressures have been carried out since the 1950s at the Zelinskii Institute of Organic Chemistry under the supervision of N I Shuikin and Kh M Minachev.[10]

The fundamental and applied aspects of the use of palladium-containing catalysts on the sibunit carbon carrier (a highly porous graphite-like material) in the reverse hydrogenation reaction and also in oxidation, carbonylation, etc. reactions have been widely discussed in recent years.[11–15] The palladium–carbon catalysts also exhibit an activity in the dehydrogenation reaction of cyclanes.[16] However, whereas the palladium catalysts are widely used in the hydrogenation reaction, they have not found so far a large-scale use in the dehydrogenation reaction. Nevertheless, the problem of the replacement in supported catalysts of platinum, which is active in the dehydrogenation of cyclanes and in the aromatisation of petrol and other fractions resulting from the processing of petroleum, by the less scarce palladium is of current interest.

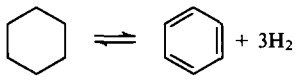
Supported palladium catalysts are also used in fine organic synthesis, which leads to new simpler procedures for the synthesis of valuable products. Heterocyclic rings constitute the structural basis of a large number of medicinal substances both of natural and of synthetic origin. The molecules of these compounds also contain various aliphatic and aromatic substituents. Derivatives of five- and six-membered heterocycles and their condensed systems constitute a class of medicinal heterocyclic compounds of practical importance.[17] Dehydrogenation reactions in the presence of supported palladium catalysts are employed to obtain some of them.

Studies designed to develop effective dehydrogenating supported palladium catalysts (monometallic and bimetallic) for the conversion of cyclanes, cyclenes, cyclohexadienes, and their derivatives and for the aromatisation of petrol fractions and the synthesis of indole, coumarin, papaverine and their derivatives, will be examined in the present review.

II. Thermodynamics of the dehydrogenation reactions of naphthenes

1. The influence of pressure

The dehydrogenation of six-membered naphthene hydrocarbons involve an appreciable increase in volume, so that an increase in pressure hinders their occurrence.



Calculations have shown[18] that the influence of pressure is particularly marked at temperatures below 500 °C. An increase in temperature from 400 to 600 °C at the same pressure shifts the equilibrium towards the formation of aromatic hydrocarbons. An increase in pressure from 14 to 56 atm at 510 °C has a negative effect on the formation of aromatic hydrocarbons, in particular on the conversion into benzene of cyclohexane and methylcyclopentane after the isomerisation of the latter to cyclohexane. The influence of pressure in this reaction is greater than in the conversion of methylcyclohexane into toluene.[19] An increase in pressure from 21 to 42 atm at 444 °C leads to a decrease in the yield of benzene obtained from cyclohexane from 70% to 33%.[20] In the presence of the Pd/Al_2O_3 catalyst at 460 °C, a space velocity (v) of 1.0 h^{-1}, and for the ratio H_2:HC = 5:1 (HC = hydrocarbon), an increase in pressure from 35 to 65 atm reduces the yield of aromatic hydrocarbons derived from ethylcyclohexane from 57.7% to 44.7%.[21]

2. The influence of temperature

In the presence of supported catalysts containing Group VIII metals, an increase in temperature from 440 °C to 510 °C (P_{H_2} = 21 atm, v = 3.0 h^{-1}, H_2:HC = 4:1) increases the yield of aromatic hydrocarbons derived from cyclohexane, methylcyclohexane, and methylcyclopentane from 70% to 93%, from 83% to 92%, and from 56% to 72% respectively.[20] In reactions involving cyclohexane and methylcyclohexane, the content of aromatic hydrocarbons in the catalytic reaction mixture reaches the equilibrium value.[22] An increase in temperature from 426 to 540 °C promotes the dehydrocyclisation of n-heptane; the yield of aromatic hydrocarbons increases from 2% to 25%.[20]

Thus, in conformity with thermodynamic postulates, an increase in hydrogen pressure inhibits the dehydrogenation reactions of six-membered cyclanes but at a higher temperature this influence becomes less marked. For example, at 510 °C the yield of benzene from cyclohexane is almost independent of pressure.[20] An increase in pressure from 10.5 to 35 atm at 496 °C also has an insignificant influence on the dehydrogenation of methylcyclohexane.[19]

Nevertheless, the reforming process is carried out in industry under a hydrogen pressure in order to suppress reactions leading to the formation of a 'carbonaceous film' on the catalysts,[23,24] which reduce their activity.[25-28]

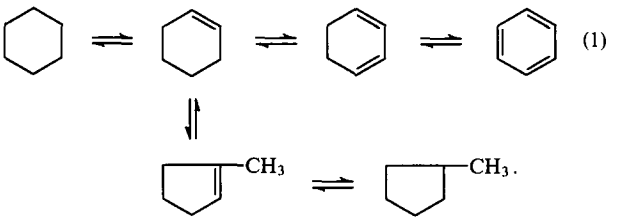
3. The influence of other factors

Apart from temperature and pressure, the aromatisation reaction is also influenced by the space velocity at which the starting material is supplied and by the starting material: hydrogen ratio.[19,29,30] As a rule, an increase in space velocity diminishes the yield of aromatic hydrocarbons. The change in the molar ratio of the circulating hydrogen and the starting material in the range (4–11):1 has little effect on the yield of the aromatisation product.[29] However, under platforming conditions, where the effluent gas consists mainly of hydrogen, the recirculating gas hinders the formation of the 'carbonaceous film' on the catalyst[24] and increases the lifetime of the latter, and thereby eliminates the need for frequent regeneration.

III. The mechanism of the dehydrogenation of cyclanes and cyclenes

At one time the sextet[31-41] and doublet[32,37,42-44] mechanisms of the dehydrogenation reaction as well as the mechanism postulating the initial formation of cyclohexene with subsequent disproportionation to cyclohexane and benzene[45-47] were widely discussed in the literature.

On metal oxide catalysts operating at an elevated pressure, the dehydrogenation of six-membered cyclanes[48,49] is to a large extent accompanied by their isomerisation with formation of five-membered cyclanes. A number of workers[50-52] considered the following scheme [scheme (1)] for the conversion of cyclohexane on metal oxide catalysts:



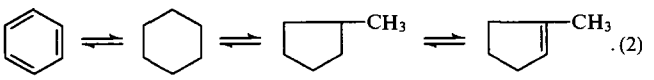
(1)

The isomerisation reaction proceeds via the carbonium ion mechanism.[53,54]

The reactions of radioactive cyclohexane have been investigated on the 1% $Pd-HF-Al_2O_3$ catalyst under reforming conditions (T = 480 °C, P_{H_2} = 21 atm, v = 1–2.5 h^{-1}, H_2:HC = 5:1).[55] In the presence of this catalyst, cyclohexane is converted into benzene (59%–63%) and methylcyclopentane (19%–23%), cyclohexene also undergoing dehydrogenation and isomerisation. However, cyclohexene, which is more reactive than cyclohexane, reacts almost completely. The specific radioactivity of the initial cyclohexene was zero and it might have been expected that it would increase with increasing degree of conversion. However, the results of the analysis of the reaction products showed that cyclohexene is almost nonradioactive, whereas benzene and methylcyclopentane are radioactive. Hence it follows that cyclohexane is not converted into cyclohexene. Thus the result failed to confirm the hypothesis that cyclohexene is an intermediate in the dehydrogenation of cyclohexane to benzene and in its isomerisation to methylcyclopentane. On a bifunctional catalyst, benzene and methylcyclopentane can apparently be obtained from cyclohexane without the intermediate formation of cyclohexene or at least without its desorption from the catalyst surface.[55]

In view of the results presented above, the role of methylcyclopentene in the expansion of the methylcyclopentane ring was investigated under the same conditions (T = 480 °C, P_{H_2} = 20 atm, v = 2.5 h^{-1}, H_2:HC = 5).[56,57] The reactions of a mixture of [6-^{14}C]methylcyclopent-1-ene and methylcyclopentane were investigated on the 1% Pd/Al_2O_3 catalyst. It was shown that the specific radioactivities of cyclohexane and benzene and also methylcyclopentane in the reaction products are similar and are in the range 2.0%–3.6% of the specific radioactivity of the initial [6-^{14}C]methylcyclopent-1-ene, whereas the specific radioactivity of the latter in the catalytic reaction mixture is much higher (12.1%–36.8%). Hence it follows that cyclohexane and benzene are obtained from methylcyclopentane without the intermediate formation of methylcyclopent-1-ene.

Scheme (2) therefore characterises the interconversions of the cyclanes more accurately than scheme (1):



(2)

But at the same time, it is necessary to take into account the possible conversion of methylcyclopent-1-ene into cyclohexane and benzene via scheme (1) as well, since the specific

radioactivities of cyclohexane and benzene exceed somewhat that of methylcyclopentane, which would be impossible for a strictly consecutive mechanism.

Thus cyclohexene is not an essential intermediate in the formation of benzene and methylcyclopentane from cyclohexane[55,57] and methylcyclopentene is likewise not an obligatory intermediate in the formation of benzene from methylcyclopentane.[56,58] This is confirmed by the experimental data for the reactions of cyclohexane and cyclohexene under reforming conditions (T = 450 °C, P_{H_2} = 21 atm, v = 10 h^{-1}, H_2 : HC = 5) where the 0.5% Pt–0.3% F–Al_2O_3 catalyst was poisoned with thiophene.[59] When mixtures of cyclohexane or cyclohexene with thiophene were passed through the system, a sharp decrease in the dehydrogenating capacity of the catalyst was observed, while the benzene content in the catalytic reaction mixtures diminished respectively from 74.2% and 90% to 15.4% and 46.6%. Thus the addition of thiophene to cyclohexane and cyclohexene diminishes the yield of benzene almost by a factor of 5 and only by a factor of 2 respectively.

The hypothesis[60] that thiophene acts predominantly on the cyclohexene dehydrogenation centres conflicts with the above results, so that the data of Hensel et al.[60] are inconsistent with scheme (1). The ratio of the concentrations of cyclohexane and methylcyclopentane in the catalytic mixtures obtained from cyclohexane is much closer to the equilibrium ratio than in the catalytic reaction mixture obtained from cyclohexene. These data also indicate that cyclohexene cannot be regarded as an essential intermediate in the isomerisation of cyclohexane to methylcyclopentane under reforming conditions.

In order to test scheme (1) and the data of Hensel et. al.,[60] a study was made of the reactions of cyclohexane and cyclohexene on the 1% Pd/AlO_3 and 1% $Pd/Al_2O_3 \cdot HF$ catalysts. The dehydrogenating functions of these catalysts were poisoned by thiophene, after which they were restored by treatment with a hydrocarbon. In contrast to the experimental conditions in the study of Isagulyants and Ryashentseva,[59] a much lower rate of supply of the hydrocarbons (5.5 h^{-1}) at 460 °C, P_{H_2} = 20 atm, and H_2 : HC = 5 was chosen to make sure that the catalytic reaction products contained also methylcyclopentene in addition to benzene and methylcyclopentane. For comparison, a study was also made of the reactions of cyclohexane and cyclohexene under the same conditions on the industrial AP-56 aluminoplatinum catalyst. On the palladium catalysts, the yield of methylcyclopentene was found to be higher by 2%–5%, whilst that of benzene was lower by 12%–16%, than on the platinum catalyst. This shows that the palladium catalysts are less active in the dehydrogenation reaction and are more active in the isomerisation process. After a mixture of cyclohexane with 1% of thiophene was passed through the system, the degree of activity of the aluminopalladium catalysts fell sharply (almost by a factor of 12), in contrast to the aluminoplatinum catalyst, while its isomerising activity remained almost unchanged. The dehydrogenating activity of the aluminopalladium catalyst was restored to the extent of 55%, while that of the fluorinated catalyst was restored to the extent of 50% relative to the initial activity after regeneration with cyclohexane for 6.5 and 8 h respectively. On the other hand, the activity of the platinum catalyst was 94% restored after passing cyclohexane for 4 h. Hence it follows that the dehydrogenating centres on the aluminopalladium catalyst are more sensitive to thiophene than the corresponding centres on the aluminoplatinum catalyst. In contrast to the platinum catalysts, the palladium catalysts convert cyclohexene into methylcyclopentenes to the extent of 12%–27%, which indicates their higher isomerising activity.[61,62] The dehydrogenating activity of the aluminopalladium catalyst fell from 13.7% to 6.9% and that of the similar fluorinated catalyst fell from 21.7% to 13.9% when cyclohexene was passed (T = 460 °C, P_{H_2} = 20 atm, v = 5.5 atm, and H_2 : HC = 5) through the system after the latter had operated for 3 h. At the same time, their isomerising activity increased: the yield of methylcyclopentenes rose from 18% to 44% and from 10% to 17.5% respectively. Up to 0.5% of cyclohexadiene was detected in the catalytic reaction mixtures. Under the same conditions, the isomerising and dehydrogenating activities of the aluminoplatinum catalyst remained unchanged.

After cyclohexene mixed with thiophene was passed over the palladium catalysts, the degree of formation of benzene fell by a factor of 2.3. Their isomerising activity (the yield of methylcyclopentenes) decreased only insignificantly under these conditions, which is inconsistent with the hypothesis[50] that dehydrogenating centres of two types are present on the catalyst surface and that cyclohexane is converted into cyclohexene on sections of the first type, while benzene is formed from cyclohexene on those of the second type. On further passage of cyclohexene, the dehydrogenating functions of the palladium catalyst are not restored, in contrast to the platinum catalysts, and the catalyst is irreversibly poisoned. The yield of benzene obtained from cyclohexene is much lower than that of the benzene obtained from cyclohexane. On the aluminoplatinum catalyst, this difference is difficult to observe owing to the high degrees of conversion. On the aluminopalladium catalysts, the yield of the benzene derived from cyclohexane was 54%–58%, whilst that of the benzene derived from cyclohexene was 18%–22%.

According to the results of Ryashentseva et al.,[61] only the centres for the dehydrogenation of cyclohexane to benzene should be poisoned. Consequently, according to scheme (1), the yields of methylcyclopentane derived from cyclohexane and cyclohexene should be similar. The experimental yield of benzene under the conditions of the conversion of cyclohexane mixed with thiophene was 3%, which indicates the inhibition of the benzene formation centres. The yield of methylcyclopentane proved to be 4%, i.e. the hydrogenation centres were also inhibited, which conflicts with the results of Isagulyants and Ryashentseva.[59] When a mixture of cyclohexane with thiophene was allowed to react, the yield of methycyclopentane did not diminish.

It follows from these data that the reactions involving the isomerisation of cyclohexane and cyclohexene proceed independently and probably on different isomerising centres.[62] This has been confirmed by the results obtained on the fluorinated aluminopalladium catalyst. In the presence of the latter, the yield of methylcyclopentane derived from cyclohexane increases, compared with the yield on the aluminopalladium catalyst, from 9.8% to 12.8% after 1 h, whereas the yield of methylcyclopentenes obtained from cyclohexene diminishes from 27.2% to 12.1%.[61] After the passage of the cyclohexene–thiophene mixture over the palladium catalysts, the content of methylcyclopentene was ten times greater than the content of methylcyclopentane. The absence of cyclenes from the products of the catalytic reaction involving cyclohexane and the presence in the latter of methylcyclopentane also cannot be accounted for by scheme (1).

All these findings confirmed the conclusion[55,59] that cyclohexene is not an essential intermediate in the conversion of cyclohexane into methylcyclopentane and benzene. On the aluminopalladium catalyst, the reactions of cyclohexane and cyclohexene proceed by independent paths, probably via different intermediates.[61] However, these is also evidence in support of the conversion of cyclohexane into benzene on metals to a large extent via the intermediate formation of cycloalkenes.[63] The difficulty of detecting the intermediate cycloalkenes is associated with the fact that their reactivity increases greatly in the sequence cyclohexane < cyclohexene < cyclohexadiene and hence cycloalkenes are present in the products in appreciable amounts only for very low degrees of conversion.

Apart from the consecutive path leading to the dehydrogenation of cyclohexane, which includes the desorption of cyclohexene, another path may also exist where cyclohexane is converted directly into benzene via a stage involving the formation of surface cyclohexene or bypassing it. The choice between these paths is apparently determined by the nature of the

chemical bond between the adsorbed hydrocarbon molecule and the catalyst surface.[63] According to the data of Tetenyi et al.,[64] the contribution of the path involving the direct hydrogenation of cyclohexane to benzene increases, while that of the dehydrogenation via the intermediate cyclohexene diminishes in the sequence

Co > Ni > Rh > Ir > Re > Pd > Pt.

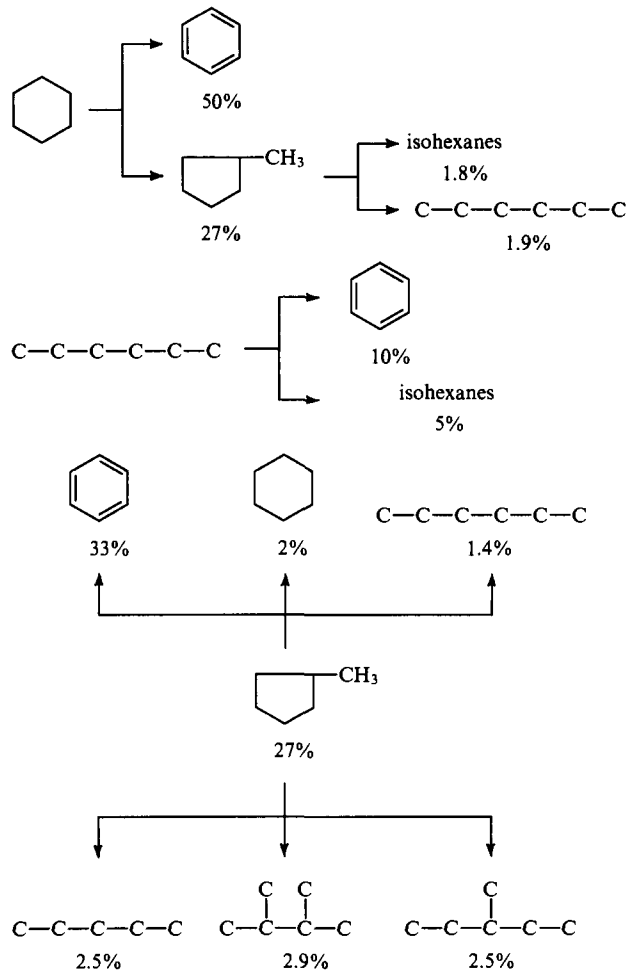
IV. Palladium-containing supported catalysts in the dehydrogenation reactions of cyclanes and their functional derivatives

According to Balandin's multiplet theory,[65] there should be a structural correspondence between the catalyst multiplet and the part of the reactant molecule oriented on it which is altered in the reaction. The hexagonal symmetry of the multiplet necessary for the hydrogenation of benzene and the reverse cyclohexane dehydrogenation reaction is achieved only on cubic face-centred and hexagonal (but not cubic) body-centred crystal lattices. Although platinum and palladium both have type *A* face-centred cubic lattices with constants of 0.27746 and 0.27511 nm respectively, their activities differ appreciably in the reactions considered.

Palladium is used widely in laboratory practice as a dehydrogenation and especially hydrogenation catalyst.[66] In Zelinskii's early studies,[66,67] palladium black without a carrier was used as the catalyst for the reactions of hydrocarbons. In subsequent investigations, palladium black was deposited on various carriers (asbestos, activated charcoal, etc.) in order to obtain catalysts with a maximum surface area. However, the concentration of the active metal was fairly high even in such cases and varied in the range 30%–40%,[68,69] sometimes attaining even 70%.[70] Such catalysts were characterised by a high activity in the hydrogenation of benzene and only a satisfactory activity in the dehydrogenation of cyclohexane. Their low dehydrogenating activity and low stability were explained by the fact that, after deposition on activated charcoal, palladium black exists in the form of a hydride (with a crystal lattice parameter of 4.04 Å instead of the normal parameter of 3.88 Å).[71] It was established that, during prolonged operation of the catalyst, this parameter remains almost unchanged. The X-ray diffraction patterns taken after prolonged operation of the catalyst were found to contain, apart from the lines due to palladium, also secondary lines which did not refer to either palladium or its hydride. The appearance of a new finely dispersed palladium phase was explained by the low stability of the palladium catalysts.[72] A phase of this kind did not appear during the employment of platinum catalysts.

The low-percentage palladium catalysts containing from 2.0% to 0.5% of Pd/C exhibit a high dehydrogenating activity.[73,74] Their X-ray diffraction study before and after use showed that they contain only one crystalline palladium phase and X-ray diffraction patterns did not reveal the appearance of any new lines after the participation of the catalyst in the reaction. The low-percentage catalysts are apparently more active and stable because their palladium lattice has favourable parameters. However, even these palladium catalysts lose their activity comparatively rapidly under the conditions of prolonged operation, especially with petrol fractions containing, in addition to the six-membered cyclanes, also five-membered cyclanes, aromatic hydrocarbons, and alkanes.

Systematic studies led to the development of a 0.5% Pd/Al_2O_3 catalyst treated with hydrofluoric acid and hydrogen sulfide,[10] which is capable of operating at an elevated H_2 pressure and a high temperature. The reactions of cyclohexane, n-hexane, and methylcyclopentane,[48] which constitute the basis of the reforming of petrol fractions, were investigated on this catalyst at $T = 480$ °C, $P_{H_2} = 20$ atm, $v = 1.0\ h^{-1}$, and $H_2:HC = 5$.



It was shown that, together with the dehydrogenation of cyclohexane, the dehydroisomerisation of methylcyclopentane and the skeletal isomerisation and dehydrogenation of n-hexane take place on this catalyst. When gumbrin (a natural aluminosilicate containing 86.89% of SiO_2 or 4.14% of Al_2O_3 and having a specific surface of 260 $m^2\ g^{-1}$) is used as the carrier, methylcyclopentane is also formed from cyclohexane together with benzene on a 0.5% palladium catalyst under reforming conditions ($T = 475–480$ °C, $P_{H_2} = 20$ atm, $v = 1.0\ h^{-1}$, and $H_2:HC = 5:1$). Under these conditions, the carrier itself (gumbrin) exhibits pronounced isomerising properties — 19.2% of methylcyclopentane is formed on this carrier from cyclohexane, the reaction being accompanied by slight cracking.[75] Treatment of the catalyst with hydrogen sulfide enhances its dehydrogenating and isomerising properties: the benzene content in the catalytic reaction mixture increases from 28.5% to 40.2%, while that of methylcyclopentane increases from 19.2% to 22.7%. This bifunctional catalyst may be useful for refining low-octane petrols.

The 0.5% Pd/Al_2O_3 and 0.5% Pd/SiO_2 catalysts have been investigated in the conversion of methylcyclohexane.[76] The experiments were performed under the following conditions: $T = 460$ °C, $P_{H_2} = 20$ atm, $v = 1.1\ h^{-1}$, and $H_2:HC = 5:1$. The toluene contents in the products when the above catalysts were used amounted to 82% and 93% respectively. Under similar conditions, ethylcyclohexane underwent various reactions on the 0.5% Pd/Al_2O_3 catalyst: dehydrogenation, hydrogenolysis of the side chain, and isomerisation with ring contraction and subsequent opening of the five-membered ring.[77] The increase in pressure from 35 to 65 atm increases the degree of conversion of ethylcyclohexane from 61.4% to 84.8%. The introduction of fluorine into the catalyst lowers its dehydrogenating activity and increases its isomerising activity. It has been suggested that

fluorine in the form of PdF_2 partially shields the catalyst active centres, diminishing thereby its dehydrogenating activity.

The kinetics of the dehydrogenation of cyclohexane have been investigated on palladium-containing supported catalysts treated with hydrofluoric acid or hydrogen sulfide.[78] The apparent activation energies and pre-exponential factors in the Arrhenius equation for the reactions on the 0.5% Pd/Al_2O_3 and 0.5% $Pd/Al_2O_3 \cdot HF$ catalysts, calculated from the initial activity, hardly differed. After the treatment of the 0.5% $Pd/Al_2O_3 \cdot HF$ catalyst with hydrogen sulfide, the activation energy increased appreciably, while the pre-exponential factor changed by several orders of magnitude.

On the most active hydrogen sulfide-treated 0.5% $Pd/Al_2O_3 \cdot \cdot HF$ catalyst at atmospheric pressure, $T = 450$ °C, and $v = 0.3$ h^{-1}, cyclohexane is 94% dehydrogenated to benzene.[79]

New palladium-containing catalysts, obtained by depositing the metal on $AlPO_4$ and $AlPO_4 \cdot SiO_2$ colloidal systems, have been used successfully for the reduction of nitrobenzene.[80] Similar modified catalysts, containing 0.5% of palladium on the SiO_2, $AlPO_4$, and $SiO_2 \cdot AlPO_4$ carriers, have been investigated in the cyclohexane and methylcyclohexane dehydrogenation reactions under pulsed conditions.[81] In terms of dehydrogenating capacity, the platinum-containing catalysts proved to be much more active than the palladium-containing ones. Table 1 presents the results of experiments on the dehydrogenation of cyclohexane on these catalysts.

Table 1. Dehydrogenation of cyclohexane on various metal-containing catalysts[81] (atmospheric pressure, $T = 425$ °C, pulse size 8.34×10^{-5} moles).

Metal	Carrier	Yield of C_6H_6(%)	Activity[a]
Pd	SiO_2	13.6	9.00
Pt	SiO_2	82.3	3.90
Pd	$AlPO_4$	5.2	2.87
Pt	$AlPO_4$	25.5	1.45
Pd	$SiO_2 \cdot AlPO_4$	13.8	4.01
Pt	$SiO_2 \cdot AlPO_4$	72.0	3.73

[a] The number of moles of cyclohexane converted per m^2 of the metal multiplied by 10^3.

During the last decades, physical methods permitting the study of highly dispersed metal particles distributed on the surface of the carrier have developed vigorously. New approaches to the selection of metal-containing supported catalysts have appeared.[82-87] The state of palladium on aluminium oxide has been investigated by the XPS method and its strong interaction with the carrier has been demonstrated.[88] The interaction of the metal with the carrier is influenced by the ligand environment. For example, impregnation catalysts obtained with the aid of $PdCl_2$ or $Pd(NO_3)_2$ solutions have different properties. The state of palladium also changes during the reduction of the catalyst. The aluminium oxide carrier is capable of retaining chlorine.

The strong interaction of $PdCl_4^{2-}$ with the acceptor centres of γ-Al_2O_3 has been observed.[89] On the other hand, palladium interacts weakly with the carrier of the Pd/SiO_2 catalyst. Zerovalent palladium is formed already at 100 °C, but the metal is not fully reduced, the most dispersed zerovalent palladium particles interacting with the carrier. According to the results obtained by transmission electron microscopy, the average Pd(0) particle size is 4.5 nm in the 1% Pd/Al_2O_3 catalyst at 300 °C and 8.5 nm in the 1% Pd/SiO_2 catalyst.

Current ideas about the interaction of the metal with the carrier were taken into account[90] when the properties of the 0.5% Pd/γ-Al_2O_3 and 0.5% Pd/sibunit catalysts were investigated in the dehydrogenation of cyclohexane. A strong interaction of the carrier with the metal is manifest in the first catalyst, while the sibunit carbon carrier hardly undergoes such interaction.[91] The specific surface of the active alumina was 225 m^2 g^{-1} for an overall pore volume of 0.68 cm^3 g^{-1}, while the specific surface of sibunit (granulated carbon) was 590 m^2 g^{-1} for a particle size of 2–2.5 mm.[91] The data concerning the dehydrogenation of cyclohexane on these catalysts are presented in Table 2.

Table 2. Dehydrogenation of cyclohexane (atmospheric pressure, $t = 1$ h, H_2 stream).[16]

Catalyst	Reaction conditions		Yield[a]	Content of C_6H_6 (%)
	T/°C	v/h^{-1}		
0.5% Pd/γ-Al_2O_3	425	0.75	51.0	87
	450	0.75	89.4	47
	480	0.75	63.7	98
0.5% Pd/γ-Al_2O_3	440	1.5	83.6	81
(treated with	440	0.7	81.2	85
H_2S)	450	1.5	91.8	85
	455	0.6	95.2	90
	460	0.5	56.6	95
	470	0.5	66.7	100
0.5% Pd/sibunit	430	1.2	75.3	83
	440	1.2	80.0	89

[a] Yield of the catalytic reaction mixture.

Cyclohexane is dehydrogenated in the temperature range 430–480 °C. Treatment of the catalyst with hydrogen sulfide increases the benzene content in the catalytic reaction mixture almost by a factor of 2 ($T = 440-450$ °C, $v = 0.75$ h^{-1}). A high yield of benzene is retained also following an increase in the space velocity at which cyclohexane is supplied by a factor of 2. The Pd/sibunit catalyst likewise exhibits a high dehydrogenating activity under similar conditions.

The dehydrogenating activity in this reaction is apparently influenced more by factors such as the porosity of the carrier, the catalyst grain size, the methods used to activate the catalyst, the composition of the reaction mixture, and other factors (which in fact determine the rate of reaction) than by the metal–carrier interaction.

Ethylcyclohexane was dehydrogenated in the liquid phase under a nitrogen atmosphere at 132 °C on suspended Pd/C and Pd/Al_2O_3 catalysts.[92] The activity of the catalyst was determined from the amount of hydrogen evolved. The results are presented in Table 3.

Table 3. Liquid-phase dehydrogenation of ethylcyclohexane (0.02 mmol per 100 ml of the catalyst) in the presence of supported catalysts containing 0.5% of the metal.[92]

Catalyst	H_2/mmol	Yield of ethylbenzene/mmol
Pd/C	9.22	3.18
Pd/Al_2O_3	3.67	1.25
Pt/C	23.93	7.75
Pt/Al_2O_3	13.04	4.15

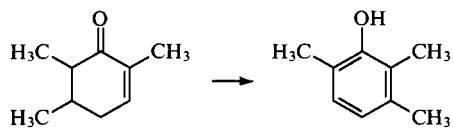
The Pd/C catalyst has a dehydrogenating activity higher by a factor of 3 than Pd/Al_2O_3. However, Table 3 shows that both catalysts are appreciably inferior to the supported platinum catalyst. Under the conditions of liquid-phase dehydrogenation with the recondensation of the ebullition products, the Pd/C and Pd/Al_2O_3 catalysts exhibit a higher activity in the preparation of cyclooctene from cyclooctane than do supported rhodium and ruthenium catalysts.[93] The activity was determined from the degree of desorption of hydrogen.

The use of the Pd/C catalyst leads to new possibilities for the preparation of silicon-containing compounds by the hydrosilylation of cyclohexadiene with subsequent dehydrogenation. Phenylsilicones can be synthesised by this procedure in one stage, in which the liquid silicon hydride and cyclohexadiene react on refluxing in the presence of the Pd/C catalyst and $C_6H_5NO_2$ as the acceptor.[94]

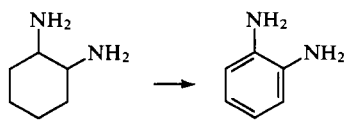
There are data concerning the use of supported palladium catalysts in the dehydrogenation reactions also of other organic compounds.[95-97] The synthesis of 8-hydroxycymene by the dehydrogenation of 8-hydroxymenthene in the presence of a palladium-containing catalyst has been described.[95]

A mixture containing 78% of α-terpineol and 10% of γ-terpineol was passed at 190–200 °C at a rate of 0.4 kg h^{-1} for 588 h over the 0.2% Pd/Al_2O_3 catalyst treated beforehand with a NaOH solution, partly dried, and reduced.[95] This yielded 231.3 kg of product, which contained 154.78 kg of 8-hydroxycymene, 49.40 kg of the dihydroterpineol isomers, 11.98 kg of *p*-cymene and 10.2 kg of the initial terpineol. The degree of conversion was 98.2%. During the tests, the catalyst did not lose its activity.

Phenol and phenol derivatives can be obtained by dehydrogenating a cyclic ketone in the gas phase in the presence of the Pd/Al_2O_3 catalyst.[96] For example, 2,3,6-trimethylphenol has been obtained in 100% yield on passing 2,5,6-trimethylcyclohex-2-en-1-one in a stream of hydrogen at 300 °C at a rate of 0.25 litre per litre of the 0.5% Pd/Al_2O_3 catalyst (the specific surface of the carrier was 4 m^2 g^{-1}). The catalyst was prepared by impregnating the carrier with an aqueous $PdCl_2$ solution and was then dried and reduced with hydrogen at 300 °C. The degree of conversion was 82.6%. The selectivity of the catalyst decreased with increase in the specific surface of Al_2O_3. The selectivity was zero for a specific surface of 170 m^2 g^{-1}.



o-Phenylenediamine has been obtained in a yield of 69% at 200 °C by the dehydrogenation of 1,2-diaminocyclohexane in the gas phase at 175–225 °C, a pressure of 0.1–10 atm, and a supply rate of 0.25 ml min^{-1} over the 5% Pd/Al_2O_3 catalyst containing 0.61% of LiOH under a nitrogen atmosphere.[97]

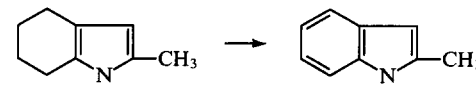


V. Palladium catalysts in the dehydrogenation reactions of heterocyclic compounds

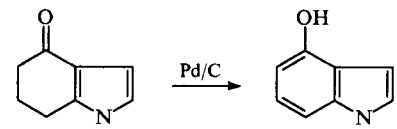
1. Dehydrogenation of tetrahydroindole and its derivatives

The selection of a catalyst for the dehydrogenation of heterocyclic compounds with a pyrrole ring is complicated by the fact that they poison catalysts containing noble metals. Indole and its derivatives were synthesised in the presence of palladium-containing supported catalysts in both liquid and gas phases. Indole and its homologues are important intermediates in fine organic synthesis. They are used as plant growth stimulators, especially β-indolylacetic acid (heteroauxin) and 3-(γ-indolyl)butyric acid.[98] Numerous medicinal preparations used in neurophysiology and psychopharmacology have been obtained from indole derivatives.[99] The principal source of indole is coal tar, which contains 2%–3% of this substance.[100]

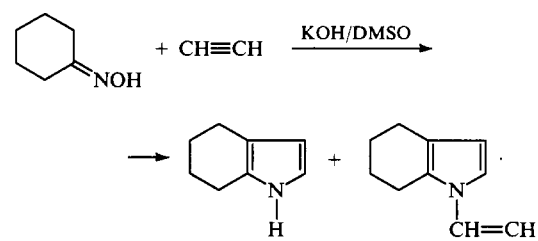
Tetrahydroindole and its derivatives are promising sources for the preparation of pure indole by dehydrogenation. 1-Methylindole has been obtained in 67% yield from 1-methyl-4,5,6,7-tetrahydroindole in the presence of the 10% Pd/C catalyst in the xylene liquid phase under a stream of nitrogen after refluxing for 18 h.[101,102]



4-Hydroxyindole can be obtained in 94% yield by the liquid-phase dehydrogenation of 4-oxo-4,5,6,7-tetrahydroindole in 2-ethylhexyl acetate in the presence of a Pd/C catalyst at 192 °C.[103] The reaction is carried out by refluxing for 7 h.



The possibility of the dehydrogenation of the cyclohexene fragment of 1-vinyl-4,5,6,7-tetrahydroindole (VTHI) and in its mixture with 4,5,6,7-tetrahydroindole (THI) under the conditions of heterogeneous catalysis on low-percentage palladium-containing supported catalysts has been demonstrated.[104] The compounds VTHI and THI became available as a result of the development of a simple method of their synthesis from ketoximes and ethyne by the Trofimov reaction.[105] In the case of cyclohexanone oxime, the process proceeds in accordance with the following mechanism:

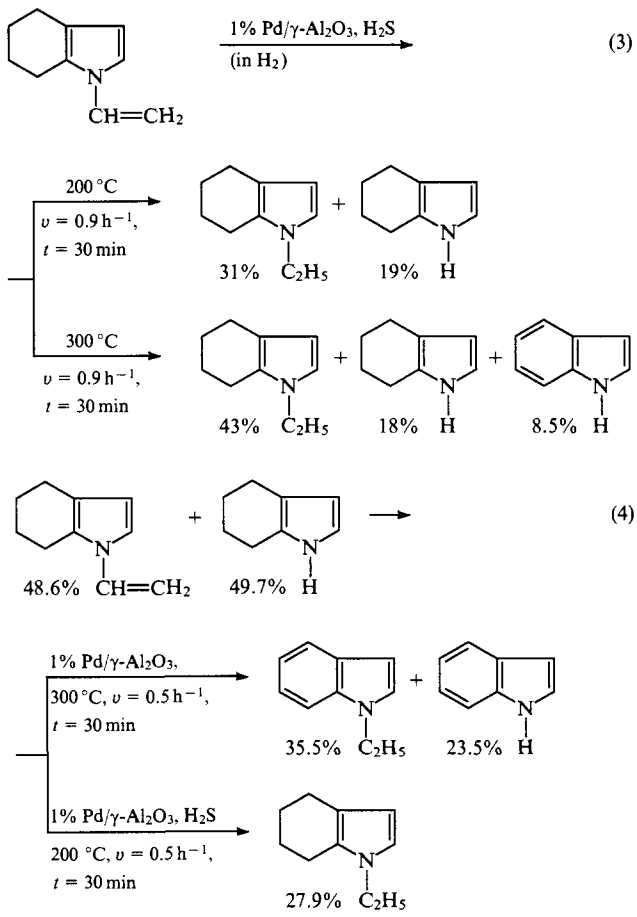


Depending on the medium in which the reaction is carried out, it is possible to obtain high yields (up to 83%–92%) of THI or VTHI.[106] The compounds THI and VTHI are promising indole synthons,[105-108] and are used, in particular, to synthesise α-substituted indoles which are otherwise difficult to obtain.[101,102]

The reactions of VTHI and its mixtures with THI in a solvent were achieved in a flow-type apparatus at atmospheric pressure in the temperature range from 100 to 525 °C, at $v = 0.3-1.2$ h^{-1}, and for a duration of the experiment ranging from 30 min to 3 h. Aluminopalladium catalysts containing 1% and 1.5% of the metal were used. The carriers were industrial γ-Al_2O_3 specimens.

A mixture of 48.6% of VTHI and 49.7% of THI (the remainder comprised cyclohexanone oxime) was obtained in a pilot plant from cyclohexanone oxime and ethyne. It was used without separation into components as the technically most readily available starting material.[109] The results are illustrated in schemes (3) and (4).

On the sulfided 1% Pd/γ-Al_2O_3 catalyst at 200 °C and $v = 1.0$ h^{-1}, 31% of 1-ethyltetrahydroindole (1-ETHI) and 19% of THI (relative to the VTHI passed through the system) are obtained from VTHI in 30 min in a hydrogen stream (3.6 litre h^{-1}), i.e. reactions involving the hydrogenation of the double bond and the cracking of VTHI, accompanied by the hydrogenolysis of the N–C bond, take place. The yield of the remaining cracking products ranges from 5% to 20%. On raising the reaction temperature to 300 °C, the yield of 1-VTHI increases to 42.7%. The six-membered ring is also dehydrogenated with formation of indole (yield 8.5%). The increase in the palladium concentration to 1.5% enhances the hydrogenating properties and weakens the cracking properties of the catalyst. The yield of 1-ETHI reaches 37%.



The principal products of the conversion of the VTHI – THI mixture are 1-ETHI, indole, and 2-ethylindole (2-EI), whose ratios depend on the composition of the catalyst. Indole is formed from VTHI in 47.2% yield on the 1% $Pd/\gamma\text{-}Al_2O_3$ catalyst at 350 °C and $\upsilon = 0.5\ h^{-1}$; the content of 2-ethylindole is 23.7%, while 1-ethylindole is virtually absent. The formation of 2-ethylindole is probably associated with the acid functions of the $\gamma\text{-}Al_2O_3$ carrier, which intensify the migration of the ethyl group to the α-position in the pyrrole ring (the thermal isomerisation of 1-alkylpyrroles to the 2-alkyl derivatives is well known).[110] The principal factor influencing the course of the above reactions on the aluminopalladium catalyst is the temperature, while the space velocity at which the mixture is supplied and the reaction time have little effect on the yield of indole and 2-ethylindole.

The selectivity of the sulfided aluminopalladium catalyst differs appreciably from that of the initial aluminopalladium catalyst. Only 1-ETHI is formed from the 1:1 mixture of VTHI and THI on the sulfided 1% $Pd/\gamma\text{-}Al_2O_3$ catalyst, i.e. the vinyl group is hydrogenated. At 250 °C, $\upsilon = 0.8\ h^{-1}$, and $\tau = 60$ min, the yield of 1-ETHI is 33.8% relative to the mixture passed over the catalyst or 72.9% relative to the reacted VTHI. The increase in temperature to 350 °C does not lead to an appreciable increase in the yield of 1-ETHI, which conflicts with data obtained using pure VTHI. These results indicate that the THI present in the initial mixture influences the reaction. The nature of the solvent (toluene or benzene) and dilution of the mixture have hardly any effect on the catalyst selectivity during the 3 h operation of the latter.[111]

By selecting the catalyst, it is possible to obtain 1-ETHI, indole, or a mixture of indole and 2-ethylindole from VTHI or its mixture with THI. On the sulfided 1.5% $Pd/\gamma\text{-}Al_2O_3$ catalyst, 47.9% of 1-ETHI is formed from VTHI ($T = 250$ °C, $\upsilon = 1.0\ h^{-1}$) and 37.6% of 1-ETHI is formed from the 1:1 mixture of VTHI and THI ($T = 250$ °C, $\upsilon = 0.5\ h^{-1}$). On the 1% Pd/Al_2O_3 catalyst ($T = 350$ °C, $\upsilon = 0.5\ h^{-1}$), 47.2% of indole and 23.7% of 2-ethylindole are formed from the same mixture. The yields of indole from the mixture of VTHI and THI show that the six-membered ring in both VTHI and THI is dehydrogenated.

The reaction of the 1:1 mixture of VTHI and THI on $Pd/\gamma\text{-}Al_2O_3$ involves, together with the reactions indicated above, the dehydrogenation of the six-membered fragment of VTHI with formation of 1-ethylindole, which isomerises to 2-ethylindole. Indole is formed mainly as a result of the dehydrogenation of THI, which reacts more readily than VTHI with the active centres on the catalyst surface. The C=C bond is reduced selectively on the sulfided $Pd/\gamma\text{-}Al_2O_3$ catalyst and 1-ETHI is obtained, while in VTHI the C–N bond undergoes hydrogenation with formation of THI.[104] Hence one may conclude that the hydrogenation and dehydrogenation reactions proceed on different active centres of $Pd/\gamma\text{-}Al_2O_3$ and the sulfided catalyst.

A study has been made of the dehydrogenation of THI on the sulfided aluminopalladium catalysts containing 0.15%, 0.2%, and 0.25% of palladium, on the 0.15% Pb/sibunit and 0.5% Pd/sibunit catalysts, and also on the mixed (0.1% Pd, 0.1% Re)/$\gamma\text{-}Al_2O_3$ catalyst.[111] The results are presented in Table 4.

The hydrogen sulfide-treated 0.5% $Pd/\gamma\text{-}Al_2O_3$ catalyst operated for 30 min at 300 °C and $\upsilon = 1.1\ h^{-1}$, exhibiting an appreciable dehydrogenating activity (the catalytic reaction mixture contained 31% of indole). Other conditions being equal, on raising the temperature to 370 and 400 °C complete conversion of THI into indole takes place. The treatment of this catalyst with hydrogen at a high temperature (650 – 700 °C) enhances its cracking properties, which is indicated by the decrease in the yield of the catalytic reaction mixture from 98% to 87%. Indole is formed already at 300 °C in 100% yield relative to the THI passed over the sulfided 0.25% $Pd/\gamma\text{-}Al_2O_3$ catalyst and the space velocity is reduced by a factor of 2 compared with the value indicated above. During the 48 – 50 min operation of this catalyst, its high activity did not change on varying the temperature from 300 to 400 °C, υ from 0.5 to 0.75 h^{-1}, and the THI content in toluene from 14.5% to 20.8%. The yield of the catalytic reaction mixture was 96% – 100% on the (0.15% – 0.2%) $Pd/\gamma\text{-}Al_2O_3(H_2S)$ catalyst at 350 – 360 °C and $\upsilon = 0.33 - 0.57\ h^{-1}$. When benzene is used as the solvent, the yield diminishes slightly. On the 0.15% $Pd/\gamma\text{-}Al_2O_3(H_2S)$ catalyst, the six-membered fragment of THI is wholly dehydrogenated, but the reaction temperature is somewhat higher compared with the catalyst containing 0.2% of Pd. On the mixed (0.1% Pd, 0.1% Re)/$\gamma\text{-}Al_2O_3(H_2S)$ catalyst, this reaction occurs only when the starting material is supplied at a low space velocity $\upsilon = 0.3 - 0.35\ h^{-1}$. Under these conditions only indole accumulates in the catalytic reaction mixture during the first 40 min, and after 115 – 126 min of operation of the catalyst up to 5% of the unreacted THI remains. The six-membered fragment of THI is fully dehydrogenated after 60 min on the 0.5% Pd/sibunit catalyst at 364 – 370 °C and $\upsilon = 0.7\ h^{-1}$; after this, the activity of the catalyst decreases somewhat. Thus, after the catalyst has been used for 186 min, 6.5% of the unreacted THI remains in the catalytic reaction mixture. Indole has been obtained in a quantitative yield on the 0.5% Pd/sibunit catalyst at 400 °C and $\upsilon = 0.85\ h^{-1}$. The decrease in the palladium concentration in the Pd/sibunit catalyst from 0.5% to 0.15% also made it possible to obtain indole in a quantitative yield during the first 73 min of the operation of the catalyst at 365 °C and $\upsilon = 0.3\ h^{-1}$. However, subsequently its dehydrogenating activity fell. The hydrogen sulfide-treated specimen containing 0.15% of palladium on $\gamma\text{-}Al_2O_3$ has a dehydrogenating activity superior to that of the analogous catalyst on sibunit after being used for 100 min.

Thus the low-percentage catalysts containing 0.15% – 0.2% of palladium, which have been developed, ensure the selective dehydrogenation of the six-membered fragment of THI. Indole is formed quantitatively at 355 – 365 °C and $\upsilon = 0.3 - 0.6\ h^{-1}$.[111]

Table 4. Dehydrogenation of 4,5,6,7-tetrahydroindole on various palladium catalysts (atmospheric pressure, toluene, H_2 flow rate 0.6 litre h^{-1}).[111]

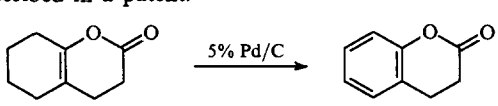
Catalyst	THI content (%)	Experimental conditions			Yield (%)		
		T/°C	v/h^{-1}	t/min	catalytic reaction mixture	THI	indole
0.5% Pd/γ-Al_2O_3	19.5	300	1.1	30	100.0	69.3	30.6
(H_2S)	19.5	340	1.1	25[a]	96.9	25.9	74.1
	20.5	370	1.2	30	96.2	–	100
	20.5	400	1.2	25[a]	97.7	–	100
0.5% Pd/γ-Al_2O_3 (H_2S)[b]	18.1	400	0.98	30	87.0	–	100
0.25% Pd/γ-Al_2O_3	17.7	300	0.6	30	100.0	–	100
(H_2S)	17.7	350	0.6	23	100.0	–	100
	14.5	350	0.5	30	97.5	–	100
	14.5	370	0.5	21	100.0	–	100
	20.8	370	0.75	30	100.0	–	100
	20.8	400	0.75	18	96.2	–	100
0.2% Pd/γ-Al_2O_3	14.3	350	0.42	35	96.2	–	100
(H_2S)	17.1	353	0.48	41	100.0	–	100
	17.3	353	0.6	65[c]	96.0	–	100
0.15% Pd/γ-Al_2O_3	15.6	300	0.52	30	100.0	14.2	85.8
(H_2S)	15.6	355	0.57	19	100.0	1.7	98.3
	19.6	355	0.6	40	99.0	–	100
	13.4	356	0.8	33	100.0	3.1	96.9
	13.3	360	0.47	38	100.0	–	100
	14.8	360	0.48	37	100.0	–	100
	14.9	361	0.48	46[d]	95.7	–	100
(0.1% Pd, 0.1%Re)/	18.0	353	0.49	36	100.0	1.5	98.5
γ-Al_2O_3 (H_2S)	14.8	362	0.44	42	98.8	6.3	93.7
	15.3	355	0.36	48	95.2	–	100
	15.5	355	0.45	36	97.2	3.0	97
	15.5	354	0.44	42	95.4	4.5	95.5
	15.3	355	0.53	66	92.9	11.9	88.1
0.5% Pd/sibunit	18.2	364	0.70	35	95.9	–	100
	18.0	367	0.70	48	93.0	1.9	98.1
	16.8	369	0.57	27[e]	95.0	–	100
0.5% Pd/sibunit[f]	18.0	400	0.85	30	98.0	–	100
0.15% Pd/sibunit	17.0	365	0.32	40	91.5	–	100
	17.3	366	0.34	33	95.0	–	100
	15.4	366	0.31	28	89.5	19.7	80.3

[a] On the same portion of the catalyst.
[b] Treated with hydrogen at 650–700 °C for 15 min.
[c] After the periodic operation of the same portion of the catalyst for 6 h.
[d] After the periodic operation of the same portion of the catalyst for 7 h.
[e] After the periodic operation of the same portion of the catalyst for 3.5 h.
[f] The specimen remaining after the experiments on the dehydrogenation of the cyclohexane for 9 h at 350–450 °C.

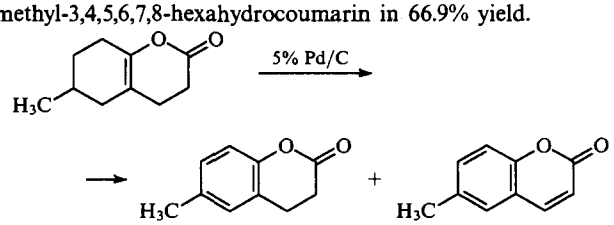
The six-membered fragment of THI is dehydrogenated on the 0.5% Pd/γ-Al_2O_3 catalyst at v = 0.75–1.2 h^{-1} and temperatures lower by 100 °C than in the dehydrogenation of cyclohexane, which makes it possible to employ catalysts with a low palladium content (0.15%–0.2%). The palladium catalyst on sibunit is also promising.

2. Dehydrogenation of dihydrocoumarins

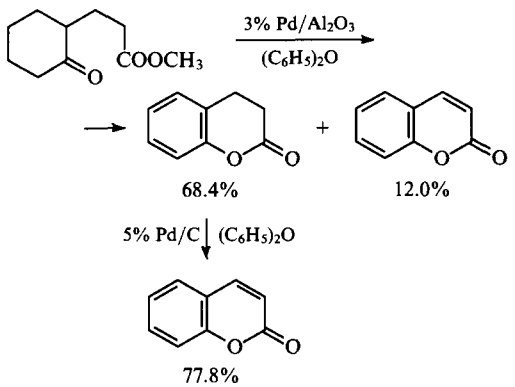
A method of synthesis of coumarin and alkylcoumarins together with the corresponding dihydrocoumarins by liquid-phase dehydrogenation in the presence of Pd/C at 260 °C has been described in a patent.[112]



For the 100% degree of conversion of 3,4,5,6,7,8-hexahydrocoumarin, the yield of 3,4-dihydrocoumarin was 70%. For a degree of conversion of 98.5%, a mixture of 6-methylcoumarin and 6-methyl-3,4-dihydrocoumarin was obtained from 6-methyl-3,4,5,6,7,8-hexahydrocoumarin in 66.9% yield.



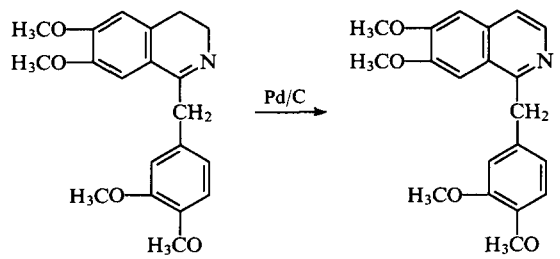
Coumarin has been obtained by the dehydrogenation of oxocyclohexanepropionic acid (OCPA) over Pd/Al_2O_3 in the liquid phase.[113]



For this purpose, OCPA in $(C_6H_5)_2O$ was heated at 250–260 °C in the presence of 3% Pd/Al_2O_3. A mixture of dihydrocoumarin (yield 68.4 mol%) and coumarin (yield 12 mol%) was obtained. Dihydrocoumarin in $(C_6H_5)_2O$ was dehydrogenated in the presence of 5% Pd/C for 14 h, which gave a mixture of 77.8% of coumarin and 22.1% of the unreacted dihydrocoumarin. After the carrier had been changed (5% Pd/Al_2O_3), the courmarin content fell to 50.8%, while that of the unreacted dihydrocoumarin rose to 49.1%.

3. Dehydrogenation of dihydropapaverine

Synthetic 1-benzyl-6,7,3',4'-tetramethoxyquinoline is identical with the natural alkaloid papaverine, which belongs to the class of opiate alkaloids and is widely used as a medicinal preparation. One of the last stages in the preparation of the synthetic papaverine is the dehydrogenation of dihydropapaverine at 200–250 °C in solution in tetralin in the presence of Pd/C under an inert gas (N_2, CO_2) stream.[17]



Dihydropapaverine was dehydrogenated on a catalyst containing 5% of palladium and deposited on an unwoven graphite material (UGM) with a volume concentration of 9.11 g cm^{-3} and a filtration coefficient of 5.3 × 10^{-2} cm s^{-1}.[114] The activity of the catalyst, determined from the evolution of hydrogen, increased after the introduction of CH_2O (to give a 1:1 mixture). The 5% Pd/UGM catalyst had the same activity as the industrial $Pd/BaSO_4$ (volume concentration 1.21 g cm^{-3}, filtration coefficient 3.5 × 10^{-5} cm s^{-1}), but a disadvantage of the latter is high hydrodynamic resistance. Papaverine can be obtained on the 5% Pd/UGM catalyst under both periodic and continuous conditions.[114]

VI. Palladium catalysts for the aromatisation of petrol fractions

The aromatisation of petrol fractions, carried out in catalytic reforming, ensures an increase in the octane number, such increase including the effect due to the dehydrogenation of naphthalenes. Aromatisation under platforming conditions is promoted by a high temperature and a low hydrogen pressure. However, when the pressure is too low, the catalyst activity falls rapidly owing to the deposition of carbon residues on its surface. The selectivity of the reaction on supported metallic catalysts is a complex function of the catalyst composition, pressure, temperature, the composition of the gas phase, etc.

The reforming catalysts possess a bifunctional activity because, together with the main reaction involving the dehydrogenation of six-membered cyclanes, reactions also occur in which five-membered cyclanes isomerise to six-membered ones with subsequent dehydrogenation, dehydrocyclisation reactions, alkane isomerisation reactions, and cracking. The presence on the catalyst surface of both the metal and of acid centres is therefore required. The platforming processes were carried out on platinum deposited on alumina, which possesses acid properties.[115-117]

Palladium, the crystal lattice of which has the same structure as that of platinum, is appreciably inferior to the latter as regards activity in reactions of both individual hydrocarbons and their mixtures.

The 0.5% $Pd/\gamma\text{-}Al_2O_3 \cdot HF$ catalyst treated with hydrogen sulfide exhibited an appreciable activity in the dehydrogenation of cyclohexane to aromatic hydrocarbons and retained its stability during operation of 262 h under the conditions of the reforming of the petrol fraction, with a boiling point of 96–114 °C, from the Il'sko-Khadyzhensk deposit (n_D^{20} = 1.4155, d_4^{20} = 0.7493, content of aromatic hydrocarbons 7.5%, sulfur content 0.0025%) at 450–460 °C, P_{H_2} = 20 atm, v = 1 h^{-1}, and H_2:HC = 5:1.[74,79] As a result of the dehydrogenation, the content of aromatic hydrocarbons rose to 36%–40%. Despite the high reaction temperature, the catalyst hardly induced any cleavage of the hydrocarbons to C_1–C_4 compounds and the effluent gas consisted of 98%–99% of hydrogen.[79]

The influence of hydrofluoric acid and of the treatment with hydrogen sulfide on the 0.5% $Pd/\gamma\text{-}Al_2O_3$ catalyst has been investigated under conditions of the reforming of the 89.5–125 °C petrol fraction containing 0.017% of sulfur compounds (calculated relative to sulfur).[118,119] The data on the composition of the fraction before and after reforming are presented in Table 5.

In the presence of the hydrofluoric acid-treated 0.5% $Pd/\gamma\text{-}Al_2O_3$ catalyst and in contrast to the initial 0.5% $Pd/\gamma\text{-}Al_2O_3$ catalyst, aromatic hydrocarbons are formed not only from six-membered cyclanes but also from five-membered cyclanes and alkenes. All the specimens also exhibit a desulfurising activity — the sulfur content decreases from 0.017% to 0.001%. The sulfided specimen is more resistant under these conditions to the action of sulfur compounds. However, when petrols containing sulfur compounds are used, the stability of the catalyst decreases with time and its aromatising capacity diminishes after 60 h of continuous operation.[119] The yield of

Table 5. Group composition of the petrol fraction with b.p. 89.5–126 °C (reforming conditions: T = 470–480 °C, P_{H_2} = 20 atm, v = 1.0 h^{-1}, H_2:HC = 12.5).[118,119]

Hydrocarbons	Content (mass %)			
	before reforming	after reforming on catalysts containing 0.5% Pd on		
		$\gamma\text{-}Al_2O_3$	$\gamma\text{-}Al_2O_3 \cdot HF$	$\gamma\text{-}Al_2O_3 \cdot HF$ (H_2S)
Alkanes:	52.7	60.2	62.3	61.8
normal	29.3	29.7	25.7	26.9
with a tertiary carbon atom	22.5	28.1	34.6	29.3
with a quaternary carbon atom	0.9	2.4	2.0	5.6
Cyclopentanes	14.6	10.8	4.4	5.4
Cyclohexanes	18.5	1.0	0.8	1.0
Aromatic hydrocarbons	5.6	20.3	26.4	24.8

aromatic hydrocarbons decreases to 12%–12.5% after 27 h on the 0.5% Pd/γ-Al_2O_3 catalyst, after 46 h on the 0.5% Pd/γ-$Al_2O_3 \cdot HF$ catalyst, and after 13 h of reforming the petrol fraction on the sulfided 0.5% Pd/γ-$Al_2O_3 \cdot HF$ specimen. It is appropriate to mention that the sulfur content in the reformates proved to be identical in all cases. It is extremely likely that the decrease in the aromatising capacity of the most active 0.5% Pd/γ-$Al_2O_3 \cdot HF(H_2S)$ catalyst is associated with the removal from the latter of part of the chemisorbed sulfur, i.e. with the decomposition of PdS at a high temperature and a hydrogen pressure of 20 atm. The specific surface of the sulfided palladium catalyst is smaller by a factor of 1.5, whilst the temperature coefficient of the rate of dehydrogenation of cyclohexane to benzene is much higher than on the other two catalysts.[78] It may be that this explains why the sulfided specimen has the highest activity under the conditions of the reforming of the petrol fraction.

Thus the introduction of hydrofluoric acid into the aluminopalladium catalyst increases its isomerising capacity, whilst treatment with hydrogen sulfide increases its resistance to the sulfur compounds present in the petrol fraction.

The reforming of the petrol fraction with a boiling point of 89.5–126 °C and containing 0.017% of sulfur has also been investigated on palladium/aluminosilicate catalysts (containing 85.35% of SiO_2 and 11.91% of Al_2O_3) with different specific surfaces (S = 263, 240, 204, 180, and 93 $m^2 g^{-1}$).[120] The aluminosilicate catalysts, which are used extensively in the petroleum processing industry for cracking, are known to possess acid properties and hence to exhibit not only a cracking activity but also an extremely high isomerising activity. The deposition on the aluminosilicate of finely disperse palladium, which possesses dehydrogenating and hydrogenating properties, made it possible to create active aromatisation catalysts. An appreciably greater increment in the content of aromatic hydrocarbons (24%–33% instead of 17%–22%) is observed on these catalysts than on the 0.5% Pd/γ-Al_2O_3 catalyst. Aluminosilicate catalysts containing 0.5% of palladium also ensure the desulfurisation of the fraction: the sulfur content falls from 0.017% to 0.001%.[121] During the first hours of the operation, these catalysts exhibit an appreciable cracking activity and therefore it is more convenient to employ them in the reforming of higher-boiling petroleum fractions. In contrast to the catalyst deposited on alumina, on the palladium/aluminosilicate catalyst five-membered cyclanes and n-alkanes are involved in the aromatisation process in addition to the six-membered cyclanes.

VII. Bimetallic supported catalysts for the dehydrogenation of cyclanes and the aromatisation of petrol fractions

Low-percentage bimetallic supported catalysts, containing palladium and rhenium, were first developed at the Institute of Organic Chemistry of the USSR Academy of Sciences in the 1960s — several years earlier than the Pt–Re reforming catalyst (see below). The behaviour of the Pd–Re catalysts in the reactions of C_6 hydrocarbons, including the dehydrogenation of cyclohexane and methylcyclohexane at elevated temperatures and hydrogen pressures, has been widely investigated.[121–123]

Table 6 presents data on the reactions of cyclohexane and methylcyclohexane on catalysts containing 1% of Pd and 1% of Re and deposited on γ-Al_2O_3 and $Al_2O_3 \cdot SiO_2$.[122,123]

Together with benzene, methylcyclopentane is also formed. Table 6 shows that the (Pd, Re)/$Al_2O_3 \cdot HF$ catalyst treated with hydrogen sulfide exhibits the highest dehydrogenating activity. When it is employed, the benzene content in the catalytic reaction mixture increases from 67% to 87% and toluene is formed from methylcyclohexane in 90% yield. The use of aluminosilicate as the carrier instead of the hydrogen fluoride-treated alumina decreases the dehydrogenating activity of the catalyst.[123] The decrease in the specific surface of the aluminosilicate from 350 to 108 $m^2 g^{-1}$ also weakens the dehydrogenating activity of the catalyst. The introduction of hydrofluoric acid (0.5% or 1.5%) enhances the acid properties of the catalyst and increases the contribution of the reactions involving the hydrocracking of n-hexane and the hydrogenolysis and dehydroisomerisation of methylcyclopentane. When the aluminosilicate carrier was used, the highest dehydrogenating activity was shown by the (1% Pd, 1% Re)/$Al_2O_3 \cdot SiO_2$ 0.5%HF catalyst treated with hydrogen sulfide. The use of active bimetallic catalysts for the reforming of petrol fractions has also been studied (see below).

The dehydrogenation of cyclohexane has been investigated on the (1% Pd, 1% Re)/Al_2O_3 catalyst containing 0.3% of fluorine and treated with hydrogen sulfide in the temperature range from 370 to 420 °C, for the molar ratio hydrogen : cyclohexane = 3 : 1, at rates of supply of cyclohexane from 0.012 to 0.04 mol $g^{-1} h^{-1}$, and at a hydrogen pressure of 10 atm.[124] At 370, 400, and 425 °C, the equilibrium yields of the benzene obtained by the dehydrogenation of cyclohexane are respectively 65%, 83.3%, and 95.2%. The kinetics of the dehydrogenation reaction were investigated in a flow type apparatus. The quantities calculated by the kinetic equation

Table 6. Reactions of cyclohexane on palladium supported catalysts (T = 480 °C, P_{H_2} = 10 atm, v = 1.0 h^{-1}, H_2 : HC = 5).[122,123]

Composition of catalyst	(1% Pd, 1% Re)/$Al_2O_3 \cdot HF$	(1% Pd, 1% Re)/$Al_2O_3 \cdot HF(H_2S)$	(1% Pd, 1% Re)/$Al_2O_3 \cdot SiO_2 \cdot HF(H_2S)$		
			A	B	C[a]
Propane–pentanes	1.3	traces (1.1)	1.7	0.2	1.5
2,2-Dimethylbutane	traces	– (–)	1.2	0.8	–
2-Methylpentane	1.3	0.5 (–)	0.6	0.2	0.4
3-Methylpentane and cyclopentane	1.2	0.4 (–)	0.4	0.1	–
n-Hexane	1.2	0.5 (–)	0.6	0.4	0.4
Methylcyclopentane	12.0	5.3 (–)	17.3	14.6	14.2
Cyclohexane	16.0	2.2 (–)	19.1	48.2	61.3
Methylcyclohexane	–	– (3.5)	–	–	–
Benzene	67.0	87.0 (5.4)	59.1	35.5	22.6
Toluene	–	4.0 (90.0)	–	–	–
Overall yield of catalyst (%)	95	95 (93)	92	96	99

Note. The numerals in brackets indicate the degree of conversion of methylcyclohexane.
[a] The specific surfaces of the catalysts were 350 $m^2 g^{-1}$ (A), 160 $m^2 g^{-1}$ (B), and 108 $m^2 g^{-1}$ (C).

agreed with experimental data. The apparent activation energy for the dehydrogenation of cyclohexane was found to be 74.5 kJ mol^{-1}. The apparent activation energies for the isomerisation of cyclohexane and for the reverse reaction (the isomerisation of methylcyclopentane) in the temperature range 370–390 °C amounted to 72.0 and 48.5 kJ mol^{-1} respectively.

The properties of the sulfided 0.5% palladium catalysts deposited on alumina and of bimetallic catalysts containing 0.5% of palladium and 0.5% of rhenium were compared in the dehydrogenation of cyclohexane at atmospheric pressure (450 °C, v = 1.4–1.5 h^{-1}).[16]

The introduction of rhenium increased the yield of the catalytic reaction mixture from 91.8% to 94.2% and the benzene content from 85% to 91% and also made it possible to reduce the reaction temperature to 400 °C. At this temperature, the benzene content was 81% for a 92.4% yield of the liquid catalytic reaction mixture. Hence it follows that the palladium–rhenium bimetallic catalyst is more active than the pure palladium catalyst.

The nature of the promoting activity of rhenium both in aluminopalladium and aluminoplatinum catalysts[125–128] is not totally clear. It has been shown[129] that, in the absence of the second metal, rhenium deposited on Al_2O_3 is reduced to the metallic state almost completely at a concentration of 4%–5% and with greater difficulty at a concentration of 0.5%. This can be explained by the fact that, on low-percentage catalysts, rhenium and its oxides are in a highly disperse state and interact strongly with the acceptor sections of the carrier surface, which hinders reduction. The addition of rhenium does not affect the mechanism of the action of the bifunctional catalyst but reduces appreciably the rate of its deactivation.[121] It may be that, in contrast to palladium, rhenium promotes the removal of the coke-formation products from the catalyst surface.

The well known ability of rhenium to increase the stability of the catalyst can be explained by the fact that rhenium oxides hydrogenate the products preceding the formation of coke during catalytic reforming.[116,117]

An attempt has been made to discover a relation between the adsorption of hydrogen on promoted palladium-containing catalysts, on the one hand, and the state of the metals and their activity in the dehydrogenation of cyclohexane, on the other.[130] For this purpose, a detailed study was made of the overall content of hydrogen on the catalyst surface, the number of forms of chemisorption, and the temperature at which the maximum rate of desorption is attained and the activation energy for desorption and its kinetic order were calculated. The state of the active phase in both one-component and modified palladium catalysts was investigated by means of a series of physicochemical methods (thermoprogrammed desorption, diffuse reflection spectroscopy, X-ray phase analysis). The palladium catalysts deposited on alumina contained 0.02 mass%–0.35 mass% of the metal and were promoted with 0.1 mass%–6.3 mass% Co, Ce, or In. It was shown that the catalysts for the dehydrogenation of cyclohexane to benzene must be capable of activating hydrogen in both weakly and strongly bound forms. Since the centres for the chemisorption of hydrogen in the weakly bound forms are unoccupied during the reaction, they can serve as the sites for the formation of the intermediate adsorption complex in the dehydrogenation of cyclohexane. The adsorption of hydrogen in the weakly bound form is characteristic of palladium catalysts modified by non-noble metals, which contain the most reduced forms of both palladium and of the promoting Ce and Co additives and also incorporate mixed centres formed as a result of their interaction.

The introduction of neodymium oxide into the aluminopalladium catalyst increases appreciably its dehydrogenating activity.[131] The dehydrogenating activity of such catalysts was investigated at atmospheric and elevated hydrogen pressures. The results are presented in Table 7.

It follows from the data presented that the 1% Pd/Al_2O_3 catalyst containing 10% of Nd_2O_3 has the maximum dehydrogenating activity. An increase in pressure increases the yield of the product on the aluminopalladium catalysts containing 4.5% and 10% of Nd_2O_3. The stability of all the specimens was tested. After 18 h operation of the first catalyst, the benzene content fell from 91.8% to 48%. The same decrease in activity on the (1% Pd, 10% Nd_2O_3)/Al_2O_3 catalyst was reached after 40 h.

Table 8 presents data concerning the influence of other cerium- and yttrium-subgroup lanthanide oxides on the dehydrogenating activity of aluminopalladium catalysts.[132]

Evidently the lanthanide oxides increase appreciably the dehydrogenating activity of the aluminopalladium catalysts. The introduction of 10% of the lanthanide oxide lowers the specific surface of the alumina slightly (in the range 15–25 m^2 g^{-1}). The catalysts prepared were characterised by similar pH values with the sole exception of the catalysts containing neodymium oxide. The introduction of the lanthanide oxide diminished slightly the acidity of the aluminopalladium catalysts virtually regardless of the nature of the lanthanide oxide. Since all nine lanthanide oxides exert almost the same influence on the activity of the catalyst, in the preparation of such catalytic systems one can employ the most readily available and cheapest lanthanides and their mixtures.

Bimetallic catalysts containing palladium and rhenium on alumina were first developed in our country.[121] The use of these catalysts in the reforming of petrol fractions was investigated in 1962.[122] Later the properties of the platinum-rhenium supported catalysts designed for reforming began to be studied in Germany and the USA.[133,134] Platinum-rhenium/carbon catalysts were described in 1965[133] and the (Pt, Re)/Al_2O_3 catalyst

Table 7. Reactions of cyclohexane on the (1% Pd, Nd_2O_3)/Al_2O_3 catalysts (atmospheric pressure, T = 480 °C, v = 1.0 h^{-1}).[131]

Catalyst	s/m^2 g^{-1}	pH[a] of catalyst	Composition of catalytic reaction mixture (mass%)			
			cyclohexane	benzene	methylcyclopentane	C_4–C_6 alkanes
Pd/Al_2O_3	112	4.7	92.1	6.0	0.9	–
Pd/Al_2O_3[b]	112	4.7	74.7	22.3	–	3.0
Pd/Al_2O_3[c]	112	4.7	51.7	34.8	12.7	0.8
(Pd, 4.5% Nd_2O_3)/Al_2O_3	157	4.0	44.4	52.7	0.5	2.4
(Pd, 4.5% Nd_2O_3)/Al_2O_3[b]	157	4.0	6.9	91.8	1.0	0.3
(Pd, 10% Nd_2O_3)/Al_2O_3	127	4.3	39.1	60.9	–	–
(Pd, 10% Nd_2O_3)/Al_2O_3[c]	127	4.3	5.6	93.3	1.1	traces
(Pd, 15% Nd_2O_3)/Al_2O_3	125	4.3	45.3	54.7	–	–
(Pd, 20% Nd_2O_3)/Al_2O_3	134	4.3	59.7	40.3	–	–

[a] The pH of the aqueous extract from the catalyst under standard conditions.
[b] v = 0.4 h^{-1}.
[c] P_{H_2} = 10 atm.

Table 8. Reactions of cyclohexane on catalysts containing 1% of Pd, 10% of a lanthanide oxide, and 89% of Al_2O_3 (T = 480 °C, v = 1.0 h^{-1}, P_{H_2} = 10 atm).[132]

Catalyst	$s/m^2\ g^{-1}$	pH[a] of catalyst	Composition of catalytic reaction mixture (mass %)				Yield of benzene at P_{H_2} = 1 atm[a]
			C_3-C_5	methylcyclo-pentane	cyclo-hexane	benzene	
Pd	147	5.3	3.5	2.7	71.4		22.4[b]
			0.8		51.7	38.4	2.8
Pd, Y_2O_3	129	6.8	4.2	2.1	11.0	82.7	50.0
Pd, Pr_2O_3	122	6.1	1.1	2.0	4.4	92.5	65.9
Pd, Nd_2O_3	151	4.3	traces	1.1	5.6	93.3	60.9
Pd, Sm_2O_3	146	6.8	1.1	1.8	8.6	88.5	55.2
Pd, Tb_2O_3	122	6.0	–	1.6	4.2	94.2	51.2
Pd, Dy_2O_3	120	6.6	1.4	4.4	10.1	84.5	49.8
Pd, Ho_2O_3	126	6.2	traces	1.6	8.0	90.4	59.9
Pd, Er_2O_3	141	6.3	1.3	1.7	10.5	86.5	73.2
Pd, Yb_2O_3	144	6.6	1.3	1.4	9.9	84.7	53.0

[a] v = 0.4 h^{-1}.
[b] residual cyclohexane.

was described in 1968.[134] The latter catalyst was prepared by the method described previously.[121] The 'rheniforming' process for improving the quality of petrol fractions was introduced in the USA in 1970.

The introduction of bimetallic catalysts is regarded as the greatest achievement in petroleum processing after the development in 1949 of the aluminoplatinum platforming catalyst. The advantage of the process on the bimetallic catalysts has been examined in detail in a monograph.[135] We shall note some of them. Rheniforming in the presence of the (Pt, Re)/Al_2O_3 bimetallic catalyst yields a reformed product with a higher octane number than that obtained in platforming on Pt/Al_2O_3. As a consequence of the high volume flow rates of the starting material, the productivity increases. The yield of the reforming product, hydrogen, and aromatic hydrocarbons rises, the useful lifetime of the catalyst increases, and the cracking of alkanes and naphthenes is reduced to a minimum. The employment of a lower pressure becomes possible, which promotes the occurrence of dehydrocyclisation and makes it possible to reduce the molar ratio of the circulating hydrogen and the starting material (H_2 : HC).[135] Preliminary purification of the petrol fractions to remove sulfur compounds is essential in rheniforming processes. The introduction of rhenium into the aluminoplatinum catalyst increases the lifetime of the latter, according to American workers, by a factor of 2–4 compared with that of the aluminoplatinum catalyst; the regeneration of the catalyst after three months' use ensures the complete restoration of its high initial activity.[135]

The influence of rhenium on the activity and stability of the aluminopalladium catalyst has been investigated under the conditions of the reforming of petrol fractions containing sulfur compounds (0.0123% of sulfur).[122] In the products obtained by reforming the Baku petrol B-70, the content of aromatic hydrocarbons increased from 5.5% to 57% after treatment for 25 h, while the concentration of sulfur compounds diminished from 0.0123% to 0.009%, i.e. by a factor of 1.4. During the initial period of the operation of the catalyst, the content of aromatic hydrocarbons reached 80%. The introduction of 1% of Re into the 1% Pd/Al_2O_3 · HF(H_2S) catalyst increased its stability almost by a factor of 4. However, after 111 h of continuous operation, the content of aromatic hydrocarbons fell to 14%.

The reforming of the 71–102 °C fraction of the Karadag petrol was investigated on the most active catalyst (1% Pd, 1% Re)/Al_2O_3 · HF(H_2S) in stationary and fluidised beds.[136] The results are presented in Table 9.

Table 9. Characteristics of the initial fraction with b. p. 71–102 °C of the Karadag petrol and the reforming products obtained with the process carried out in stationary and fluidised catalyst beds (T = 480 °C, v = 0.8–3.5 h^{-1}, P_{H_2} = 10 atm, H_2 : HC = 5–20).[136]

Component	Composition of fraction (mass %)	Composition of reforming products (mass %)		
		after treatment in a stationary bed for 25 h	after treatment in a fluidised bed for	
			25 h	100 h
Isopentane	1.4	1.2	1.1	0.9
n-Pentane	2.7	2.1	2.5	1.9
2,2-Dimethyl-butane	0.3	0.4	0.7	0.5
2-Methylpentane and 2,3-dimethyl-butane	5.9	6.3	6.1	5.8
3-Methyl-pentane	4.8	3.9	4.6	4.5
n-Hexane	12.4	10.9	11.6	10.3
n-Isoheptanes + dimethylcyclo-pentanes + cyclohexane + methylcyclo-pentane	48.9	36.7	30.7	37.4
Methylcyclo-hexane	15.4	1.1	0.8	2.8
Benzene	3.7	15.1	18.7	12.9
Toluene	4.5	21.3	23.2	23.0

It follows from Table 9 that, after 25 h of the operation of the catalyst, the content of aromatic hydrocarbons in the reforming products in the stationary and fluidised beds is 36%–42%. The content of benzene has then been increased by a factor of almost 4, whilst that of toluene increased by a factor of 5. The contents of the C_5 and C_6 alkanes remained almost unchanged. The fraction of isomeric hexanes (total hexanes) is ~50% in the initial petrol fraction. Approximately the same fraction of hexanes was attained earlier[121] on the same catalyst in the isomerisation of n-hexane in a stationary bed. Thus aromatic hydrocarbons are mainly formed as a result of the dehydrogenation of

six-membered cyclanes and to a slight extent as a result of the dehydroisomerisation of alkylcyclopentanes. The activity of the stationary catalyst bed gradually diminishes and, after it has worked for 40 h, the content of aromatic hydrocarbons in the reforming products falls to 29%, whilst in the fluidised bed their content after the catalyst has worked for 100 h diminishes only to ~36%. Hence it follows that the stability of the catalyst in the fluidised bed is 4 times greater than in the stationary bed. This can apparently be accounted for by the fact that in the fluidised bed the catalyst has a much larger macrosurface than in the stationary bed.

After 100 h of operation, the catalyst was regenerated with air in the fluidised bed at atmospheric pressure and 400 °C, was treated with hydrogen, and the experiment was again carried out at a pressure of 10 atm, a space velocity of 1.5–2.0 h^{-1}, and H_2 : HC = 10. The content of aromatic hydrocarbons in the reformate increased by a factor of 5, as before. Consequently, the hydrogen sulfide-treated rhenium–aluminopalladium catalyst fully recovers its activity as a result of regeneration.

VIII. Certain characteristic features of the catalytic and physical properties of palladium-containing supported catalysts

The available information about the physicochemical properties of supported palladium and palladium-rhenium catalysts for the dehydrogenation of cyclanes in the reforming of petrol fractions is extremely limited.[137–139] X-Ray diffraction analysis of the 0.5% Pd/Al_2O_3 catalyst, the same catalyst containing 0.5% of fluorine, and the fluorinated specimen subjected to an additional treatment with hydrogen sulfide showed that the palladium in all the specimens and the aluminium oxide in the first two specimens are in a crystalline state. The lattice constant of the aluminium oxide in these two cases is virtually the same, amounting to 7.91 and 7.90 Å respectively. The crystal dimensions are in the range 50–100 Å. The absence of Al_2O_3 reflections not coinciding with the palladium reflections (d = 2.349 and 1.384) is characteristic of the X-ray diffraction patterns of the sulfided specimen. It is therefore impossible to regard it as strictly demonstrated that the aluminium oxide in this specimen is in the crystalline state (lattice constant 7.86 Å).[78] The chemical treatment with hydrofluoric acid and hydrogen sulfide probably alters markedly the size and shape of the crystals and leads to the dispersion of the aluminium oxide. The palladium in the sulfided specimen is less saturated by hydrogen than in the first specimen. The rate of conversion of cyclohexane into benzene increases most markedly (by a factor of 4) with increase in temperature from 300 to 350 °C at atmospheric pressure in a flow system on the sulfided palladium-containing catalyst. The results obtained in tests of the activities and stabilities of these specimens under the conditions of the reforming of petrol fractions (see above) are related to the temperature coefficients of the rate of reaction.

Since the specific surfaces of the test specimens hardly changed during the dehydrogenation of cyclohexane, it follows that the differences between the activities and stabilities are induced by the chemical composition of the catalyst and not by structural features. It follows from data on the phase composition[78] that the impurities which are bound to be present in the specimens by virtue of the characteristics of the method of preparation can exist only in the form of surface compounds (AlF_3 or $HAlF_4$ and also PdS) or, which is less probable, in the form of an amorphous phase. Even at low concentrations, these compounds can influence significantly the activities and stabilities of the catalyst. It may be that the high activity and stability of the sulfided palladium specimen is due to the presence of PdS on the latter. The partial or complete sulfiding of the palladium surface apparently increases the temperature coefficient of the rate of dehydrogenation. This appears entirely probable, because sulfides are known to be active at higher temperatures than the metals forming part of their composition. For example, nickel sulfide hydrogenates the carbon–carbon bond at temperatures above 150 °C, whereas metallic nickel in the active form hydrogenates it already at room temperature.

Table 10. The contents of sulfur and carbon in the catalysts after prolonged operation under the conditions of the reforming of the petrol fraction with b.p. 89.5–124 °C (sulfur content in the fraction 0.017%).[78]

Catalyst	Duration of operation of catalyst/h	Content (%)	
		S	C
0.5% Pd/Al_2O_3	27	0.040	0.25
0.5% $Pd/Al_2O_3 \cdot HF$	46	0.035	0.28
0.5% $Pd/Al_2O_3 \cdot HF(H_2S)$	73	0.039[a]	0.27

[a] The initial reduced catalyst contained 0.125% of sulfur.

Data on the contents of sulfur and carbon in palladium-containing catalysts are noteworthy (Table 10).[78]

Regardless of the duration of the operation under the conditions of the reforming of petrol, the contents of sulfur and carbon remain almost unchanged in all the catalysts. If the accumulation of carbon had been limited by the coke saturation of the cracking surface centres, it would have been difficult to expect identical amounts of it on catalysts to have different properties. Therefore the data in Table 10 concerning the content of carbon are more likely to indicate that, after the formation of the 'carbonaceous film', the rate of hydrogenation of the film becomes equal to the rate of its formation on the catalyst surface, i.e. a certain equilibrium is established. Since the sulfur content in the catalyst does not increase with increase in the productivity in the operation of the latter, one may reach the unambiguous conclusion that the rupture of the sulfur compounds in petrol with formation of elemental sulfur on the catalyst does not occur and that sulfur is evolved in the form of hydrogen sulfide. The sulfur content in the initial sulfided catalyst was 0.125%. After the transition of the catalyst to the deactivated state as a result of performing the petrol reforming process on the latter, the sulfur content fell to 0.04%. Under these conditions, the sulfur content could have decreased only as a result of the formation and removal of H_2S.

It is appropriate to note that, when the activity fell to the same value, the sulfur contents in all the catalysts were also identical. It is extremely likely that the decrease in the activity of the sulfided catalyst is associated with the removal from the latter of part of the chemisorbed sulfur (the decomposition of PdS at a high temperature and hydrogen pressure).

The catalytic properties of metal oxide supported catalysts are known to be greatly influenced by the recrystallisation of the active phase. The specific surface of the metal in the alumino-palladium and aluminopalladium-rhenium catalysts has been estimated by a modified method involving the gas titration of the chemisorbed hydrogen by ethene[140,141] and also by the oxygen chemisorption method. Heat treatment of the Pd/Al_2O_3 catalyst at 640 °C increases the specific surface of palladium from 106 to 446 $m^2\ g^{-1}$.[137] The high H : Pd = 0.95 ratio shows that palladium is present on the carrier in a virtually atomic state. Oxygen titration yields lower specific surfaces (S increases on heat treament from 91 to 360 m^2 per gramme of palladium).

The specific surface of the metal (52 $m^2\ g^{-1}$) on the (Pd, Re)/Al_2O_3 catalyst is smaller than on Pd/Al_2O_3. Heat treatment of the catalyst increases the overall specific surface of palladium and rhenium. The specific surface of palladium in the bimetallic specimen is four times greater than in the palladium specimen. Thus in air rhenium does not inhibit the recrystallisation of palladium on the carrier but increases the thermal stability of the catalyst.

The effect of coke on the crystallisation of palladium and rhenium on different carriers has been examined.[138] X-Ray

diffraction study of palladium-rhenium catalysts on silica before and after saturation with coke (4%–5% of coke) under the conditions of the aromatisation of hydrocarbons at atmospheric pressure and 500 °C led to the identification only of lines corresponding to palladium. The introduction of rhenium into the Pd/SiO_2 catalyst retards the crystallisation of palladium on saturation with coke.

The relation between the activity of the $(Pd, Co)/Al_2O_3$ bimetallic catalyst in the dehydrogenation of cyclohexane and its adsorption capacity with respect to hydrogen has been investigated.[139] The dehydrogenation was carried out at 300–480 °C and atmospheric pressure under pulsed conditions. The specimen was subjected to a preliminary treatment in a stream of hydrogen at 520 °C for 15 min. The adsorption properties of the catalyst in relation to hydrogen (adsorption capacity, number of chemisorbed forms of hydrogen, the strength of the bond between hydrogen and the metallic catalyst surface) were determined by the thermoprogrammed desorption method. The conversion of cyclohexane on the 0.1% Pd/Al_2O_3 catalyst began at 340 °C and the maximum yield of benzene, equal to 38%, was attained at 480 °C. The Co/Al_2O_3 systems containing 1.66%, 3.0%, and 4.28% of the metal proved to be inactive. The activity of the $(Pd, Co)/Al_2O_3$ bimetallic catalyst is determined to a large extent by the concentration of the non-noble metal in the latter. The dehydrogenating activity of the palladium catalyst increases sharply after the introduction of 1% and 1.66% of cobalt: the yield of benzene at 480 °C reaches 83.4% and 68.4% respectively. At lower (0.1% and 0.5%) and higher (3.0% and 4.28%) cobalt concentrations, the degrees of conversion of cyclohexane into benzene are appreciably lower. C_1-C_6 hydrocarbons—cyclohexane cracking products—are formed on the bimetallic catalyst, in contrast to Pd/Al_2O_3.

The spectrum of the desorption of hydrogen from the Pd/Al_2O_3 catalyst contains one temperature range (600 to 700 °C) with a temperature of the maximum rate of adsorption of 660 °C. Kinetic calculations showed that hydrogen is desorbed in accordance with a second-order equation ($n = 2$) and that the activation energy for desorption is $E_{des} = 480$ kJ mol^{-1}. This indicates the atomic nature of the chemisorbed hydrogen and a high strength of the hydrogen–metal bond. The adsorption capacity of palladium in Pd/Al_2O_3 is low (0.1 ml per gramme of the catalyst), which corresponds to the ratio H:M = 0.54. Data have been obtained also for the Co/Al_2O_3 catalyst. On thermal desorption of hydrogen from the (0.1% Pd, 1.66% Co)$/Al_2O_3$ catalyst (the most effective in the dehydrogenation of cyclohexane), two forms of chemisorbed hydrogen (I and II) were detected. Hydrogen begins to be evolved at a lower temperature (300 °C) and the evolution takes place over a much wider temperature range (300 to 700 °C) than on the one-component palladium and cobalt catalysts. These results indicate a greater energy nonuniformity of atomic hydrogen and a weaker hydrogen–metal bond in the $(Pd, Co)/Al_2O_3$ catalyst. The strongly bound hydrogen (form II) is desorbed with $E_{des} = 280.5$ kJ ml^{-1}, whilst the weakly bound hydrogen (form I) is desorbed with $E_{des} = 118.5$ kJ mol^{-1}. The centres which bind hydrogen more strongly ($T_{des} > T_{reaction}$) are coated by adsorbed hydrogen on the catalysts showing a lower activity in the dehydrogenation of cyclohexane, whilst the centres for the weak chemisorption of hydrogen are virtually absent and their surface is coated only by the strongly bound forms.

The modifying effect of rhenium in the platinum-rhenium supported catalyst can be accounted for by the formation of bimetallic (alloyed) Re–Pt particles on the catalyst surface[125,126] or by the localisation of the platinum clusters on the low-valence rhenium ions bound to the carrier surface.[127] It is also possible to create catalysts containing transition metal complexes fixed on the carrier surface.

Bimetallic catalysts containing discrete surface structures of predominantly one composition can be obtained by the thermal decomposition of fixed surface complexes incorporating the atoms of the active metal and of the modifying element. Organic ligands are easily removed on reduction of the catalyst, which makes it possible to investigate the influence of the modifying element under conditions which rule out the uncontrollable modification of the deposited metal and of the carrier surface by the decomposition products. In the case of platinum-containing catalysts, the low-valence Group IV–VIII elements bound to the SiO_2 surface can serve as centres for the stabilisation of the reduced platinum atom or clusters.[128] By virtue of the formation of a chemical bond with the element of the additive, the deposited platinum is not sintered over a wide range of reduction temperatures.

The formation of zerovalent compositions[142] on the surface of the (0.5% Pd, 1.2% Si, 1.2% Cr)$/Al_2O_3$ specimen obtained by the method of Ermakov and coworkers[127,128] has been demonstrated by laser micromass spectrometry. Peaks corresponding to Cr_2O^+, $Cr_2O_3^+$, and SiO^+ are absent from the mass spectrum, which indicates the absence of chromium and silicon oxides. The presence of zerovalent silicon has been confirmed by XPS data. The presence of zerovalent chromium and silicon under the conditions of the preparation of the specimens favoured the formation on the surface of intermetallic compounds of the type of Pd_3Cr and Pd_2Si, which should promote an increase in the selectivity and stability of the catalyst in the dehydrogenation and aromatisation reactions as a result of the suppression of side processes involving the cleavage of the C–C bonds and saturation by coke.[142] On the Pd/Al_2O_3 catalyst modified by chromium and silicon compounds, it is possible to aromatise unsaturated cracking petrols containing alkenes and alkadienes without the preliminary hydropurification of the starting material.[142]

The formation of the alloy may improve the properties the platinum–rhenium catalyst compared with the platinum reforming catalyst usually employed.[143] The palladium–rhenium alloy was first investigated in the 1950s.[144] The limit of the solubility of rhenium in palladium corresponds to a ~20% rhenium content. The alloys remain single-phase up to a rhenium concentration of 7.4 mass% (12.8 at.%). When small amounts of rhenium (0.35 mass% and 2.24 mass%) are introduced into palladium, the electrical resistance of the specimen increases. Palladium and rhenium are transition metals with incomplete *d* shells. The valence of palladium is higher than that of rhenium, since the number of electrons in the $d+s$ levels in it is greater. The phase diagram for the palladium–rhenium system, like that for the platinum–rhenium system, belong to the peritectic type and reveals the presence of two limited solid solutions and no chemical compounds. The principal factors determining the nature of the interaction of the elements according to Tylkina et al.[145] are their position in the Periodic System, the isomorphous nature of the crystal structures, and the difference between the atomic dimensions and electronegativities. According to the Hume–Rothery rule, the formation of a continuous series of solid solutions requires that the difference between the atomic radii does not exceed 7%–8%, while the appearance of limited miscibility requires that the difference should not be greater than 15%. The platinum group metals and rhenium have virtually identical atomic radii. The size factor does not exceed 3%.

Another condition for miscibility is the similarity of the crystal lattices. This is why palladium, which has a face-centred cubic lattice, forms only limited solid solutions with rhenium, which has a hexagonal close-packed lattice. A significant characteristic of the elements is their electronegativity[146] because it is a function of the atomic radius and valence and may serve as a measure of the electron binding energy in the atom. It is known that, for a difference between the electronegativities of 0.2 e.u., one should expect continuous miscibility, while for a difference of 0.4 e.u. limited miscibility is to be expected. The electronegativities of rhenium and palladium are identical and equal to 2.08 e.u.

In the interaction of metals, the difference between their melting points plays a significant role. When the difference between the melting points is small (up to ~20 °C), there is a continuous miscibility, whereas in the case where it is considerable (up to ~50 °C) limited miscibility obtains. The difference between the melting points and the peritectic transformation temperature are also related. The greater the difference between the melting points of the two metals, the lower the peritectic transformation temperature, and the greater the extent of the two-phase region. The difference between the melting points of rhenium and palladium is 51 °C and that between the melting points of rhenium and platinum is 44 °C. For other platinum group metals, this difference is much smaller.

The above considerations suggest that the high effectiveness of the palladium–rhenium catalyst is associated with the formation on its surface of a palladium–rhenium alloy.

The formation of the surfaces of bimetallic catalysts is complex and takes place in several stages. It depends both on the carrier and on the conditions in the preparation of the catalyst. Furthermore, as a consequence of the specificity of the interaction of the components in small clusters, the composition of the catalyst surface may differ from that of the bulk-phase of the alloys.

The reasons for the promoting effect of the second metal in bimetallic supported catalysts have not been ultimately elucidated. There is a possibility of the interaction of the carrier with rhenium, the stabilisation of some kind of intermediate oxidation states by alumina, fusion, or the formation of metal clusters. However, one must assume that, since the coke deposition process is very slow, it is a consequence of side reactions. The second metal may more effectively catalyse the removal of the corresponding intermediates than palladium.

The prediction of the catalytic effect and selection of catalysts with specified properties is still one of the current problems in hetereogeneous catalysis.[147–153] Studies carried out by Boreskov's school[149–151] and other investigators have shown that, for a constant chemical composition of the catalyst, the specific catalytic activity depends slightly on the dispersity of the active component, the degree of its crystallinity, and the method of preparation. A stationary composition of the catalyst is established under the influence of the reaction mixture and its catalytic activity is independent of its initial state. For the majority of reactions, the postulate of the approximate constancy of the specific activity of the catalyst holds. These reactions belong to the class of the so called structure-insensitive reactions. On the other hand, the reactions for which appreciable deviations are observed are structure-sensitive.[154, 155]

Together with nickel, palladium is one of the most active hydrogenation catalysts. The advantage of palladium over nickel consists in the fact that it readily dissolves hydrogen, which diffuses through the metal.[148] The hydrogenation reaction is structure-insensitive.

Analysis of the data presented in the review suggests that dehydrogenation on palladium-containing supported catalysts belongs to the class of structure-sensitive reactions, the rate of which depends on the accessibility and structure of the active centres. For such a reaction, the method of preparation of the catalyst is much more important than for the structure-insensitive reverse hydrogenation reaction. In particular, much attention must be devoted to the selection of the carrier, the regulation of its porosity, the preliminary treatment, the determination of the depth of impregnation, and other similar factors.[153]

Sulfur- and nitrogen-containing heterocyclic compounds are known to be catalytic poisons for platinum group metals. The catalyst is poisoned as a result of the stable chemisorption of such compounds on the surface of the deposited metal. Apparently, more strongly chemisorbed sulfur- and nitrogen-containing intermediates are formed on palladium catalysts than on sulfided palladium-containing catalysts and the higher activity and stability of the latter in the aromatisation reactions of petrol fractions containing sulfur compounds and in the dehydrogenation of heterocyclic molcules are associated with this factor. The greater stability of the hydrogen sulfide-treated palladium-containing catalysts compared with the untreated catalysts may also be associated with the formation on the surface of palladium sulfide, which, like other metal sulfides, is more resistant to the poisoning effect of sulfur and nitrogen compounds. Furthermore, metal sulfides are much less subject to saturation by coke than the metals themselves, as a result of which, nickel sulfide may prove to be more active, for example in the hydrocarbon hydrogenation reaction, than metallic nickel. Sulfide catalysts are bifunctional in their nature. They exhibit both hydrogenating-dehydrogenating and acid properties.[149] The great interest in sulfide catalysts is associated with their wide-scale application in hydropurification processes. The nature of the active component in metal sulfide supported catalysts and the mechanism of the activation of the C–S bond and of the hydrogen molecule in the hydropurification process still remain obscure.[156] A certain amount of attention has also been devoted to problems of the catalytic elimination of nitrogen-containing compounds, but their content, for example, in petroleums, is much lower than the content of sulfur compounds and the number of obscure and unsolved problems in that field remains even greater.

The modification of palladium supported catalysts with rhenium may induce an increase in the activity of palladium as regards reduction and promotes the attainment of a higher dispersity of the metal particles than in the Pd/Al_2O_3 catalyst.[135] Rhenium ensures a high thermal stability of alumino-palladium–rhenium catalysts, diminishes coke deposition, and can be more effective than palladium in removing the sulfur- and nitrogen-containing intermediates from the catalyst surface.[137, 157]

Sulfided palladium and palladium-containing bimetallic supported systems are active catalysts for the dehydrogenation of cyclanes, cyclenes, cyclohexadienes, and their functional derivatives and may be used both for the synthesis of aromatic hydrocarbons and for the refinement of petrol fractions. Severe requirements as regards the content of aromatic hydrocarbons in the fuel have now begun to be imposed in certain developed countries.[158, 159] One of the methods for the reduction of the concentration of such hydrocarbons may involve the use of sulfided palladium — rhenium supported catalysts for the hydrogenation of petroleum fractions.[160] Palladium-containing supported catalysts exhibit a high activity and selectivity in the dehydrogenation reactions of nitrogen- and oxygen-containing compounds in processes involving the preparation of valuable products of fine organic synthesis, such as indole, coumarin, their derivatives, and papaverine. The heterocyclic nuclei of the above compounds are known to serve as the structural basis for a large number of medicinal compounds, perfumes, dyes, etc.

The search for new ways of preparing supported catalysts containing a metal in a highly disperse state, modification, the synthesis of new carriers, the discovery of a relation beween the catalytic activity and the adsorption properties of the deposited metal and its valence state on the carrier, and other similar studies will promote the development of the scientific foundations for the selection of catalysts with specified properties in particular reactions. Further continuation of these researches by application of the latest physicochemical methods is one of the most important problems in heterogeneous catalysis.

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The mechanism of the adsorption of water molecules on carbon adsorbents

R Sh Vartapetyan, A M Voloshchuk

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Abstract. The results of studies on the mechanism of the adsorption of water molecules by nonporous and microporous carbon adsorbents carried out using various physicochemical methods are surveyed. The influence of the chemical state of the surface and of the porous structure of adsorbents on the heat of adsorption and the mechanism of filling of the carbon surfaces of micro- and mesopores of carbon adsorbents are analysed. The nature of the primary adsorption sites and the influence of the adsorption of water molecules on the X-ray diffraction parameters (microcrystalline structure) of carbon adsorbents are studied. The methods of investigation of the porous structure and chemical state of the surface of carbon adsorbents based on the analysis of water vapour adsorption isotherms are considered. The bibliography includes 80 references.

I. Introduction

The adsorption of nonpolar molecules, in particular argon, krypton, nitrogen, oxygen, carbon dioxide, and various hydrocarbons on carbon adsorbents (CA) has been studied rather extensively. These adsorbable substances are widely used to determine the parameters of the porous structures and adsorption properties of CA.[1] For example, argon is used for determining the specific surfaces of solids having low specific surfaces; carbon dioxide is used to characterise ultramicroporous adsorbents, including coal. The 'subtraction' method developed in recent years, which is based on the simultaneous analysis of adsorption isotherms of carbon dioxide and nitrogen, is employed for the determination of the structural parameters of micropores of various types.[2] Benzene has been accepted as a standard vapour for characterising CA in the former USSR countries. In European countries, Japan, and USA, nitrogen and carbon tetrachloride are usually employed for this purpose.

The methods for the determination of the porous structure parameters from the adsorption isotherms of the above compounds are based on the use of physical adsorption equations. These are primarily the well-known Dubinin–Radushkevich, Dubinin–Astakhov, and Dubinin–Stoeckli equations of the theory of volume filling of micropores (TVFM), developed by the school of Academician Dubinin,[3–5] and also various equations of polymolecular adsorption theory, in particular, the Brunauer–Emmett–Teller (BET) equation,[1,5] and the Mikhail–Brunauer–Bodor (MP) equation, etc.[1]

The adsorption of water on carbon adsorbents has some peculiarities, compared with the adsorption of nonpolar substances. The characteristic features and peculiarities of the adsorption of water vapour on CA are primarily caused by the tendency of polar water molecules to form hydrogen bonds, the dispersion interactions with the carbon surface being relatively weak.

The attempts to develop methods for the analysis of the porous structures of CA using the water vapour adsorption isotherms published in the literature are based on various, sometimes mutually exclusive, views on the adsorption mechanism.

A distinctive feature of carbon adsorbents, which determines to a substantial degree the fields of their application, is their relative hydrophobicity. However, depending on the porosity and the chemical state of the surface, which can vary on prolonged storage or prolonged use of an adsorbent, the humidity of the medium may noticeably influence the adsorption capacity of CA toward substances of various types.[6,7] Therefore, the study of the general rules and peculiarities of the adsorption of water vapour on CA has acquired practical significance.

The study of the mechanism of the adsorption of water vapour on CA is supposed to answer the following questions: what is the role of the primary adsorption sites of CA in the adsorption of water molecules, what are these sites from a chemical viewpoint, where are they located, how do the molecules being sorbed interact with these sites, in what manner are the surface and the micropore volume of CA filled, and what changes in the adsorbent itself accompany the adsorption process?

Although a large number of studies dealing with the adsorption of water vapour on CA have appeared in the literature,[8–22] at present there are no unanimous views on the mechanism of the adsorption, the role of the chemical state of the surface, or the nature of the adsorption sites. The initial views on the mechanism of adsorption of water vapour can be divided into two main groups: (1) the concept of the capillary condensation mechanism of the filling of micropores (Juhola[11–13] is the most consistent adherent of this theory) and (2) the concept of primary adsorption sites and the specific interaction of water with the carbon surface (Pierce and Smith[14] and Dubinin[15] have

R Sh Vartapetyan, A M Voloshchuk Laboratory for the Kinetics and Dynamics of Adsorption, Institute of Physical Chemistry, Russian Academy of Sciences, Leninskii prosp. 31, 117915 Moscow, Russian Federation, Fax (7-095) 952 53 08, Tel. (7-095) 955 46 24

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developed this concept independently of one another). Dubinin and coworkers[15] have reported on the surface oxides of CA, which play an important role in the adsorption of water molecules. In addition, it has been suggested[16,17] that the specific features of the adsorption of water vapour on CA are due to changes in the properties of the adsorbate caused by an increase in the average number of hydrogen bonds. It has also been noted[18] that the peculiarity of the adsorption of water is due to the fact that the carbon networks move apart and water molecules penetrate into the interlattice space of the CA by the 'collective' adsorption mechanism.

Within the framework of the concept of primary adsorption sites (PAS), there are also several views on the mechanism of further filling of the adsorption space: (1) the 'island' mechanism, according to which the PAS serve as nuclei for the formation of micro-drops, whose coalescence results in the formation of the bulk phase[14,19,20] and (2) the monomolecular-layer mechanism, according to which hydrogen bonds play a prominent role in the formation of a monomolecular layer.[21,22]

The studies published in recent years also did not completely clarify the problem of the mechanism of the adsorption of water vapour on carbon adsorbents, in particular on activated carbon (AC). Some authors apply widely the Kelvin[13] and Sircar[23] equations, based on the capillary condensation mechanism of adsorption, while other workers draw attention to the fact that the presence of acidic oxygen-containing complexes in the CA increases the adsorption of water vapour and facilitates the filling of micropores.[24-27] At the same time, the presence of non-acidic oxygen complexes does not influence the polarity of the CA surface and does not increase the adsorption of water vapour.[28]

In the present review, attention is concentrated on the role of the chemical state of the surface and of the microporous structure of the CA in the adsorption of water vapour, the nature of the PAS, the character of the interaction of the adsorbed molecules with the PAS, and the mechanism of the filling of the pore volume. Therefore, we carried out a systematic analysis of experimental data on the adsorption of water vapour on CA differing in porosity and chemical state of the surface, as well as adsorption on identical CA studied by various physicochemical methods. A total of about 300 samples of CA obtained from various materials by a variety of procedures were studied.

All the CA studied were characterised in terms of the adsorption of nitrogen vapour at 77 K. The specific surfaces (S_{sp}) of nonporous CA were calculated by the BET equation or determined from comparative plots, which have been surveyed and described by Greg and Sing.[1] The so-called 'absolute' adsorption isotherm on the surface of graphitised thermal carbon black was adopted as the 'reference' isotherm in the analysis of graphitised CA samples,[29] while in the analysis of other CA, the averaged adsorption isotherm for nonporous technical carbon black samples[30] was used.

The parameters of the porous structures of microporous AC (the limiting volume of the adsorption space of micropores W_o and the characteristic adsorption energy E_o) were calculated from the equations of the theory of the volume filling of micropores[5] using the comparative γ/F method of determining the surface area of mesopores.[30,31] The width of the micropores ($2x$) for the slit model was determined from the generalised Stoeckli equation,[32] which relates $2x$ (nm) to the characteristic adsorption energy E_o (kJ mol^{-1}).

$$2x = \frac{10.8}{E_o - 11.4}$$

From the W_o/x relationship, the geometric surface area of the slit-shaped micropores (S_g) was found.[4]

The parameters of mesoporous AC were determined by the MP method.[1,33]

Water vapour adsorption isotherms on technical carbon blacks and also on some AC (especially in the region of small relative pressures) were obtained in a vacuum adsorption unit using a beam microbalance having a sensitivity of 1.0 μg with weighed portions of about 2 g; adsorption on the other AC was measured using a McBain-type quartz spring balance having a sensitivity of about 3 μg with weighed portions of 100 mg. Low adsorbate pressures (less than 1.3 Pa) were measured by a capacitance membrane manometer with a sensitivity of 0.013 Pa.

Most of the experimental data on the adsorption of water vapour have been analysed by a comparative method,[34] which is widely used to determine the parameters of the porous structures of adsorbents from the adsorption isotherms of nonpolar substances.[1] In this case, the water vapour adsorption isotherm on nonporous graphitised carbon black was adopted as the 'reference' (standard) isotherm.[34]

II. Adsorption of water molecules on the surface of nonporous carbon adsorbents

1. Adsorbents with low concentrations of primary adsorption sites

In conformity with the concept of primary adsorption sites, when water molecules are sorbed on a nonporous carbon surface, they initially form hydrogen bonds with the PAS and, as the relative vapour pressure p/p_s (p_s is the saturated vapour pressure) increases, they form hydrogen bonds with one another too. Consequently, clusters of associated water molecules are formed around the PAS.[14] Kiselev and Kovaleva[35] have noted that the adsorption of water vapour on graphitised carbon black over the whole region of relative pressures remains insufficient for covering the entire surface with a continuous monomolecular layer. Apparently, the formation of 'islands' or clusters can account for the fact, observed by these authors, that the limiting adsorption at saturation of water molecules on surfaces of various carbon black samples, pretreated in a stream of hydrogen at 1973 K, is about 8 μmol m^{-2}, which is equivalent to approximately 50% of the surface being covered by a continuous water monolayer.[36] This value was obtained by plotting the absolute water vapour adsorption isotherms on various carbon black samples.[36]

Analysis of the data obtained by Golovko et al.[37], who studied the adsorption of water vapour on the surface of highly dispersed graphite, indicates that in this case too no continuous monomolecular layer is formed. One may suggest that, depending on the surface concentration of the PAS, the adsorption of water vapour may end in the formation of either separated clusters, existing in equilibrium with the saturated vapour, or of a continuous adsorption film on the surface. In the former case, the distance between the PAS (l_m) should be larger than a certain limiting size of the water clusters formed on the carbon surface, and the limiting adsorption at saturation (a_s) should be proportional to the number of PAS rather than to the surface

Table 1. The specific surfaces (S_{sp}), the numbers of primary adsorption sites (a_m), the distances between them (l_m), the total amounts adsorbed at saturation (a_s), and the numbers of statistical monomolecular layers (N_s) for the graphitised CA studied (samples *1–8*).

Sample	S_{sp}/m^2 g^{-1}	a_m/μmol g^{-1}	l_m/nm	a_s/μmol g^{-1}	N_s[a]
1	47	0.5	12.5	240	0.32
2	50	8.0	3.22	1200	1.50
3	51	12.0	2.66	1790	2.20
4	47	5.0	3.96	610	0.82
5	63	15.0	2.65	1790	1.80
6	50	2.5	5.76	390	0.49
7	33	1.6	5.85	250	0.48
8	100	4.0	6.44	590	0.37

[a] The N_s value was calculated for the area of the water molecule (0.105 nm^2) determined from the bulk density of water.

area of the CA. In the latter case, l_m should be smaller than the limiting size of the clusters and a_s should be proportional to the surface area of the CA.

A number of adsorbents prepared from ultradisperse technical carbon[38] with subsequent graphitisation at a temperature of 3073 K have been used as CA with low surface concentrations of PAS. As shown by mercury porosimetry, the initial sample *1* (Table 1) possessed a pore volume of 0.425 $cm^3\ g^{-1}$ with a narrow pore size distribution having a maximum near 25 nm. In order to deposit OH groups, sample *1* was chlorinated and then hydrolysed (samples *2* and *3*) by the procedure reported for a diamond surface.[39] Samples *4* and *5* were prepared by the oxidation of sample *1* in concentrated HNO_3 at 298 K and 373 K, respectively. In addition, sample *6*, prepared by treating the CA with phenol, was studied. Sample *7* differed from the initial sample *1* only by a lower specific surface and a higher PAS concentration. For comparison, Vulkan-7H carbon black graphitised at 3073 K (sample *8*), adopted as the 'reference' sample, was also studied.

Fig. 1 presents comparative plots for the adsorption of nitrogen vapour on samples *1–7* at 77 K. In these plots, the 'absolute' isotherm for adsorption on the surface of graphitised thermal carbon black was adopted as the reference isotherm.[29] For all the samples *1–7* studied, these plots are straight lines passing through the origin of coordinates. This indicates that the mechanisms of nitrogen adsorption on the samples studied and on the standard nonporous carbon surface are identical and that the surfaces of the adsorbents studied are energetically and structurally uniform. From the slopes of the comparative plots for the adsorption of nitrogen, the specific surfaces of the adsorbents (S_{sp}) may be determined.[29,30] Fig. 2 shows water vapour adsorption isotherms on some of these samples at 293 K, and Fig. 3 presents the comparative plots for the adsorption of water vapour. In this case, the water vapour adsorption isotherm on sample *8* was adopted as the standard. The slopes of the comparative plots for the adsorption of water are proportional to the concentration of the PAS (a_m).[34] The distance between the PAS (l_m) was calculated on the assumption that they are uniformly distributed over the surface.

From Table 1, one can see that the number of PAS on the initial sample *1* is significantly smaller than that on the 'reference' graphitised carbon black and that this number increases sharply when the CA is oxidised. The S_{sp} values for samples *1–4* and *6* are virtually identical, while S_{sp} for sample *5*, obtained by boiling sample *1* in concentrated HNO_3, is somewhat higher. The values of a_s for samples *1*, *4*, *6*, *7*, and *8* correspond to the fractions of the close packed monolayer.

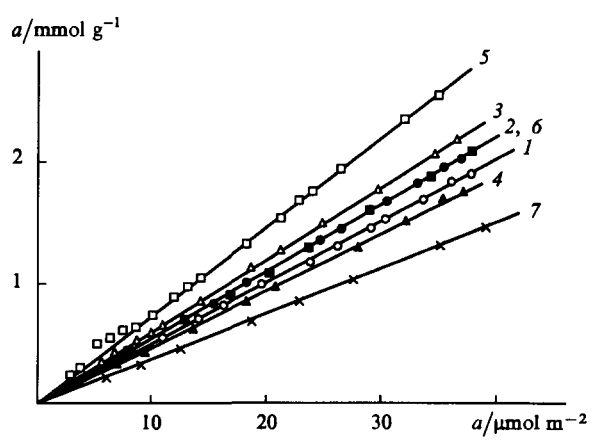


Figure 1. Comparative plots for the adsorption of nitrogen vapour on graphitised CA samples (*1–7*) at 77 K. The numbering of the samples in Figs 1–4 corresponds to that in Table 1.

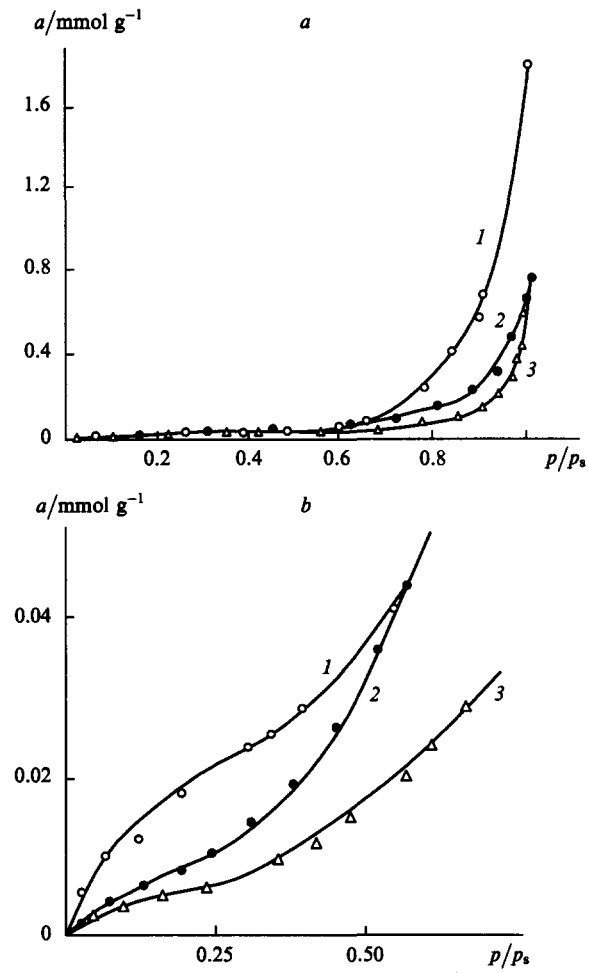


Figure 2. Water vapour adsorption isotherms at 293 K on the graphitised samples *3* (curve *1*), *4* (curve *2*), and *8* (curve *3*). The overall form of the isotherms (*a*) and the isotherms at low coverages (*b*).

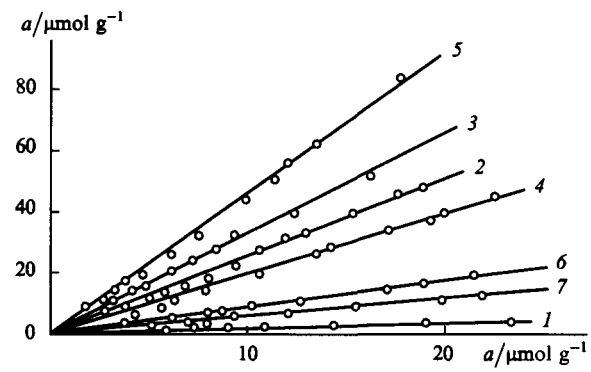


Figure 3. Comparative plots for the adsorption of water vapour on the graphitised samples *1–7* at 293 K.

The dependence of the total amount adsorbed at saturation a_s on the concentration of PAS a_m on graphitised CA is shown in Fig. 4. It is a straight line starting from the origin of coordinates. The slope of this straight line corresponds to the average number of water molecules in a cluster formed around a PAS at $p/p_s = 1$, which is approximately 150 molecules per site. The size of such a cluster can be evaluated from data on the numerical modelling of the adsorption of water molecules on a carbon surface.[40] If one assumes that the adsorbed water clusters are geometrically similar (a cluster consisting of 19 water molecules is a hemisphere 1.4–1.5 nm in diameter and 0.7 nm high[40]), a

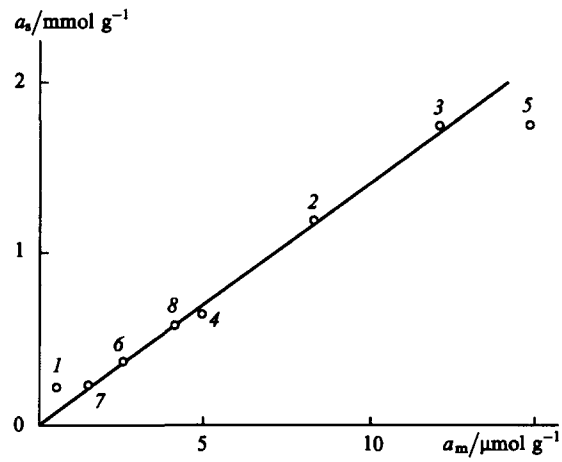


Figure 4. Dependence of the total amount of water vapour adsorbed at saturation on the number of primary adsorption sites (a_m) on graphitised CA samples.

cluster on a surface incorporating 150 water molecules should be about 3.0 nm in diameter and 1.5 nm high.

Thus, if the distance between the PAS l_m is larger than 3 nm, no continuous adsorption layer is formed on the surface of the graphitised CA. This result is supported by independent calorimetric measurements of the heats of immersion in water of sample *7* containing various quantities of preadsorbed water (Fig. 5).[41] From Fig. 5, one can see that the heats of immersion increase continuously as the quantity of preadsorbed water increases up to the total uptake at saturation, and reach 1.5 J g^{-1}. This means that the differential heats of adsorption calculated from the heats of immersion are lower than the heat of condensation over the whole range of coverages (curve *2* in Fig. 5). At low coverages, the differential heats agree with the isosteric heats calculated from the water vapour adsorption isotherms on this sample at 298, 293, and 273 K (curve *3*).

Taking into account the surface energy of normal water (118 mJ m^{-2}), one can infer that the heat of immersion equal to 1.5 J g^{-1} corresponds to the disappearance of 12.7 m^2 g^{-1} of the water surface, i.e. if the limiting quantity of water has been preadsorbed, the water molecules occupy about 40% of the whole surface of the graphitised sample, which amounts to 33 m^2 g^{-1} (see Table 1).

Thus, if the distance between the PAS is greater than the critical size of the clusters formed from water molecules adsorbed on the carbon surface, the clusters grow independently of one another until the amount adsorbed at saturation is achieved. By determining the amount of water vapour adsorbed at saturation, one can evaluate the number of PAS on the carbon surface.

It is noteworthy that the correct determination of the number of PAS for water molecules is very important in the approach outlined. The number of PAS on the CA can be calculated from the Langmuir equation for localised adsorption:

$$a = \frac{a_m bp}{1 + bp},$$

where p is the equilibrium pressure and b the energetic factor. This equation describes experimental adsorption isotherms in the region of low relative pressures where adsorption is mainly caused by the interaction of water molecules with PAS. The resulting number is identical with the number of acidic surface functional groups, which is determined by an independent method involving the neutralisation of these groups with a solution of Na_2CO_3. Determination of the number of PAS using the Dubinin–Serpinskii equations yields, as a rule, higher values of a_m,[42] which finally results in smaller distances between the PAS and, consequently, in lower values of the critical size of a cluster on the carbon surface.

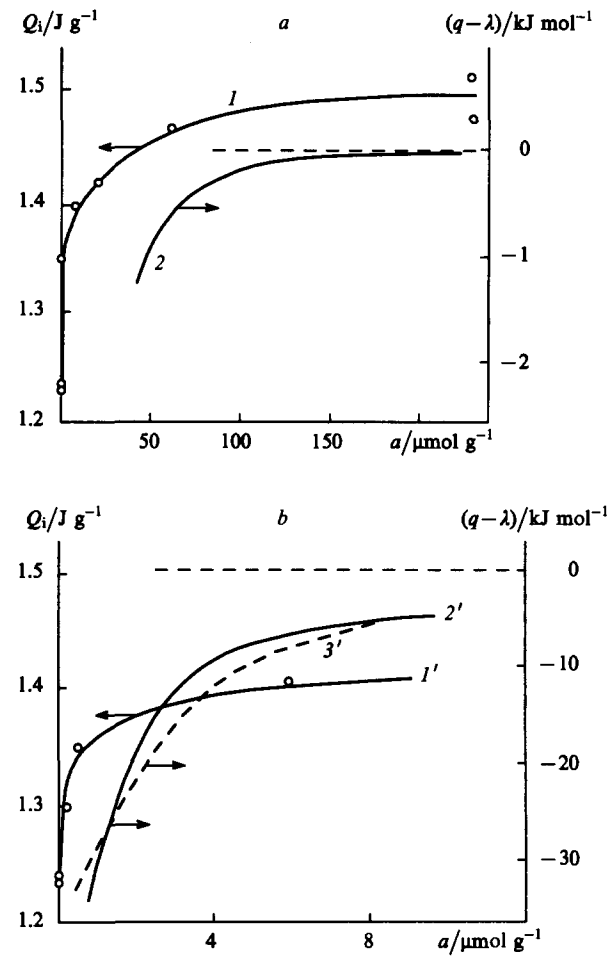


Figure 5. Dependence of the heat of immersion of sample *7* in water (Q_i) at 298 K on the quantity of preadsorbed water (curves *1* and *1′*) over the entire range of coverages (*a*) and in the initial section (*b*). The 'pure' differential heats of adsorption of water vapour ($q - \lambda$) were calculated from the Q_i values (curves *2* and *2′*). The isosteric heats of adsorption of water vapour on the same sample (curve *3′*) were calculated from the adsorption isotherms measured at 273, 293, and 298 K.

The first Dubinin–Serpinskii equation (DS-1) can be written as follows:

$$a = \frac{a_m ch}{1 - ch},$$

where c is a constant equal to the ratio between the adsorption and desorption rate constants and h the equilibrium relative pressure (p/p_s).

Allowance for the variation of the number of PAS present as new water molecules are adsorbed results in the second Dubinin–Serpinskii equation (DS-2):

$$h = \frac{a}{c(a_o + a)(1 - ka)},$$

where k is determined from the condition $a = a_s$ at $h = 1$, i.e.

$$k = \frac{1}{a_s} - \frac{1}{c(a_o + a_s)}.$$

Here a is the amount adsorbed at the relative pressure h, and a_s the amount adsorbed at $h = 1$.

2. Adsorbents with a relatively high concentration of primary adsorption sites

The adsorption of water vapour on CA with relatively high concentrations of PAS may result in the formation of a continuous adsorption layer. In this case, the total amount adsorbed at saturation should be proportional to the specific surface of the CA.

Table 2 presents the values of S_{sp}, a_s, l_s, and a_s as well as the number of statistical monomolecular layers N_s for such carbon black samples. The designations of the samples and the specific surfaces of the majority of carbon blacks studied were taken from two papers[29,30] (the values of S_y are given as the S_{sp}). In addition, samples of technical carbon PM-75, Ukhta channel carbon black (UKhT-K), and C-7 type acetylenic carbon black[29] with 5.5% of deposited pyrocarbon (AC-5.5) were studied. All the samples were subjected to preliminary heat treatment at 1273 K. As can be seen from Table 2, the l_m values for these samples are smaller than the critical cluster size, which indicates that the formation of a continuous adsorption film is possible. The a_s values for these carbon blacks correspond to the formation of 1.7 ± 0.3 statistical close-packed monolayers.

The plot of a_s against S_{sp} for the CA listed in Table 2 is shown in Fig. 6. This plot is linear and starts from the origin of coordinates. In this case, the slope of the straight line makes it possible to determine the amount of water vapour adsorbed at saturation per unit carbon surface: it is equal to approximately 26 μmol m^{-2}.

Table 2. The specific surfaces, the numbers of PAS, the distances between them, the total amounts adsorbed at saturation, and the numbers of statistical monomolecular layers for carbon blacks with high concentrations of PAS.

Sample	Carbon black	S_{sp}/ $m^2\ g^{-1}$	a_m/ μmol g^{-1}	l_m/ nm	a_s/ μmol g^{-1}	N_s
1	S-3	31	0.013	1.99	0.85	1.75
2	PM-75	68	0.061	1.36	1.85	1.74
3	S-4	73	0.027	2.11	1.90	1.66
4	ST-4	84	0.283	0.70	2.85	2.16
5	ST-6	87	0.023	2.50	2.25	1.65
6	ST-7	91	0.060	1.59	2.50	1.75
7	S-8	95	0.220	0.85	2.20	1.48
8	AS-5.5	97	0.022	2.71	2.75	1.81
9	ST-8	112	0.337	0.74	3.25	1.85
10	UKhT-K	120	0.311	0.80	2.90	1.54
11	ST-10	126	0.068	1.75	2.95	1.49
12	S-9	126	0.132	1.26	2.50	1.27

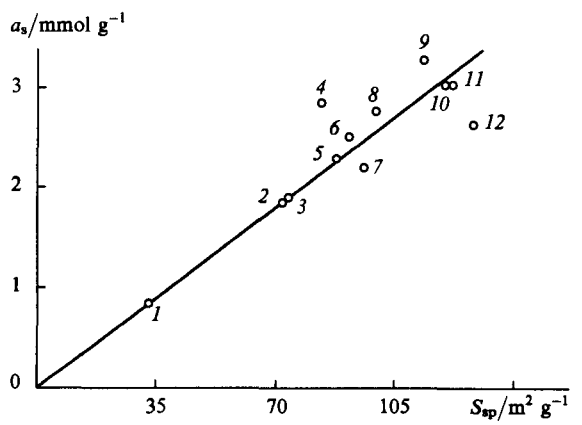


Figure 6. Dependence of the total amount of water vapour adsorbed at saturation on the specific surfaces of nonporous CA. The numbering of the samples corresponds to that in Table 2.

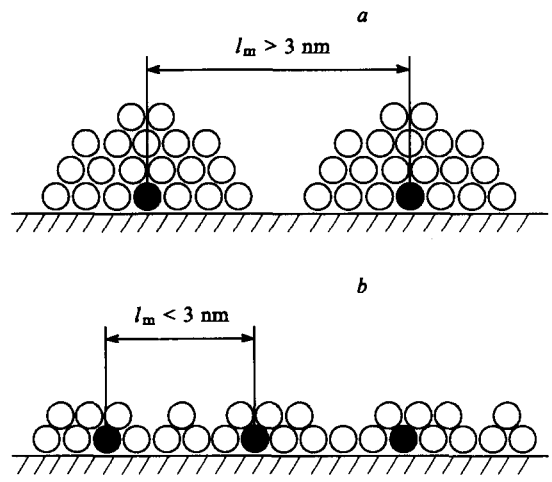


Figure 7. Schematic illustration of the coverage of the surfaces of nonporous CA with different surface concentrations of PAS: (*a*) l_m > 3 nm; (*b*) l_m < 3 nm.

The linear relationship between the amount of water vapour adsorbed at saturation and the S_{sp} of nonporous carbon adsorbents makes it possible to determine the surface areas of nonporous and mesoporous carbon adsorbents. This method has also been used[43] to evaluate the surface area of the mesopores of AC containing micro- and mesopores.

Thus, depending on the surface concentration of PAS on nonporous CA, two schemes for the filling of the surface can be suggested (Fig. 7). The first scheme (Fig. 7*a*) corresponds to a concentration of PAS below the critical concentration, when clusters of adsorbed molecules are formed and grow independently of one another until a limiting value of approximately 150 molecules per site is reached. The second scheme (Fig. 7*b*) corresponds to a rather high surface concentration of PAS, when a continuous adsorption layer is formed.

III. Adsorption of water molecules on activated carbons

The parameters of the porous structures of some typical representatives of the AC studied are listed in Table 3. The AC-1 and AC-5 samples were prepared from coal by steam activation, and their properties are close to those of industrial AC samples of AG-3 and AG-5 types. The peat-based AC-2 and AC-3 samples are similar in their properties to industrial recovered AC of the ART type. The AC-6, AC-7, and AC-8 samples were prepared under laboratory conditions from furfural. AC-4 is an industrial AC of the MSC-5 type (Japan), and AC-10 and AC-11 are industrial AC of the SKT-6A and SKT types, respectively. AC-9, AC-Ts, and AC-U-3 were obtained under laboratory conditions; the former two samples were prepared by the carbonisation of silicon and zirconium carbides respectively, while the latter (AC-U-3) was prepared from polyacrylonitrile.

Apart from the microporous AC listed in Table 3, ultramicroporous AC-U-1 (based on polyacrylonitrile) and AC-U-2 (an AC with MSC-4A molecular-sieve properties) samples, a supermicroporous coal-based AC-U sample, and a mesoporous AC-M (from molybdenum carbide) sample have also been studied. The specific surfaces of AC-M and AC-U are 470 and 1870 $m^2\ g^{-1}$ respectively. The total amounts of nitrogen adsorbed at saturation W_s on these samples are 0.85 and 1.44 $cm^3\ g^{-1}$, and the average pore sizes (the half-widths x) calculated from these values for the slit model are 1.8 and 0.77 nm, respectively. AC-U-1 and AC-U-2 virtually do not adsorb benzene.

Table 3. Porous structure parameters of typical representatives of the activated carbons studied.

Sample	S_m /m^2 g^{-1}	W_o /cm^3 g^{-1}	E_o /kJ mol^{-1}	x/nm
AC-1	100	0.28	19.0	0.71
AC-2	35	0.40	24.4	0.42
AC-3	140	0.26	19.5	0.67
AC-4	18	0.20	32.4	0.28
AC-5[a]	–	0.18	23.6	0.85
		0.38	10.4	
AC-6	30	0.32	34.0	0.24
AC-7	120	0.60	19.8	0.64
AC-8	300	0.67	17.6	0.87
AC-9	30	0.47	21.8	0.52
AC-10	–	0.55	21.4	0.54
AC-11	20	0.49	21.5	0.53
AC-Ts	25	0.82	17.8	0.84
AC-U-3	~0	0.10	29.2	0.30

[a] The calculation was carried out using the two-term equation of the theory of volume filling for a bidisperse porous structure; the x values have been averaged.[4] The calculation by the Dubinin – Stoeckli equation yields S_m = 300 m^2 g^{-1}, W_o = 0.38 cm^3 g^{-1}, x = 0.73 nm.

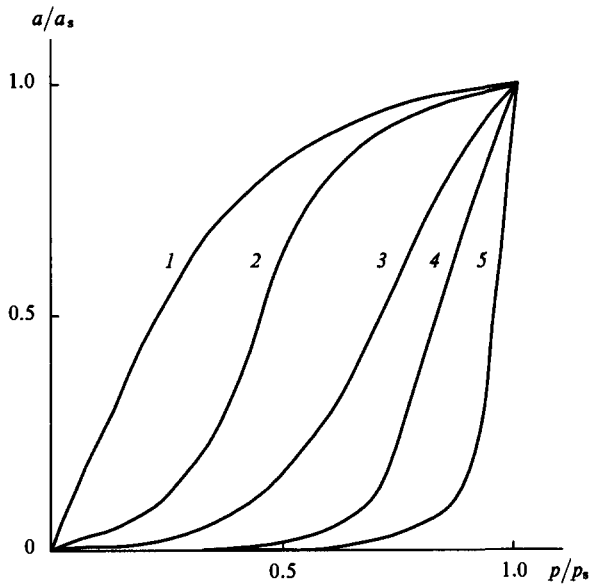


Figure 8. Water vapour adsorption isotherms in relative coordinates for typical AC: AC-U-1 (*1*), AC-2 (*2*), AC-1 (*3*), AC-7 (*4*), AC-M (*5*).

The parameters of the porous structures of other AC will be presented as required.

The adsorption isotherms for water vapour on the AC studied cover almost the whole range of known adsorption isotherms. Fig. 8 shows adsorption isotherms on typical AC in relative coordinates, a/a_s against p/p_s. The shapes of these adsorption isotherms vary from the atypical curve for the ultramicroporous AC-U-1, which is convex over the whole pressure range, to the concave curve for the mesoporous AC-M.

1. Adsorption isotherms at low coverages

While studying the adsorption of water vapour on AC, particular attention was concentrated on the initial sections of the adsorption isotherms, since this region had scarcely been investigated before, though it may provide valuable information concerning the number and nature of PAS and the mechanism of the interaction of water molecules with PAS.

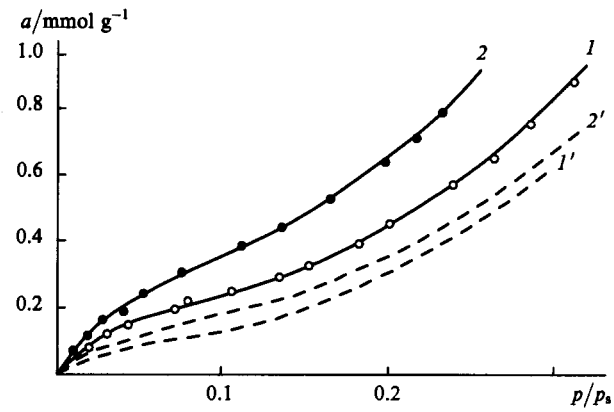


Figure 9. Initial sections of water vapour adsorption isotherms at 293 K on AC-1 and AC-2 evacuated at 293 K (curves *1* and *2*) and 673 K (curves *1'* and *2'*). The circles represent the adsorption isotherms for samples containing 0.6 and 1.8 mmol g^{-1} of firmly bound water respectively.

In Fig. 9, the initial sections of the isotherms for the adsorption of water vapour on two AC evacuated at 293 and 673 K are shown as examples. It can be seen that they have noticeable convex sections at relative pressures below 0.05 – 0.10. The presence of the convex sections indicates that, in the region of low relative pressures, the adsorption occurs predominantly on PAS. The number of PAS can be determined from the known Langmuir equation for localised adsorption. It is equal to the parameter a_m of the Langmuir equation. As a rule, the numbers of PAS for various AC are close to the amounts adsorbed at $p/p_s = 0.1$.

The numbers of PAS found from the Langmuir equation have been compared with those determined using the Dubinin – Serpinskii equation.[42] It was shown that a_m calculated from the Langmuir equation differs appreciably from and is virtually always lower than the number of PAS (a_o) found from the Dubinin – Serpinskii equation. In our opinion, a_m has a more clear physical meaning than a_o, since it is determined from the initial section of the adsorption isotherm, whose character is governed by the interaction of adsorbed molecules with PAS. This is also supported by the data reported[44-46] for oxidised AC for which the degree of adsorption of water vapour at $p/p_s = 0.1$ is practically identical with the number of acidic functional groups determined using the Boehm method, by neutralising these groups with bases of various strengths.[47]

Fig. 9 indicates that, when the temperature of preliminary evacuation is increased from 293 to 673 K, the water vapour adsorption isotherm is located in a lower position, which is associated with the decrease in the number of PAS on heating an AC.

In order to study the influence of the conditions in the preparation of the samples in more detail, AC-1 was evacuated at 673 K at a pressure of 10^{-2} Pa to constant weight, and, after cooling the sample to 293 K, three adsorption (to $p/p_s = 0.2$) and desorption cycles were carried out successively. The results of these experiments are shown in Fig. 10. In the fourth cycle, measurements were continued until the saturated vapour pressure was achieved, and, starting from the fifth cycle, a reproducible curve was obtained. As a result, the full adsorption isotherm (Fig. 11) was obtained, characterised by the so called 'open' hysteresis in which the desorption branch lies above the adsorption branch over the whole range of relative pressures (curve *1* in Fig. 11). The next adsorption-desorption cycle (curve *2* in Fig. 10) virtually did not lead to an increase in the quantity of firmly bound water, and the adsorption isotherm became reversible at low p/p_s with 'closed' hysteresis in the region $p/p_s = 0.3 - 1.0$.

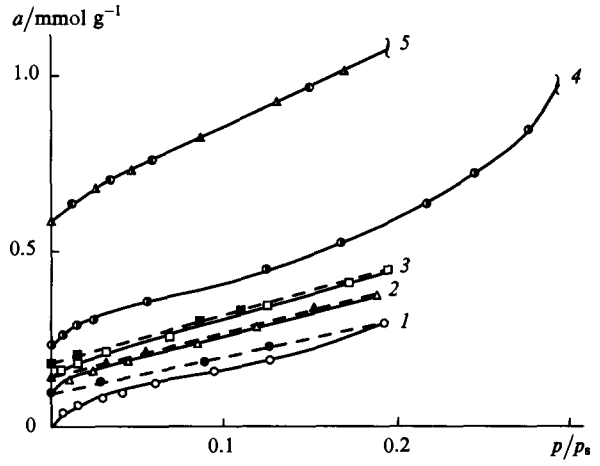


Figure 10. Water vapour adsorption (open symbols) and desorption (filled symbols) isotherms at 293 K on a AC-1 sample evacuated at 673 K. The numbers denote the numbers of adsorption-desorption cycles.

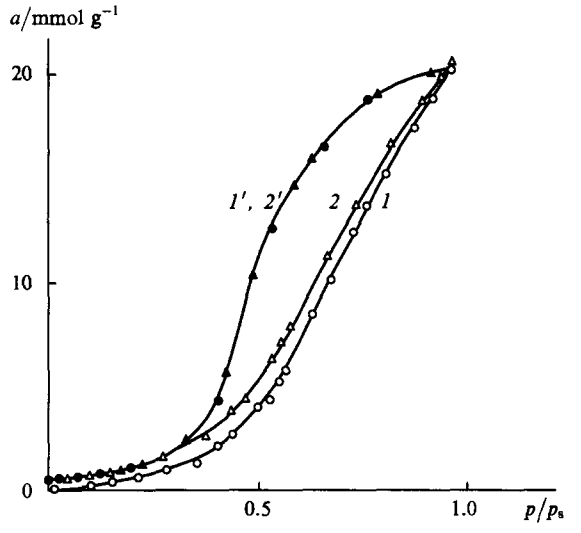


Figure 11. Full isotherms for the first (curves *1* and *1'*) and second (curves *2* and *2'*) adsorption (*1* and *2*) and desorption (*1'* and *2'*) cycles on AC-1 at 293 K.

The results presented in Figs 9 and 10 indicate that, after the thermal desorption of a sample at an elevated temperature (600–700 K), irreversible sorption (chemisorption) of water occurs synchronously with physical adsorption. Chemisorption also takes place at pressures of $10^{-1}-10^{-2}$ Pa during intervals between adsorption measurements. Therefore, each subsequent adsorption-desorption cycle occurs with a larger initial mass of the sample than the previous one. This chemisorption process causes the 'open' hysteresis on the water vapour adsorption isotherm on an AC subjected to preliminary evacuation at an elevated temperature.

The increase in the number of PAS with increase in the quantity of firmly bound water indicates that the firmly bound water acts as PAS. Irreversible adsorption of water vapour on AC was observed previously;[9,48,49] it has also been observed in a study of the interaction of an atomically pure graphite surface with water.[50]

Apart from the initial sections of the water vapour adsorption isotherms on AC-1 and AC-2 evacuated at 293 and 673 K, Fig. 9 also shows the adsorption isotherms on samples that have been evacuated at 673 K and then rehydrated. As one can see, preliminary heating of the samples results in a decrease in the amount of water adsorbed in the region of low p/p_s. After the rehydration of AC, the adsorption isotherms obtained for unheated and rehydrated samples coincide. Thus, a substantial proportion of the PAS are destroyed when the sample is heated to 673 K, and are almost entirely restored when the sample is rehydrated.

The numbers of PAS for some AC evacuated at 293 and 673 K and also for a number of AC, modified through oxidation in moist air at 623 K, deashing in HCl, successive deashing in HF and HCl, and heat treatment in an argon atmosphere at temperatures between 1273 and 2073 K, are presented in Table 4. It can be seen from this table that preliminary heating results in a decrease in the number of PAS for all the initial AC, except AC-9. In the case of AC-9, the number of PAS does not change on preliminary heating.

Table 4. The numbers of PAS (a_m/mmol g^{-1}) on the initial and modified AC at various evacuation temperatures (T_{evac}).

Sample	Method of pretreatment	The number of PAS after evacuation at	
		293 K	637 K
AC-1	None	0.30	0.16
	Oxidation	0.32	0.43
	Deashing with HCl + HF	0.40	–
	Heat treatment at		
	1273 K	0.10	0.10
	1473 K	0.08	0.08
	1673 K	0.07	0.07
	1773 K	0.06	0.06
	1873 K	0.05	0.05
	2073 K	0.03	0.03
AC-2	None	0.41	0.21
	Oxidation	0.44	0.44
AC-6	None	0.60	0.20
AC-7	"	0.41	0.08
AC-8	"	0.21	0.05
AC-9	"	0.20	0.20
AC-10	"	0.53	0.20
AC-U-1	"	1.24	0.34
AC-S	"	0.19	0.16
AC-M	"	0.70	0.20

The role of oxidation in air at 623 K does not reduce merely to an increase in the number of PAS. In fact, when the preliminary evacuation of AC-1 and AC-2 is carried out at 293 K, the numbers of PAS on the initial and oxidised samples are close, while in the case of evacuation at 673 K, the a_m values for oxidised samples are much larger than those for the initial ones. The major distinction in the adsorption behaviour of the initial and oxidised AC is that for samples oxidised in moist air, the change in the number of PAS on heating the AC from 293 to 673 K is substantially less pronounced. The oxidation not only leads to a change in the total concentration of PAS, but results in an increase in the ratio between the relatively unstable oxygen-containing surface compounds that are removed by moderate heating (in particular, chemisorbed water) and more thermally stable surface groups.

As can be seen from Table 4, heat treatment of AC in an argon atmosphere at 1273–2273 K leads to a continuous decrease in a_m.[42] When the treatment temperature is higher than 1273 K, the adsorption isotherms do not depend on the

conditions in which the sample is prepared for the experiment, i.e. the numbers of PAS on the heated and unheated samples are identical.

Extensive deashing by successive treatment with HCl and HF of the compounds evacuated at 293 K results in an increase in the number of PAS; i.e. the adsorption properties of the AC during their deashing are mostly influenced by the chemical modification of the surface, leading to an increase in the number of surface functional groups acting as PAS, rather than by the removal of oxygen-containing ash elements.

2. Heats of adsorption of water vapour at low coverages

The results obtained in studies of the adsorption of water vapour on CA in the region of low relative pressures attest to a substantial role of PAS in the adsorption. Useful information about the character of the interaction of adsorbed water molecules with PAS can be gained from the heats of adsorption of water vapour. Fig. 12 presents the dependences of isosteric heats (q_{st}) on the amount of adsorbed water vapour for some AC.[51] They all have a characteristic shape: in the range of low coverages, the q_{st} values are lower than the heats of condensation, but they increase with increase in coverage, and for high degrees of adsorption the q_{st} are constant and somewhat higher than the heats of condensation. For some AC, the $q_{st}(a)$ dependence goes through a maximum. A similar form of the dependence of the heat of adsorption on the amount adsorbed has been previously postulated in a study of the characteristic features of water vapour adsorption on CA.[17] We may note that our data are supported qualitatively by a calorimetric measurement of the heat of adsorption of water vapour on an AC previously evacuated at 298 K.[52]

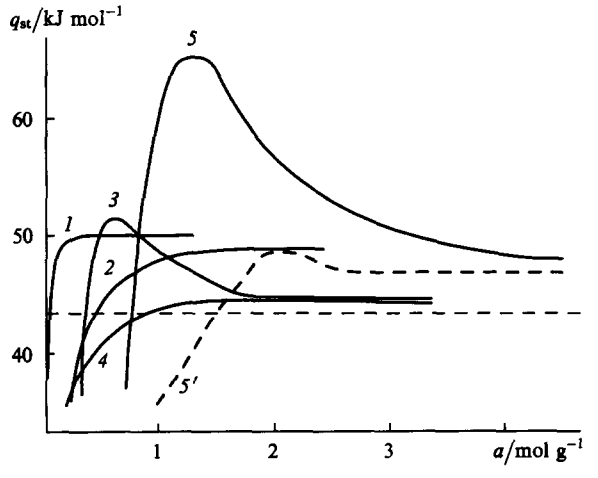


Figure 12. Dependence of isosteric heats of adsorption on the amount of adsorbed water for AC-1 (*1*), AC-2 (*2*), AC-N (*3*), AC-U-2 (*4*), and AC-U-3 (*5* and *5′*). Here and in Fig. 13, the dashed line represents the heat of condensation of water vapour.

It should be noted that the relationships for differential and isosteric heats of adsorption are applicable only to reversible adsorption cycles. As was shown above, the adsorption of water may be complicated by chemisorption, which distorts the results obtained in calculations of heats of adsorption. Strictly speaking, samples of a particular AC evacuated at different temperatures differ from one another in the chemical state of the surface and the concentration of PAS. For example, for AC-U-3, the variation of the temperature of experiments from 283 to 303 K leads to a substantial loss of the firmly bound water, and, as this takes place, the number of PAS considerably decreases. Therefore, two dependences of q_{st} against the amount adsorbed are shown in Fig. 12 for the AC-U-3 sample. One of them corresponds to the temperature range 283–293 K (curve *5*) and the other is for 293–303 K (curve *5′*). It has been shown[51] that the nonlinearity of adsorption isosteres, typical for most AC, hampers a precise quantitative determination of the isosteric heat of adsorption (q_{st}); however, the situation remains qualitatively the same.

In the region of low coverages, water molecules are mainly adsorbed on PAS, and the number of PAS is not invariable for a particular AC but depends on the temperature.

In this respect, it is expedient to refer the quantity of adsorbed water (a) to the number of PAS (a_m), which should be found separately for each temperature. This approach to the determination of heats of adsorption is equivalent to allowance for the temperature dependence of the adsorption-active surface of an adsorbent. The quantity a/a_m characterises the average number of water molecules adsorbed on one PAS.

To determine q_{st}, adsorption isotherms are plotted in terms of the a/a_m–p coordinates. The differential heats of adsorption q_Θ determined from these relationships for small a/a_m are given in Fig. 13. From this figure, one can see that in the region of small a/a_m the heats of adsorption virtually do not depend on the amount adsorbed within the limits of experimental error and are lower than the heat of condensation of water vapour. The method of determining heats of adsorption described can be used only in the region of low coverages, when there is less than one adsorbed water molecule per single PAS and the assumption that adsorption mostly occurs on PAS is obeyed sufficiently rigorously. When more than two or three water molecules are adsorbed on each PAS, the q_Θ values are also invariable and are somewhat higher than the heat of condensation of water vapour.

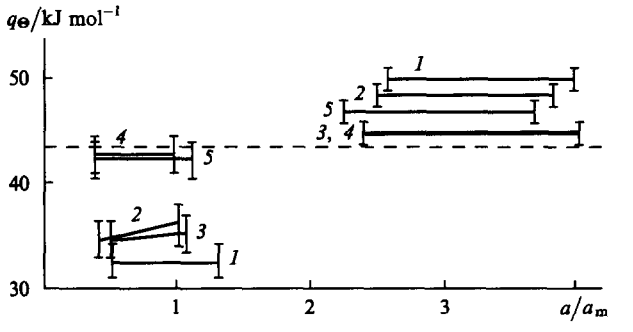


Figure 13. Dependence of the heats of adsorption of water vapour q_Θ on a/a_m for AC-1 (*1*), AC-2 (*2*), AC-N (*3*), AC-U-2 (*4*), and AC-U-3 (*5*).

From our viewpoint, the general character of the dependence of the heats of adsorption on the amount adsorbed agrees well with the mechanism of the adsorption of water vapour on CA considered above. Since the heat of adsorption on a PAS is related to the energy of formation of a hydrogen bond, the heat of adsorption should be equal to the energy of one hydrogen bond plus the energy of dispersion interaction. The energy of interaction of water molecules with a model PAS (a carbonyl group), found by numerical modelling,[40] is ~ 32 kJ mol^{-1} for the optimum arrangement of water molecules. Thus, it is reasonable to expect that in the region of low coverages the heat of adsorption should be smaller than the heat of condensation (~ 44 kJ mol^{-1}), which is itself somewhat greater that the energy of formation of two hydrogen bonds.

The fact that the heats of adsorption of water vapour at low coverages are lower than the heat of condensation implies that adsorbed molecules do not interact with one another and, in this sense, water molecules are adsorbed like the molecules of a gas. A similar suggestion was made previously[48] judging from kinetic data. However, some authors including those just cited[48] have obtained heats of adsorption at low coverages, larger than the heat of condensation. Among other reasons, this may be due to

the fact that, in most of these studies, measurements were carried out with CA evacuated at elevated temperatures. As has already been noted, in this case, apart from physical adsorption, chemisorption of water molecules takes place. It is this effect that has most probably been observed in the above studies.[48,53,54] The substantial energy evolved during chemisorption (the possibility of a chemical reaction also cannot be ruled out)[49,55] results in high calorimetric heats of adsorption in the region of low coverages. For high coverages, all the authors have obtained nearly constant heats of adsorption, which are somewhat higher than the heat of condensation of water vapour. This is explained by the fact that, as the clusters around the PAS grow, the average number of hydrogen bonds per molecule increases, and, consequently, the heat of adsorption also increases and can exceed the heat of condensation, owing to the contribution of the dispersion interactions of water molecules with the adsorbent.

The results obtained in another study[53] agree qualitatively with the scheme considered. It was found that, for relatively low temperatures (243–293 K), the heat of adsorption is nearly equal to the heat of condensation over the whole range of coverages studied; when the temperature is increased to 333–491 K, the quantity of firmly bound water acting as PAS decreases noticeably. In addition, when the temperature of the experiments is increased, one can study the region of low coverages at normal water vapour pressures. Under these conditions, the q_{st} values for small amounts adsorbed are much smaller than the heat of condensation, and grow rapidly as the degree of adsorption increases.[53]

3. Adsorption in the region of moderate and high coverages

The influence of the concentration of PAS on the full adsorption isotherm can be demonstrated by studying the adsorption of water vapour on various AC with similar microporous structures but different concentrations of PAS. The different types of interaction of the nonpolar nitrogen molecules and the polar water molecules with CA should lead to dissimilar mechanisms of adsorption on the surface and also to dissimilar mechanisms of the filling of the pore volume of a CA. Adsorbents that adsorb nitrogen in like manner can be essentially dissimilar towards the adsorption of water vapour. Fig. 14 shows relative isotherms for the adsorption of water vapour and nitrogen on two AC samples (AC-3 and AC-1). It can be seen that the degrees of adsorption of nitrogen on these two samples are close to one another over the whole p/p_s range (i.e. the samples possess similar porous structures). However, the amounts of water vapour adsorbed are significantly different, and only at $p/p_s \approx 1$ do they converge. These distinctions are due to the fact that the number of PAS on AC-3 is smaller than that on AC-1 by a factor of approximately six.

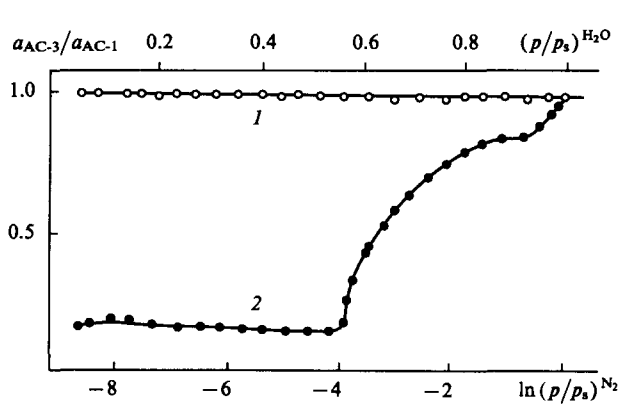


Figure 14. The ratios of the amount of nitrogen vapour adsorbed at 77 K (curve *1*) and the amount of water vapour adsorbed at 293 K (curve *2*) on AC-3 to the corresponding amounts adsorbed on AC-1.

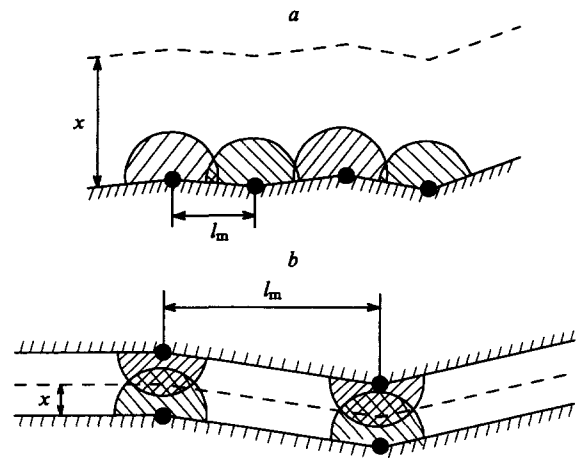


Figure 15. Schematic illustration of the filling of the pore volume of AC with various ratios of the average distance between the PAS (l_m) to the half-width of slit-like pores (x).

Thus, in the initial range of p/p_s, the adsorption of water on AC, similarly to that on nonporous CA, occurs on PAS, around which clusters of adsorbed water molecules can in principle form and grow. Generally, two schemes can be suggested to describe how the pore volume is filled as the clusters around PAS grow (Fig. 15). If the distance between the PAS is smaller than the width of a pore and smaller than the critical size of a cluster on a carbon surface, the clusters can coalesce as they grow to give a continuous adsorption layer on the surface of pores (Fig. 15*a*). For relatively narrow pores and a low concentration of PAS, one should expect that water molecules adsorbed on opposite walls of a pore would interact, forming bridge bonds (Fig. 15*b*).

The schemes presented indicate that the manner in which pores are filled depends both on the structure and on the chemical nature of the surface. At the same time, for low coverages, the mechanisms of the adsorption of water molecules on nonporous, mesoporous, and microporous CA are identical and are governed by the interaction with PAS. Fig. 16 shows isotherms for the adsorption of water vapour (referred to the numbers of PAS) on Vulkan-7H carbon black graphitised at 3073 K, mesoporous AC-M, ultramicroporous AC-U-3, and microporous AC-1, AC-2, AC-5, and AC-N. The data reported for some nonporous carbon blacks of the Graphon type[19,56] are also shown in this figure.

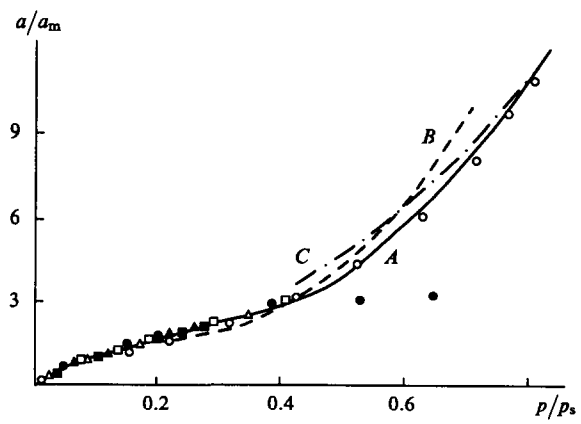


Figure 16. Water vapour adsorption isotherms in terms of the $(a/a_m) - (p/p_s)$ plots on Vulkan-7H carbon black (curve *A*), the mesoporous AC-M (*1*), the ultramicroporous AC-U-3 (*2*), the microporous AC-1 (*3*), AC-2 (*4*), AC-5 (*5*), AC-N (*6*), and also on Graphon carbon blacks (curves *B* and *C*).

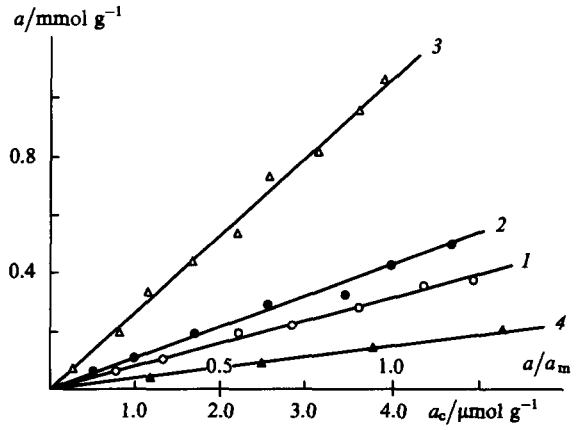


Figure 17. Comparative plots for the adsorption of water vapour in the region of low coverages for AC-1 (*1*), AC-2 (*2*), AC-U-1 (*3*), and AC-5 (*4*).

The similarity of the mechanisms by which water molecules are adsorbed on all CA in the range of small p/p_s is manifested, in particular, as follows. If the adsorption isotherm on separate PAS (or, to a first approximation, on a graphitised carbon black) is adopted as the reference isotherm, the comparative plots obtained for low coverages are straight lines starting from the origin of coordinates. The slopes of these straight lines are proportional to the concentrations of PAS. The initial sections of the comparative plots for some AC are shown in Fig. 17. Deviations of these plots from linearity should be expected in those cases where the mechanism of adsorption on a particular sample departs from independent cluster formation.

The coalescence of clusters yielding a continuous film should be shown on the comparative plots by a sharp downward deviation from the linear dependence. Among all the AC studied, these deviations from linearity were observed only for two adsorbents with relatively wide pores. Comparative plots for mesoporous AC-M and for AC, prepared by heat treatment of AC-1 at 2073 K [AC-1(2073)], with a specific surface of 110 $m^2\ g^{-1}$ are shown in Fig. 18. Adsorption on a continuous adsorption film apparently occurs less effectively than on free clusters. The abscissae of the break points allow one, in principle, to calculate the specific surfaces of adsorbents from the relationship $S = L^2 a_m N$, where L is the diameter of clusters at the instant they coalesce, a_m concentration of the clusters, and N the Avogadro number.

The validity of the adsorption scheme considered can be more clearly demonstrated by determining the amount adsorbed at the instant the clusters coalesce from the concentration of the PAS,

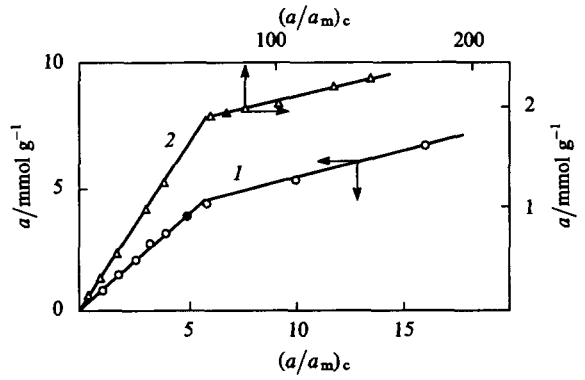


Figure 18. Comparative plots for the adsorption of water vapour on the mesoporous AC-M (*1*) and AC-1 (at 2073 K) (*2*).

from the specific surface of the sample (found by using nitrogen adsorption), and from the cluster sizes calculated by numerical modelling,[40] and by comparing the result with the ordinate of the break on the comparative plot. The adsorbed amounts calculated by this procedure for the AC-M and AC-1(2073) samples are 3.6 and 1.9 mmol g^{-1}. These values are close to the ordinates of the break points in Fig. 18, which confirms the validity of the adsorption mechanism suggested.

For adsorption on microporous AC, deviations from linearity (breaks) are seen on comparative plots even for low coverage, and they are directed upwards (Fig. 19*a*). This shape of comparative plots shows that interaction between water molecules adsorbed on the opposite walls of pores (i.e. the formation of bridging bonds) results in an increase in adsorption compared with that on separate sites. In addition, the narrower the micropores, the smaller is the abscissa of the break point. This is more clearly seen in Fig. 19*b*, where the comparative plots are given in reduced coordinates: the amounts adsorbed, expressed as numbers of molecules per adsorption site for the AC studied, are plotted as the ordinate, and the corresponding values for the reference carbon black Vulkan-7H(3073) are plotted as the abscissa.

Fig. 20 presents the correlation between the abscissa of the break point and the cube of the average size, x, of the micropores, calculated from the nitrogen vapour adsorption isotherms.

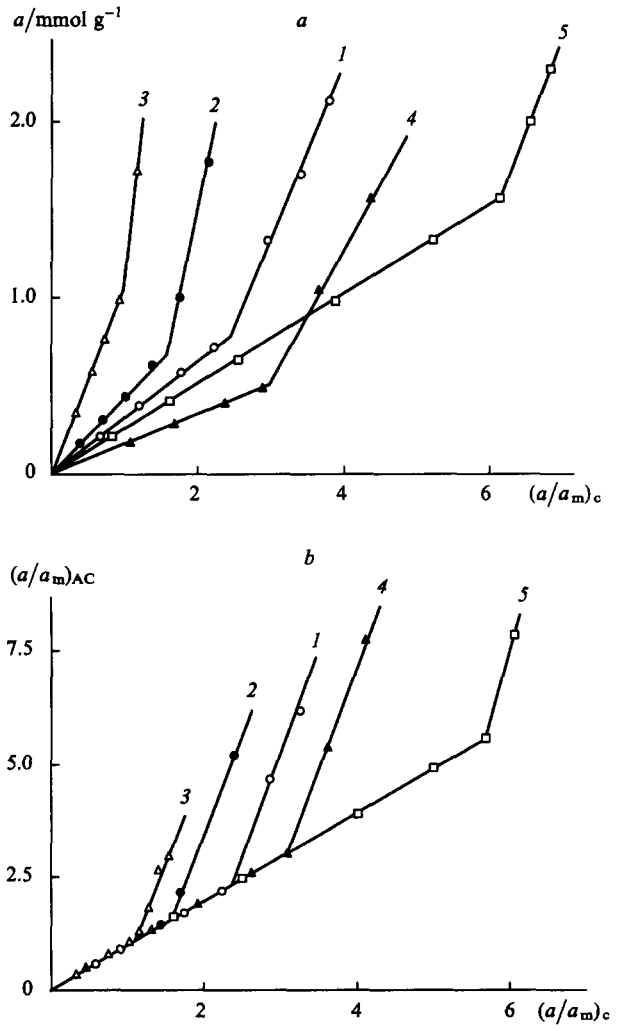


Figure 19. Comparative plots for the adsorption of water vapour on the microporous AC-1 (*1*), AC-2 (*2*), AC-U-1 (*3*), AC-5 (*4*), and AC-8 (*5*) in terms of the normal (*a*) and reduced (*b*) coordinates.

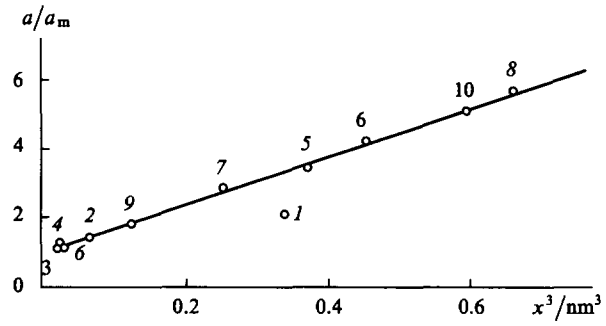


Figure 20. Correlation between the abscissa of the break point on comparative plots and the cube of the average size of micropores in AC-1 (*1*), AC-2 (*2*), AC-U-1 (*3*), AC-4 (*4*), AC-5 (*5*), AC-S (*6*), AC-7 (*7*), AC-8 (*8*), AC-9 (*9*), and AC-N (*10*).

The value of x can be found from the initial and middle sections of the water vapour adsorption isotherms on microporous AC.

The results obtained show that, when the micropores of the AC are filled with water, bridge bonds are formed. As this takes place, a relatively loose openwork structure, a 'lace', is produced in which the density of water is lower than that in the bulk phase. This can account for the fact that calculations of the limiting sorption volumes of AC from water vapour adsorption isotherms using the density of bulk-phase water usually afford smaller micropore volumes than calculations from the adsorption isotherms for other substances.[57] In principle, if the density of the adsorbed water is known, one can evaluate the size of the micropores by the foregoing procedure.[57]

Another method of evaluating the sizes of micropores of AC from adsorption and desorption isotherms for water vapour has also been reported.[58] The method is based on determining the width of the hysteresis loop between particular points on the adsorption and desorption isotherm branches. All the adsorption isotherms considered in this study have saturation sections, and the sharp rise of these isotherms ends at relative pressures of 0.8–0.9, and this limits the field of application of this method. In addition, it is known[59] that water vapour adsorption isotherms on ultramicroporous AC exhibit no hysteresis at all. One should also take into account the fact that repetition of the adsorption-desorption cycle for the same AC increases the amount of water adsorbed at saturation and diminishes the hysteresis loop,[60] which also hampers the use of this method.

The method of determining a porous structure from water vapour adsorption isotherms based on the formation of a monomolecular layer[4,22] at relative pressures of about 0.6 has been advantageously used for some AC. A common drawback of all the methods of calculation of specific surfaces based on the adsorption of water molecules is that for these calculations one must know the cross-sectional area of a water molecule; this value in its turn depends substantially on the oxidation state of the surface. It is likely that, for AC having typical micropores with diameters of the order of 4–5 water molecules, the overall adsorbed amounts are identical, whether a dense monomolecular layer or a loose 'openwork' packing is formed. In other words, the density of adsorbed water forming bridge bonds is approximately half that of liquid water. Hence, about two loose layers of the openwork packing are equivalent to a continuous monomolecular layer.[22] This is indirectly supported by the fact that the cross-sectional areas of water molecules differ by a factor of almost two: calculations give 0.06–0.08 to 0.13 nm^2 depending on the method, while the experimental results are 0.128 ± 0.54 nm^2.[61] A value of 0.148 nm^2 has been adopted as the cross-sectional area for a water molecule on carbon black.[20] Data on the linear dimensions of various molecules including water, obtained by various authors who have used different computational methods, have been analysed and systematised.[62] For a water molecule, values ranging from 0.276 to 0.348 nm were reported.

Dubinin and coworkers[63,64] later restricted the field of application of the previously suggested method[4,22] to activated carbons with a 'normally' oxidised surface and a narrow size distribution of micropores, while for a broader region of micropore sizes they suggested a calculation for a monomolecular layer from the point of inflection, determined with the aid of the Weibull equation,[63] which is used to describe experimental water vapour adsorption isotherms. The authors[63] showed that the inflection points, indicating, in their opinion, the formation of monomolecular layers on various AC, lie at p/p_s from 0.5 to 0.75, which expands significantly the applicability of this method of determining the porous structure of an AC. However, it should be noted that, since the experimental water vapour adsorption isotherms on ultramicroporous and mesoporous AC (see Fig. 7) have no normal inflection points, the approach suggested can scarcely be applied to these materials. For the same reason, this method cannot in principle be applied to nonporous CA.

Methods of determining the porous structure parameters based on the formation of a monomolecular water layer in the micropores of an AC are also not general, as the amounts of water adsorbed on various AC at the same relative pressure can differ appreciably, depending on the chemical state of the surface. For example, it has been shown[65] that the proportion of the surface of carbon blacks occupied by water at a relative pressure of 0.6 can vary from 10% to 450%, that is, 0.1 to 4.5 monomolecular layers are formed. Some authors dispute altogether the possibility of formation of a monomolecular layer on the surface of nonporous CA during adsorption of water vapour.[26,43]

As regards the above result,[65] it should be noted that the amount of water vapour adsorbed at saturation, which corresponds to the formation of more than two monomolecular layers, is associated, in our opinion, with the filling of the surface ultramicropores formed on oxidation of carbon blacks. Oxidation can not only be carried out by special treatment, but can also occur during storage in air, and may be accompanied by the formation of surface ultramicropores.[65] The presence of these surface ultramicropores can be demonstrated by a joint analysis of water vapour adsorption isotherms on ultramicroporous AC and Spheron-6 carbon black.[59]

It should be noted that the determination of the parameters of the microporous structure from water vapour adsorption isotherms by any method, including that suggested by us, is somewhat conventional, because the results obtained are compared with data on the adsorption of other substances (nitrogen or benzene), and for this purpose a particular model of the porous structure is introduced. Unfortunately, up to now, there are no other direct and reliable methods of studying the microporous structures of CA. The use of tunnelling electron microscopy may prove to be promising in this field; however, no systematic studies of CA by this method have yet been carried out.

IV. The nature of the primary adsorption sites

The nature of the PAS has been studied by temperature-programmed desorption with mass spectrometric analysis of substances being evolved, by neutralising surface oxides with bases of various strengths, and by X-ray photoelectron spectroscopy.

1. Temperature-programmed desorption

The substances evolved during the heating of AC have been analysed using mass spectrometry with a linear variation of the temperature of samples (a MAT-311A spectrometer, Varian, USA). Prior to heating, the samples were evacuated at 293 K and a pressure of 10^{-5} Pa for 12 h. Figs 21 and 22 show the temperature dependences of the rate of H_2O, CO_2, and CO evolution at heating rates of 5 K min^{-1} for initial and rehydrated

AC-U-1. As can be seen, the H_2O/CO_2 ratio depends on the type of AC. Some overlapping peaks on the curves correspond to various functional groups and their fragments. Joint desorption of H_2O and CO_2 is typical of AC-1. Analogous spectra were obtained for AC-2. It may be assumed that water is chemisorbed on these AC via lactone type groups, which accounts for the joint desorption of H_2O and CO_2.[67] Actually the groups being desorbed can be regarded as a complex carbonic acid $H_2O:CO_2$. In our opinion, the presence of an H_2O peak and a low-temperature CO_2 peak in the spectrum of the rehydrated substance is evidence in support of the chemisorption of water. The evolution of CO at high temperatures may occur either via the decomposition of the corresponding groups or via the chemical reaction with the lattice carbon of CO_2, formed on decomposition of carboxylic or lactone groups.

The spectrum recorded for the polymer-based AC-U-1 differs essentially from those for AC-1 or AC-2. The CO_2 band contains two peaks, one of which (in the high-temperature region) is close to the CO peak. Therefore, the following scheme can be proposed. Water is evolved due to decomposition of two carboxy-groups, yielding an anhydride structure. The low-temperature CO_2 peak results from decomposition of separate carboxy-groups, and the joint desorption of CO and CO_2 is associated with the decomposition of the anhydride structures at high temperatures. This scheme is in full agreement with the results of a study of IR spectra of Saran-type AC,[68] which are similar to the AC-U-1 studied by us.

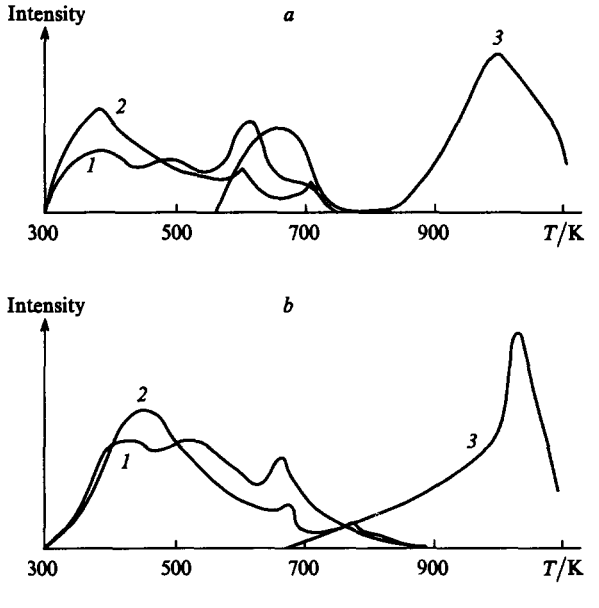


Figure 21. Temperature dependence of the rate of H_2O (*1*), CO_2 (*2*), and CO (*3*) evolution during the heating of the initial AC-1 (*a*) and the AC-1 rehydrated in water vapour after preliminary evacuation at 673 K (*b*) at a rate of 5 K min^{-1}.

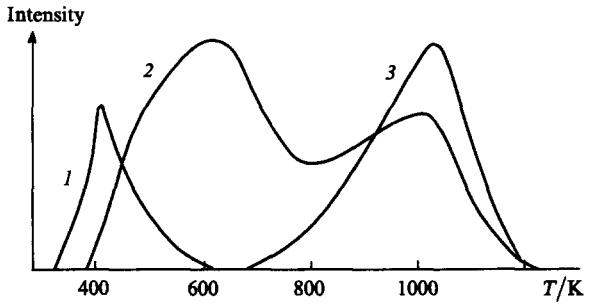


Figure 22. Temperature dependence of the rate of H_2O (*1*), CO_2 (*2*), and CO (*3*) evolution during the heating of AC-U-1 at a rate of 5 K min^{-1}.

Oxidation of these AC yields initially anhydride groups, which undergo hydrolysis by atmospheric moisture to give acid groups. These COOH groups are linked in pairs by hydrogen bonds.

A study on the nature of oxygen-containing functional groups in oxidised AC carried out recently by temperature-programmed desorption[69] has confirmed the existence of acidic carboxy-groups yielding a CO_2 peak at 600 K, and of anhydride groups with a CO_2 peak at 900 K. A significant role in the formation of 'CO_2 complexes' is played by the temperature of the oxidation of the AC in air or in nitric acid.[69] It has been found[44,70] that the quantity of CO_2 evolved is usually equivalent to the amount of alkali required to neutralise the acidic groups of AC.

From the adsorption results and data derived from temperature-programmed desorption, one may conclude that a part of the PAS (as a rule, the smaller one) are acidic carboxy-groups, thermally stable below 673 K. Adsorption on heated AC at low p/p_s occurs predominantly on these sites. The majority of the PAS on the AC prepared from natural raw materials (peat, coal, or wood) are chemisorbed water molecules, which are removed during heating simultaneously with CO_2. In this case, water molecules are apparently chemisorbed on lactone type groups, which can be regarded as complex carbonic acid adsorbed on the AC surface.

Water molecules chemisorbed on anhydride groups (carboxy-groups linked in pairs via hydrogen bonds) and individual carboxy-groups act as the PAS on Saran and other polymer-based AC.

2. Neutralisation of surface groups with bases of various strengths

The nature of the PAS has also been studied by the familiar Boehm[47] procedure, consisting in the neutralisation of the acidic groups with bases of various strengths. This procedure is being advantageously used to analyse the composition of acidic surface groups on oxidised AC, carbon blacks, and graphites. When the acidic groups being neutralised are weak, the interpretation of the titration data is more complicated, since neutralisation may be accompanied by the simultaneous ion exchange and direct hydrolysis of nonprotonated surface groups. We have carried out potentiometric titrations with a 0.05 N HCl solution of 0.05 N solutions of $NaHCO_3$, Na_2CO_3, NaOH, and C_2H_5ONa after they had been shaken with samples of AC.

Fig. 23 shows the potentiometric titration curves for the titration of solutions of NaOH (*a*) and Na_2CO_3 (*b*) with 0.05 M HCl after 20 ml of this NaOH or Na_2CO_3 solution had been shaken with 1 g of AC-1, AC-2, or AC-9 for two days. From Fig. 23*a*, one can see that in the case of AC-1 and AC-2, the titration curves for NaOH are similar to those for Na_2CO_3. One may assume that the surfaces of AC-1 and AC-2 contain the chemisorbed complex carbonic acid, $H_2O:CO_2$, which passes into the alkaline solution as Na_2CO_3 during interaction with water. This agrees with the data obtained by temperature-programmed desorption.

This characteristic of the titration of an NaOH solution, after shaking it with some of the AC, hampers a quantitative determination of the concentration of acidic groups of different strengths on the AC surface. In addition, it is known that inert electrolytes, for example KCl, added to a KOH solution substantially influence the results of the titration carried out after shaking the AC with this alkaline solution.[71] Since the mechanism of the action of inert electrolytes remains unclear, the authors[71] mostly used the data obtained on neutralisation of relatively strong acidic groups with a solution of Na_2CO_3.

Table 5 presents the concentrations of acidic surface groups neutralised by a solution of Na_2CO_3 (a_N), together with the number of PAS determined from water vapour adsorption isotherms on AC preliminarily heated at 673 K. One can see that these values are rather close, and it is quite probable that the convex section of the water vapour adsorption isotherm on the AC evacuated at 673 K is caused by the adsorption of water

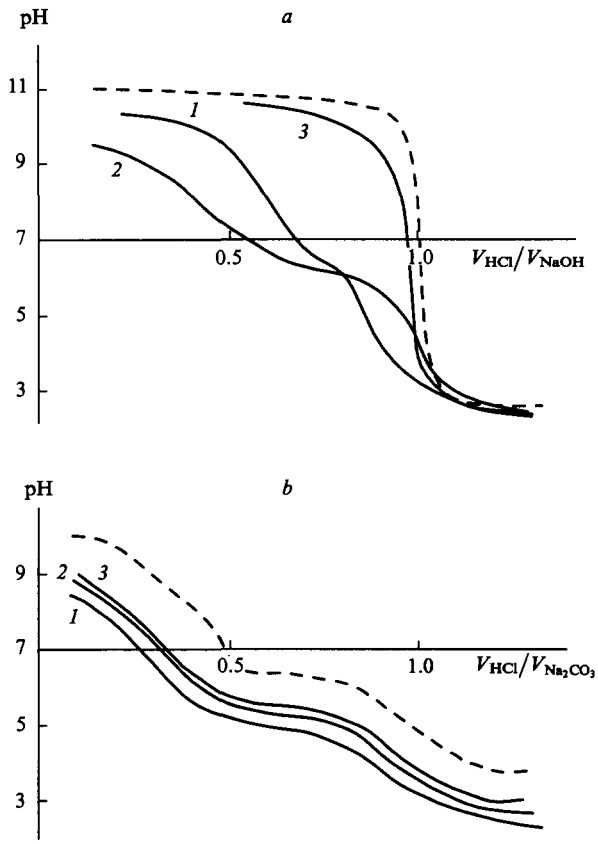


Figure 23. Curves for potentiometric titration with 0.05 N HCl of the NaOH (*a*) and Na_2CO_3 (*b*) solutions resulting from shaking 20 ml of 0.05 N NaOH and Na_2CO_3 respectively with 1 g of AC-1 (*1*), AC-2 (*2*), and AC-9 (*3*). The titration curves for the initial solutions of NaOH and Na_2CO_3 are shown by dashed lines.

molecules on relatively strong acidic carboxy-groups, which are not destroyed on heating to 673 K, as the PAS.[47] For nonporous graphitised Vulkan-7H carbon black, the number of surface groups neutralised with a Na_2CO_3 solution is 0.005 ± 0.002 mequiv. g^{-1}, which agrees with the data on the adsorption of water vapour ($a_m = 0.004$ mmol g^{-1}).

A correlation between the number of acidic groups determined by conductimetric titration and the amount adsorbed at point *b* (according to the BET equation) on the convex section of the water vapour adsorption isotherm has also been noted in a study[45] of the heats of immersion of a polymeric AC in water.

Despite the fact that quantitative analysis of the results of the titration of weakly acidic groups is difficult, one can make some qualitative conclusions. The titration curves for AC-9 have the normal shapes typical for the titration of a strong base with a strong acid. The numbers of acidic groups, neutralised with NaOH and Na_2CO_3, are close, i.e. the surface of AC-9 mostly contains strongly acidic groups, which are not removed on heating to 673 K. The adsorption properties of AC-9 with respect to water vapour almost do not depend on the evacuation temperature, i.e. adsorption occurs on thermally stable strongly acidic groups.

Table 5. The number of acidic surface groups neutralised by a solution of Na_2CO_3 (a_N) and the number of PAS (a_m) on the AC samples evacuated at 673 K.

Sample	a_N/mequiv. g^{-1}	a_m/mmol g^{-1}
AC-1	0.12	0.16
AC-2	0.16	0.21
AC-2 (oxidised)	0.50	0.44
AC-6	0.18	0.20
AC-7	0.09	0.08
AC-8	0.04	0.05
AC-9	0.18	0.20

It was shown previously that evacuation of AC-1 at 673 K leads to an appreciable decrease in the number of PAS, and the chemisorption of water molecules virtually restores the number of the PAS. In our opinion, the results obtained by the neutralisation of acidic groups are consistent with this assumption. When AC-1 is shaken with NaOH, some of the surface groups pass to the solution as Na_2CO_3. This results from the interaction of NaOH with weakly acidic groups on the surface of AC-1 (the complex carbonic acid, $H_2O:CO_2$). A relationship between the quantity of water, irreversibly adsorbed by the AC, and the number of oxygen-containing surface groups that decompose on heating to evolve CO_2 has also been observed in a study of the adsorption of water on AC modified with potassium permanganate and nitric acid.[44]

3. X-Ray photoelectron spectroscopy

The adsorption properties of AC with respect to water vapour are determined by an active part of the oxygen present, rather than by its total amount. The proportion of active oxygen can be evaluated by X-ray photoelectron spectroscopy. For this purpose, an AC sample was ground in an agate mortar and deposited as a suspension in water or ethanol on a support. After the evaporation of the liquid, the supported sample was introduced into the sluice compartment of an ESCA-3 MARK-2 spectrometer (VG, UK). The analysis was carried out after evacuation of the AC to a pressure of 10^{-9} Pa. X-Rays (magnesium K_α line) with $h\nu = 1253$ eV served as the ionisation source. The spectra were calibrated against an external standard [C 1*s* peak (285.0 eV) from a hydrocarbon layer on a gold support]. The O 1*s* spectra were recorded prior to and after heating the supported sample in the spectrometer compartment to 650 K. The O/C relative concentration was determined from the ratio between peak surface areas with allowance for the corresponding ionisation cross-sections. Simultaneously with the O 1*s* spectrum, the mass spectra of the desorbed substances were recorded using a built-in mass spectrometer. The oxygen spectrum is complex. Its detailed interpretation is complicated by difficulties associated with the calibration of the peak components; however, it may be noted that when the sample is heated, the spectrum component with a higher bond energy diminishes sharply [72] and evolution of H_2O and CO_2 occurs. The quantity of oxygen removed is estimated from the O : C ratios in the initial and heated AC.

Table 6 presents the O : C ratios for some AC as examples and also these ratios for AC-1 heat treated in argon at 1273 to 2273 K, oxidised in moist air at 623 K, and deashed with HCl or with HCl and HF in succession. As can be seen from the table, when the initial AC-1 is heated to 673 K, most of the oxygen remains in the AC, whereas the number of PAS is almost halved, as was shown above from the adsorption data (see Table 4). This indicates that most of the PAS on this AC are unstable oxygen-containing groups removed during heating to 673 K, in particular chemisorbed water. The overall amount of oxygen in AC-1 ensures a number of PAS a_m of 0.30 mmol g^{-1}. When 14% of the oxygen is removed, the number of PAS diminishes to 0.16 mmol g^{-1}, i.e. the adsorption-active oxygen comprises about a quarter of its overall content, which agrees with the data obtained by Boehm.[47]

Treatment of the AC in a moist air flow at 623 K does not result in an increase in the overall oxygen content (see Table 6); it actually decreases somewhat, due to the removal of some of the surface oxygen-containing groups on heating the sample. However, the relative change in the O/C concentration caused by heating decreases from 0.14 to 0.11 under these conditions.

Table 6. The O:C ratios calculated for some AC from X-ray photoelectron spectra prior to and after heating of the AC.

Sample	Method of treatment	O:C ratio (%)	
		before heating	after heating
AC-1	None	13.7	11.8
	Heat treatment at		
	1773 K	8.0	8.0
	2073 K	3.0	3.0
	Oxidation	12.3	10.9
	Deashing with		
	HCl	12.5	10.5
	HCl + HF	7.4	5.1
AC-2	None	20.0	–
AC-U-1	"	15.0	–
AC-10	"	39.0	–

Thus, oxidation in a moist air flow at 623 K results in an increase in the proportion of thermally stable oxygen-containing groups, rather than in the overall amount of oxygen on the AC. It is this effect that stabilises the number of PAS on the oxidised AC when it is heated from 293 to 673 K (see Table 4).

V. The influence of the adsorption of water vapour on the parameters of the microcrystalline structure of activated carbons

Valuable information about the mechanism of the adsorption of water molecules, the location of the PAS, and also the relationship between microporous and microcrystalline structures of adsorbents can be obtained from X-ray diffraction studies of AC adsorbing water vapour.

Carbon adsorbents normally consist of amorphous carbon and crystalline areas (crystallites), whose faces can form the walls of micropores. In X-ray diffraction patterns, the amorphous part is manifested as background scattering, while the structure of crystallites is characterised by two reflections: a more intense (002) reflection, the angle of which allows one to determine the distance between the graphite-like layers (d), and a weak (10) reflection corresponding to the ordering of atoms in the graphite-like layers.[73] The (10) reflection is actually a band that usually incorporates several unresolved lines — (100), (004), and (110). From the width of the (002) reflection, the X-ray diffraction parameter L_c characterising the 'height' of crystallites, i.e. the dimensions of the prismatic faces of the crystallites, can be estimated, while the width of the (10) band makes it possible to find the L_a parameter characterising the dimensions of the basal faces of crystallites. The relative intensity of the reflection provides information about the degree of crystallinity of the carbon material.[73, 74]

Since the X-ray diffraction patterns of the AC do not change when the surface is covered with oxides, it has been assumed[75] that oxygen is located at the corners of hexagons made up of carbon atoms. If we accept this assumption and take into account the fact that a proportion of the oxygen must be incorporated in the PAS, we find that the distances (l_m) between them should be of the same order of magnitude as the sizes of the crystallites L_a. To a first approximation, l_m can be estimated on the assumption that the PAS are uniformly distributed over the total surface of the AC ($S_g + S_m$).

The total surfaces ($S_g + S_m$) of AC found from nitrogen adsorption isotherms at 77 K, the numbers of the PAS (a_m) determined from water vapour adsorption isotherms at 293 K, and the distances between them (l_m) are listed as examples in Table 7. The L_a parameters and half-widths (x) for the slit model of pores are presented for comparison. One can see that the average distances between PAS for the majority of AC vary over a rather narrow range and are close, on average, to the sizes L_a of the crystallites forming the structure of the AC. The L_a parameters of the AC studied are consistent with the values reported[76] for various AC.

Table 7. The total specific surfaces ($S_g + S_m$), the numbers of PAS (a_m), the distances between them (l_m), the X-ray diffraction parameters L_a, and average half-widths x for some of the CA studied.

CA	(S_g+S_m)/ $m^2\ g^{-1}$	a_m/ mmol g^{-1}	l_m/nm	x/nm	L_a/nm
1	494	0.30	1.65	0.71	2.10
2	987	0.41	2.00	0.42	2.20
4	435	0.48	1.23	10.28	1.86
5[a]	820	0.16	2.92	0.73	–
6	1363	0.60	1.94	0.24	2.20
7	1058	0.41	2.07	0.64	3.30
8	1070	0.21	2.90	0.87	3.70
9	934	0.20	2.79	0.52	–
10	1019	0.53	1.79	0.54	2.36

[a] The calculations were carried out using the Dubinin – Stoeckli equation. Calculation by the two-term equation of the theory of volume filling yields a total specific surface of 713 $m^2\ g^{-1}$ and $x = 0.85$ nm.

A comparative X-ray diffraction study of various CA adsorbing water vapour makes it possible to identify the changes in adsorbents caused by the adsorption of water molecules. The adsorption of water vapour on some of the AC leads to a decrease in the interplanar spacing;[77] however, it is not clear whether this is a common characteristic feature of all AC and what is the physical meaning of these changes.

The results of a comparative X-ray diffraction analysis of CA are presented in Figs 24 and 25. The X-ray diffraction patterns were obtained on a DRON-3M diffractometer using CuK_α radiation (a Ni filter) by reflection from a flat sample, ground up beforehand and rubbed into a round cell. The measurements were carried out at room temperature; prior to the measurements, the samples were dried at 373 K and saturated with water vapour for 48 h. The interplanar spacings d and the intensities I of the (10) band, relative to the background, were determined for samples dried at 373 K and for samples saturated with water vapour.

Figs 24 and 25 present, among other data, the results of X-ray diffraction studies for those CA which are not listed in Tables 2 or 3. The d parameters for the dried samples studied varied from 0.355 nm for the P267-E carbon black to 0.462 nm for supermicroporous AC-S.

These figures indicate that the changes in the interplanar spacings (Δd) and intensities (ΔI) of the (10) band occurring after saturation of various AC with water vapour have some features in common. The average interplanar spacing d always decreases on adsorption of water molecules, and moist samples have closer d values than the dry ones. It is likely that water molecules, whose size is only slightly smaller than the distance between the graphite-like layers, influence the arrangement of the edge carbon atoms, located on the defective surfaces of crystallites, which makes a contribution to the change in the average interplanar spacing.

The Δd values increase as d increases up to a certain limiting value, after which they diminish (Fig. 24). At the same time, the intensity of the (10) band referred to the background increases for some of the samples (ΔI is positive) and decreases for others (ΔI is negative) (Fig. 25). The dependence of ΔI on d for moist samples of most of the AC studied is nearly linear (the samples with the maximum d value deviate from the general relation). This type of variation of Δd and ΔI with d can be explained in terms of the following scheme (Fig. 26). In the case of samples with small d values, the adsorption of water molecules on the edge dislocations of the graphite-like layers leads to a decrease in

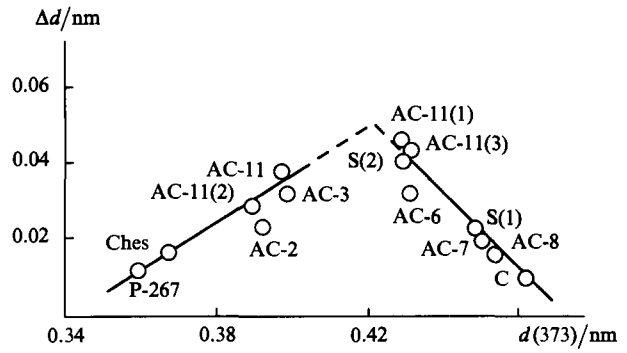


Figure 24. Dependence of $\Delta d = d(373) - d(H_2O)$ for samples dried at 373 K [$d(373)$] and samples saturated with water vapour [$d(H_2O)$] on $d(373)$. The points are labelled in conformity with the designations of the CA used in Tables 2 and 3. Additional designations are as follows: P is an industrial carbon black of the type P267-E, 'Ches' is a 'Chesacarb' type carbon black produced in the Czech Republic, S(1) is a modification of the supermicroporous AC-S, S(2) is AC-S treated with concentrated HNO_3, AC-11(1) and AC-11(2) are samples of AC-11 treated at 1173 K in an Ar or NH_3 atmosphere respectively, and AC-11(3) is AC-11 treated with concentrated HNO_3.

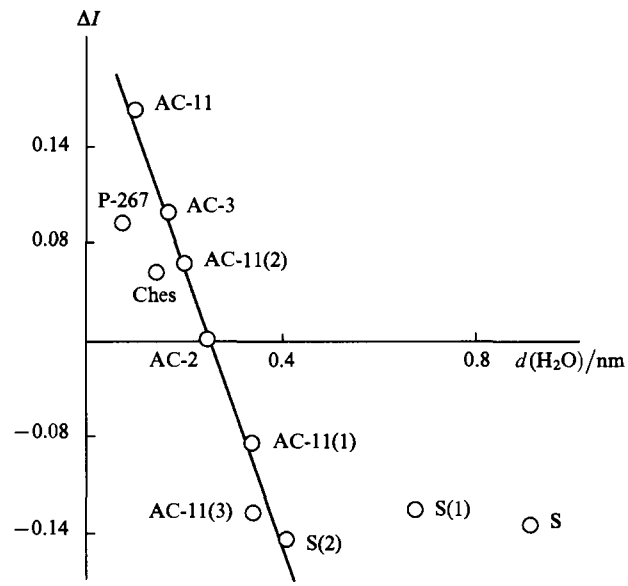


Figure 25. Dependence of the intensity difference $\Delta I = I(H_2O) - I(373)$ for samples saturated with water vapour [$I(H_2O)$] and those dried at 373 K [$I(373)$] on $d(H_2O)$ for moist samples. The designations are the same as in Fig. 24.

the interplanar spacing and simultaneously makes the mutual arrangement of the layers more ordered (Fig. 26*a*). For samples with medium d values, a decrease in d, virtually unaccompanied by an ordering of the networks, is possible (Fig. 26*b*). For samples with large d values, the adsorption of water molecules may result in a decrease in the interplanar spacing with a simultaneous distortion of the mutual arrangement of the layers (Fig. 26*c*). When d is further increased, the adsorption of water molecules does not influence it.

Thus, the character of the variation of the interplanar spacing d and of the relative intensity I of the (10) band after the adsorption of water vapour confirms the hypothesis that the adsorption occurs from the sides of the prismatic faces of the crystallites, where edge defects are located. This conclusion is also supported by the data on the influence of the adsorption of water

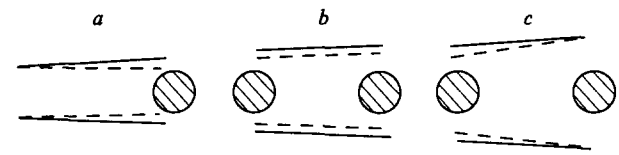


Figure 26. Schematic arrangement of water molecules near graphite-like layers at the edges of crystallites. The solid and dashed lines show the corresponding arrangement of the graphite-like layers prior to and after the adsorption of water molecules.

molecules on the L_a parameter characterising the size of the basal faces of the crystallites. Table 8 presents the L_a and L_c parameters for some AC dried at 373 K and saturated with water. One can see that L_a increases due to the adsorption of water vapour in all cases, and the larger the value of L_a, the larger the relative increase in $\Delta L/L_a$. At the same time, L_c varies slightly and irregularly. These results indicate that the adsorption of water molecules leads to the elongation of the carbon layers, and improvement of the latter.

Table 8. X-Ray diffraction parameters L_a and L_c for samples dried at 373 K and saturated with water.

Sample	L_a/nm		L_c/nm	
	373 K	H_2O	373 K	H_2O
AC-1	2.10	2.55	1.82	1.79
AC-6	2.20	3.10	0.98	1.02
AC-7	3.30	4.39	0.89	0.94
AC-8	3.70	5.00	0.75	0.94
AC-10	2.36	2.64	1.02	1.02
AC-S	2.14	3.67	0.89	0.86
AC-U-2	1.78	2.34	1.64	1.58

The combination of X-ray diffraction analysis in the study of the adsorption of water vapour with the determination of adsorption isotherms in the study of the formation of the porous structure of the AC in the carbonisation and activation stages makes it possible to demonstrate in some cases a bimodal size distribution of the micropores of some AC, associated with the presence of two independent structures.[78] Apart from the normal micropores, revealed by nitrogen vapour adsorption isotherms, some AC can contain ultramicropores revealed by water vapour adsorption isotherms.[78] This is due to the sensitivity of the adsorption of water vapour at low relative pressures to the size of very small micropores. The water vapour adsorption isotherm on these AC has a typical 'wave-like' shape, whereas the nitrogen vapour adsorption isotherm at 77 K has the normal shape.[78,79]

Thus, it may be stated that the water vapour adsorption isotherms are more sensitive in a certain sense to the features of the porous structure than adsorption isotherms for other adsorbable substances; this allows one to identify fine details of CA structures. Later, Naono and Hakuman[80] arrived at the same conclusion while studying the porous structures of silica gels and also iron and titanium oxides.

In general, one may conclude that the differences between the mechanisms of the adsorption of nitrogen and water vapours on CA are manifested by different effects of the chemical state of the surface and the porous structure of the CA on the form of the nitrogen and water vapour adsorption isotherms. Therefore, experimental data concerning adsorption of nitrogen and water vapour complement each other and provide more comprehensive and detailed characteristics of the porous structure of the CA.

The data obtained by X-ray diffraction agree with the previously suggested schemes for the filling of the micropore volume with water. The similarity of the L_a and l_m values, on the one hand, and their comparison with the x values, on the other hand, imply (see Tables 7 and 8) that for the majority of AC the distances between the PAS are larger than the half-widths of the micropores, so that the filling of the micropore volume with water molecules involves the formation of bridge bonds between the PAS located on the opposite walls of micropores. Thus, the character of the filling of the pore volume with water depends on the ratio between the widths of slit-like pores and the surface concentration of the PAS, which is determined, in its turn, by the average size of the crystallites forming the porous structure of the activated carbons.

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Organic reactions on the surface of silicon dioxide: synthetic applications

V A Basiuk

Contents

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Abstract. The literature data on the specific features of organic reactions in the presence of silicon dioxide (predominantly in the unmodified form) and its use for synthetic purposes are analysed. Oxidation (including dry ozonisation), reduction, alkylation and acylation, halogenation, elimination, hydrolytic and dehydration reactions, intermolecular cycloaddition and other cyclisation reactions, three-membered ring opening reactions, and peroxide decomposition reactions, as well as certain photochemical reactions are considered. In the processes investigated, the surface of silicon dioxide can function as a catalyst, as a solid medium for the occurrence of reactions, and/or as a matrix influencing the stereospecificity. The bibliography includes 214 references.

I. Introduction

Silicon dioxide is one of the most important inorganic compounds used in catalytic organic synthesis. In industrial catalysis, it is employed in the vast majority of cases as a carrier for substances with more pronounced catalytic properties.[1] However, in contrast to industrial organic synthesis, in organic synthesis as a whole the role of silicon dioxide is by no means restricted to its use as a simple more or less inert carrier. Like other generally known inorganic oxides (for example, Al_2O_3), it can be used not only in industrial processes such as hydrocarbon cracking but also in many heterogeneous reactions at the laboratory scale. Such reactions frequently take place under mild conditions (< 100 °C) and their characteristic features are more selective transformations (chemo-, regio-, and stereoselective) and simplified (compared with homogeneous analogues) methods for the isolation of the final products.[2] Many specialists in the field of laboratory fine organic synthesis are known to prefer commercially available silicon dioxide (usually silica gel) to catalytic systems with a platinum metal deposited on the oxide.

Many publications describe comparative studies on series of inorganic oxides in order to find optimum conditions for reactions and the optimum yield of their products. In some cases, the composition of the oxide may not affect the process or may affect it insignificantly, i.e. the oxides (for example, silicon and aluminium oxides, pure or mixed) are 'mutually replaceable'. Here it is appropriate to refer to certain studies involving the use of aluminium oxide (pure or with deposited reagents),[3-16] silicon–aluminium oxides,[17] zeolites,[18-23] and clays[24,25] in fine organic synthesis. A number of reviews[26-33] deal with processes with participation of various oxides. However, none of them presents complete information either about the employment of SiO_2 or about other oxides (for example, in the latest review[33] devoted to silicon and aluminium oxides, only about 50 publications were covered); furthermore, the data in the majority of these studies have become obsolete.

Bearing in mind the foregoing considerations, it appears entirely justified and timely to analyse in greater detail the role of silicon dioxide in fine organic synthesis. Attention is concentrated here on reactions involving the use of unmodified commercially available silicon dioxide (as a rule silica gel), in which its surface actually exhibits a catalytic effect (or other useful properties). Examples of the employment of SiO_2 as a carrier for any other catalyst (see, for example, Refs 34–39) are not considered in detail. However, sometimes it is extremely difficult to classify silica gel as a catalyst or as an inert carrier. Furthermore, in the literature considered certain terminological inaccuracies are encountered. In particular, it has been reported[40] that iron(III) chloride deposited on silica gel is an effective 'reagent' for the rapid and selective dehydration of alcohols and also for rearrangements of the pinacol and acyloin types. The use of the term 'reagent' is apparently illegitimate because a typical case of catalysis is considered. A still more striking example of a nonrigorous terminology is provided by the title of the book[41] *Catalysis of Organic Reactions by Supported Inorganic Reagents*. Nevertheless, these terms have become established and continue to be used, sometimes admittedly with the stipulation that the expression 'supported reagent' is understood both as a reagent, i.e. a stoichiometric agent, and as a catalyst.[42]

The classification of organic reactions used below (like virtually any classification) involves an arbitrary feature, reflecting synthetic aspects which are discussed in the literature analysed. For example, although dry ozonisation reactions formally belong to oxidation processes, they have been segregated in an independent section because they are of great synthetic value and are based on an unusual experimental approach.

Finally, a characteristic feature of the vast majority of publications on this topic is a purely practical approach, in which the main task (although not the only one) is to obtain the maximum yields of the target products, and is in no way concerned with the elucidation of the mechanism of the catalytic (or any other) action of silicon dioxide in the reactions employed.

V A Basiuk Department of Radiation Chemistry and Radiochemistry, Instituto de Ciencias Nucleares, Universidad Nacional Autonoma de Mexico, Circuito Exterior C.U., A. Postal 70-543, 04510 Mexico, D.F., Mexico. Fax (525) 616 22 33.
e-mail: basiuk@roxanne,nuclecu.unam.mx

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Because of this, the present review is inevitably one-sided in a certain sense: whilst there are numerous examples of synthetic applications of organic reactions on the surface of silicon dioxide, it is at present impossible to make serious generalisations about the characteristic features of their occurrence. Thus the data presented in this review will be more useful to specialists in synthetic organic chemistry rather than those engaged in catalysis and in the chemistry of the surfaces of inorganic oxides.

II. Organic reactions carried out in the presence of silicon dioxide

1. Dry ozonisation

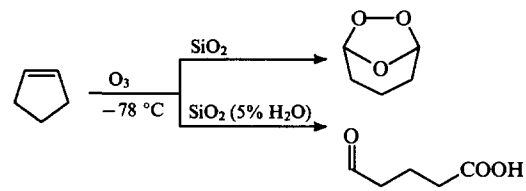
Dry ozonisation is one of the most important processes carried out in the presence of silicon dioxide and has great synthetic value because it makes it possible to introduce oxygen atoms into nonactivated C–H bonds.[43,44] Ozone is known to react slowly with saturated hydrocarbons at the C–H bonds, oxidising them to hydroxy- and keto-groups. Such insertion of oxygen takes place predominantly at tertiary carbon atoms with retention of the configuration of the substrate. However, the potential synthetic possibilities of these reactions are restricted by a number of factors, the most important of which is the low solubility of ozone in organic solvents and its high reactivity with respect to them.

These limitations can be removed by employing silica gel as the adsorbent and as the solid medium for the reaction.[45,46] The typical method proposed involves the preliminary deposition of the substrate (~1 mass%) on silica gel and the passage of a stream of ozone at −78 °C until saturation. A virtually quantitative conversion of the hydrocarbons (methyl- and dimethyl-cyclohexanes, decalins, adamantane, etc.) into the corresponding tertiary alcohols is achieved under these conditions with a virtually complete retention of the configuration of the *cis–trans* isomers and the absence of polyoxygenated products. Yet another important advantage of this method is the possibility of further stepwise oxidation of the product by repeating the ozonisation procedure. This has been demonstrated in relation to the introduction of a second hydroxy-group into monohydroxylated products (or their acyl derivatives) or in their oxidation to ketones.

According to the data of Proksch and de Meijere,[47–49] in the dry ozonisation of substituted cyclopropanes the attack by ozone is directed predominantly to the C–H groups in the α-position in the three-membered ring. This made it possible to develop a new approach to the α-functionalisation of the hydrocarbons indicated. The strained bicycloalkanes, containing a cyclopropane fragment, behaved differently under these conditions.[50] For example, the ozonisation of bicyclo[2.1.0]-pentane results in the formation of a 2 : 5 mixture of cyclopropylacetic acid and succinic dialdehyde. Comparison of the behaviour of aliphatic hydrocarbons and their cyclic analogues, led Tal et al.[51] to the conclusion that the degradation of the C–C bonds in the first case is more appreciable and the oxidative abstraction of alkyl groups results in the yields of the tertiary alcohols being lower and those of the ketones being higher.

The dry ozonisation of mono-, di-, and tri-alkyl-substituted alkenes leads to the formation of a mixture of ozonides (or polymeric peroxides) and carbonyl compounds.[52] Phenylethyl-alkenes afford almost exclusively aromatic aldehydes and ketones under these conditions, while alkynes give rise to a mixture of carbonyl and carboxy-compounds.

It has been shown in relative to the dry ozonisation of a series of alkenes adsorbed on silica gel[53] that the composition of the reaction products depends greatly on the presence of water in the system. In particular, the oxidation of cyclopentene on silica gel dehydrated beforehand affords the normal monomeric ozonide, which can be isolated in 80% yield whereas after the addition of 5% of water oxidative cleavage of the double bond takes place with formation of 5-oxopentoic acid in approximately the same yield.



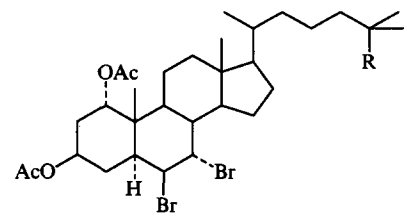
We may mention for comparison that, when the ozonisation is carried out in the usual way, the main product is a polymer.

Aromatic compounds without strong electron-accepting groups also undergo oxidative degradation under the conditions indicated.[54] For example, phenyl- and mesityl-cyclohexanes give rise to cyclohexanecarboxylic in 90% and 70% yields respectively (degrees of conversion of 95% and 90%), while tetralin affords adipic acid in 50% yield (degree of conversion 95%). The addition of 25% of water to the silica gel in the last case leads to an increase in the yield of adipic acid to 75%.

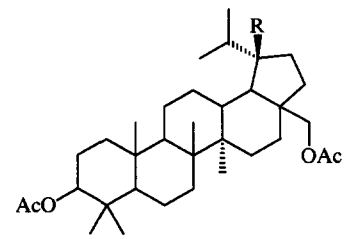
The possibility of the wide-scale employment of dry ozonisation on the silica gel surface for hydroxylation at tertiary aliphatic carbon atoms (which is particularly important in the chemistry of natural products) is limited by the reactivity to ozone of the double bond present in the molecule.

Since C–H bonds interact with ozone more slowly than C=C bonds, the latter must be protected by readily removable groups. It has been shown[55] that C–Br groups are less reactive to ozone than tertiary C–H groups, so that the bromination of the C=C bonds may be employed for protection.

Subsequently the dry ozonisation method was applied by the same investigators in the synthesis of the 1α,25-dihydroxy-derivative of vitamin D_3, for the oxidation of the dibromo-derivative **1** to the hydroxy-derivative **2** (yield 11%),[56] and also for the introduction of a functional group at the C(25) atom in other cholestane derivatives.[57] The dry ozonisation of 3β,28-diacetoxy-lupane **3** led to the 19-hydroxy-derivative **4**;[58] a mixture of 18β,19β-epoxyfriedelane **6** and the products of the oxidation of the CH_2 groups in the 19-position (compound **7**), the 15-position (compound **8**), and the 16-position (compound **9**) to the keto-groups (in 48%, 2%, 11%, and 11% yields respectively) was obtained from friedelane **5**.[59]

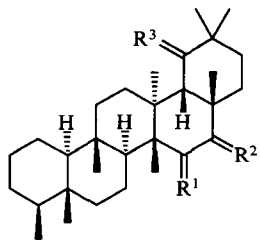


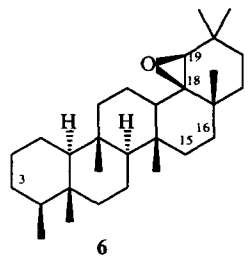
1, 2



3, 4

R = H (**1**, **3**), OH (**2**, **4**).



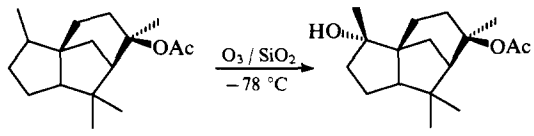


5, 7, 8, 9 6

5: $R^1 = R^2 = R^3 = H_2$; 7: $R^1 = R^2 = H_2$, $R^3 = O$;
8: $R^1 = O$, $R^2 = R^3 = H_2$; 9: $R^1 = R^3 = H_2$, $R^2 = O$.

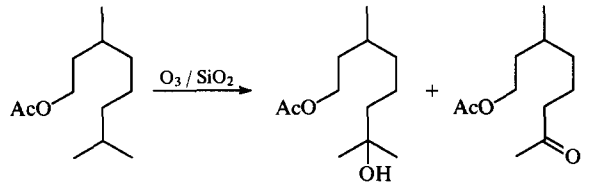
The dry ozonisation of friedelin (3-oxofriedelane) afforded analogous derivatives.[60]

This method has also been used to synthesise the hydroxy-derivative of cedrol acetate **10** and other sesquiterpenes.[61,62]



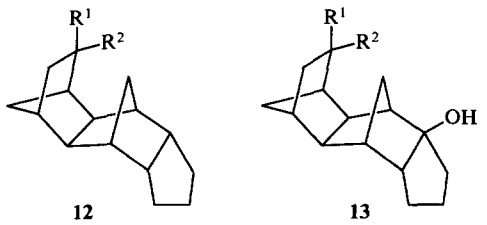
10 **11**

In contrast to ozonisation in solution, in the dry ozonisation of 3,7-dimethyloctyl acetate adsorbed in silica gel, the carboxy- or oxo-group is introduced predominantly in the 7-position, which is at a considerable distance from the functional group already present,[63,64] while oxidation in the 3-position is suppressed.

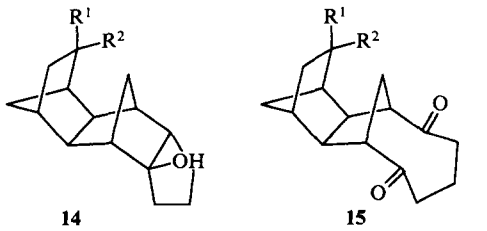


41%–69% 18%–31%

The maximum regioselectivity is attained when the initial compound is deposited on silica gel as a coating resembling a close-packed monomolecular layer. These results confirm the hypothesis that, by carrying out the reaction in adsorption layers, it is possible to increase the regioselectivity as a result of the mutual orienting effect of the substrate molecules. The ozonisation of cyclododecyl acetate under these conditions led to the formation of a mixture of its 5-, 6-, and 7-oxo-derivatives in 15%, 27%, 9% yields respectively.[65] The oxidation of the substituted cyclopentadiene trimers **12** led to the formation of the alcohols **13** and **14** and of the diketone **15**.



12 **13**



14 **15**

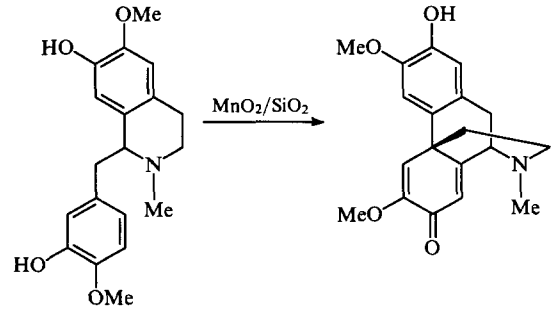
Substituents	(Yield %)		
	13	**14**	**15**
$R^1 = OAc$, $R^2 = H$	35	25	20
$R^1 + R^2 = O$	18	12	18

However, the authors[65] concluded that the proposed method of synthesis suffers from a series of disadvantages (difficulty of monitoring the course of the reactions, poor reproducibility, etc.) and subsequently modified it by introducing Freon 11 [trichlorofluoromethane (Ed. of Translation)] into the reaction medium and also by depositing the substrates on silica gel in the form of succinates to ensure their firmer fixation.[66] The advantages of the new approach were demonstrated by the authors in the ozonisation of the succinates of 6-methylheptan-2-ol, 3,7-dimethyloctanol, adamantan-2-ol, and two hydroxydecalins.

Among other reactions which take place effectively on treatment with ozone in the presence of silica gel, mention should be made of the oxidation of primary aliphatic amines to the corresponding nitro-compounds.[67] The synthesis lasts from several minutes to tens of minutes and the yields of the nitro-compounds reach 70%. The formation of more far-reaching oxidation products—ketones and carboxylic acids—is also possible, but their yields do not exceed 6%.

2. Other oxidation reactions

The use of solid inorganic oxidants in organic synthesis is limited by their insolubility in weakly polar media. This limitation can be overcome by the preliminary deposition of the oxidant on inert solid carriers, for which silica gel has been recommended among other substances. The first example of the use of SiO_2 in such reactions was the oxidation of a substituted benzyltetrahydroisoquinoline **16** by deposited manganese dioxide[68] with formation of isosalutaridine **17** (yield 4%).



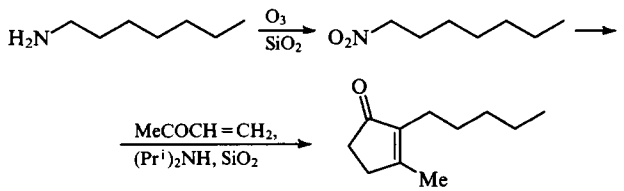
16 **17**

The oxidation of alcohols to aldehydes and ketones by potassium permanganate is a typical example.[69] The oxidation of benzyl alcohol to benzaldehyde,[70] of alkynes to diketones, of cyclic ketones to dicarboxylic acids, of acylated amines to acylimides, and of sulfides to sulfones,[71] as well as the conversion of ethers into lactones, of cyclic ketals into ketones, and of nitro-groups into carbonyl groups[72] on treatment with potassium and zinc permanganates have been investigated.

Chromic acid adsorbed on silica gel can also serve as a convenient reagent for the oxidation of alcohols to aldehydes and ketones in high yields (68%–90%).[73] Deposited potassium dichromate oxidises selectively benzyl alcohols and halo-derivatives to the corresponding ketones, the reactions being carried out in a neutral medium.[74] Chromic acid adsorbed on silica gel can be employed also for the synthesis of menthone from menthol (yield 96%). It has also been reported that deposited pyridinium chromate is suitable for the effective oxidation of a wide variety of secondary and primary alcohols containing labile acid groups.[75]

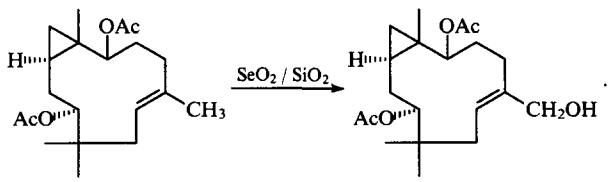
A mild method of synthesis of quinones from hydroquinones and catechols with the aid of deposited cerium(IV) and chromium(VI) salts has been described.[76] The homogeneous oxidation of 1-naphthol by cerium(IV) ammonium nitrate leads to 2,4- and 4,6-dinitro-derivatives.[77] However, the above reaction on silica gel leads to the formation of 2- and 4-nitro-1-naphthols in 42% and 38% yields respectively. Polynuclear arenes afford under these conditions the mononitro-derivatives and not quinones; for example, phenanthrene is converted into 2- and 3-nitrophenanthrenes (45% and 28%).

It is believed[78] that sodium methoxide deposited on silica gel is an ideal medium for the Nef reaction. Aldehydes and ketones may be obtained from primary and secondary nitro-compounds in yields exceeding 60%. The method has been used in the last stage of the synthesis of dihydrojasmone **18** from n-heptylamine and for the conversion of 1-(nitromethyl)cyclohexene into the corresponding aldehyde in 82% yield.[79]

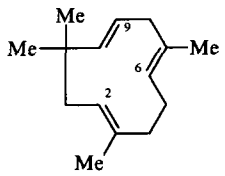


18

Among other inorganic oxidants deposited on silica gel and used in similar syntheses, mention should be made of sodium metaperiodate ($NaIO_4$, see, for example, the synthesis of quinones from hydroquinones[80]), potassium dimesoperiodate ($K_4I_2O_9$), and paraperiodic acid (H_5IO_6),[81] as well as selenium dioxide, which oxidises selectively allylmethyl groups to the corresponding primary alcohols and aldehydes.[82]

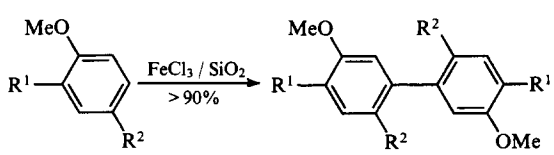


The oxidation of humulene (a sesquiterpene)



by perbenzoic acid and silver nitrate on silica gel[83] leads to the epoxidation of the double bonds in the 2,3-positions (the main product), the 6,7-positions, and the 9,10-positions; the $\Delta^{2,3},\Delta^{6,7}$-diepoxide is formed simultaneously. On the other hand, the dominant product in the homogeneous oxidation of this sesquiterpene is the $\Delta^{6,7}$-epoxide.

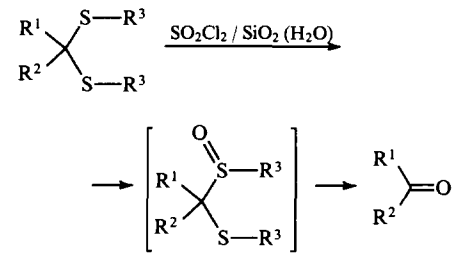
Iron(III) chloride deposited on silica gel can be used as the carrier for methoxy-substituted aromatic compounds.[84]



R^1, R^2 = Me, OMe.

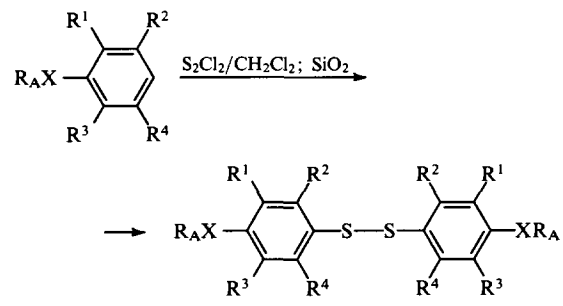
The rate of reaction increases after the complete removal of the solvent.

In a number of studies,[85-89] silica gel was regarded not as the reaction medium but as a catalyst of oxidation processes. Sulfuryl chloride is known to interact with methyl phenyl sulfide to form chloromethyl phenyl sulfide. It was found that, when reactions of this type are carried out in the presence of small amounts of moist silica gel, the corresponding sulfoxides are formed exclusively, while the chlorination of the alkyl groups is fully suppressed under these conditions.[85] The oxidation reaction takes place at room temperature in methylene dichloride; the yields of the sulfoxides exceed 80% (up to the quantitative yields for the unpurified products). When thioacetals are treated with sulfuryl chloride, the oxidative elimination of the thioacetal group takes place, the corresponding carbonyl derivatives being formed in almost quantitative yields at room temperature.[86,87]



These results[86,87] have been used to develop a convenient method of synthesis of sulfoxides and carbonyl compounds labelled with the ^{18}O isotope.[88] The source of the isotope was the water $H_2{}^{18}O$ deposited on silica gel.

The interaction of adsorbed reagents of the type RSCl, $RSCH_2Cl$, and S_2Cl_2 with aromatic compounds has been investigated.[89] For example, when durene is acted upon by chloromethyl phenyl sulfide, a ring-substitution product — phenylthiomethyldurene — is formed (28%). The reaction of S_2Cl_2 with mesitylene leads to a mixture of dimesityl sulfide (29%) and dimesityl disulfide (52%). In the analogous method of synthesis of aryl disulfides, patented by Japanese investigators,[90] the formation of sulfides is suppressed.

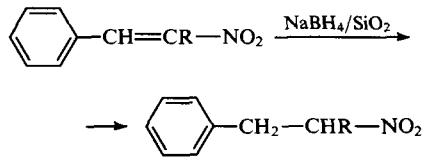


R^1, R^2, R^3, R^4 = H, Alk, AlkO; R_A = 4-BrC_6H_4; X = O, S.

For example, when X = O and $R^1 = R^2 = R^3 = R^4$ = H, the yield of the disulfide reaches 61% (25 °C, 20 h).

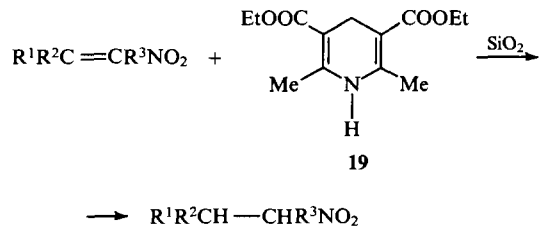
3. Reduction

The use of inorganic reagents for the reduction of organic compounds is not always possible, as in the case of solid oxidants, owing to their poor solubility in weakly polar solvents. One of the first reductants employed in the form deposited on silica gel was sodium tetrahydroborate.[91,92] Being commercially available, it proved to be extremely convenient for a wide variety of selective reactions involving the reduction of functional groups of one kind in the presence of others. However, a significant disadvantage of this reagent is its sensitivity to the presence of adsorbed water on silica gel — up to complete deactivation. An alternative stable and effective reductant proved to be tetrabutylammonium tetrahydroborate deposited on silica gel from solution in tetrahydrofuran.[93] The following reaction may serve as an example of selective reduction by tetrahydroborates on the surface of silica gel:[94]

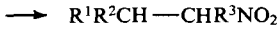


In contrast to the analogous homogeneous reaction, the formation of dimeric reduction products is almost fully suppressed under these conditions and high yields of nitroalkanes (92%–98%) are attained.

Another approach to the synthesis of nitroalkanes from nitroalkenes involves the interaction of the latter with the Hantzsch ester **19** in benzene in the presence of silica gel.[95]



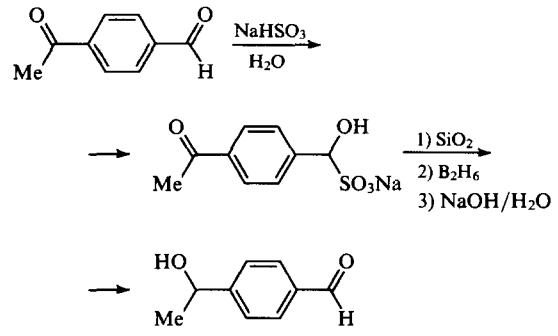
19



The reduction of aliphatic and aromatic nitroalkenes proceeds smoothly and is not accompanied by the reduction of the nitro-groups and the dimerisation of the olefinic groups. Other groups, such as the ester groups, are inert under the given conditions; only the C=C bonds conjugated with the nitro-group are reduced.

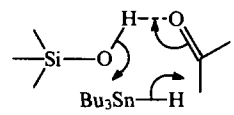
The deposition of the pyridine–borane complex on silica gel makes it possible to carry out the reduction of aldehydes and ketones under milder conditions.[96] For example, the heterogeneous reduction of benzaldehyde to benzyl alcohol in cyclohexane takes place at room temperature and is completed after 45 min with a yield in excess of 95%, whereas in the homogeneous system is takes place on refluxing in toluene or benzene and the yields are by no means always satisfactory.

The use of sodium bisulfite as the protecting agent for aldehyde groups and of silica gel as a solid matrix made it possible to carry out the selective reduction of 4-acetylbenzaldehyde.[97,98]



4-(1-Hydroxyethyl)benzaldehyde is formed with a selectivity of 70%–93% [4-acetylbenzyl alcohol and 1-(4-hydroxymethylphenyl)ethanol are minor products]. Positive results were also achieved when Al_2O_3 was used as the carrier. 4-Acetylbenzophenone was reduced in accordance with a similar scheme to 4-acetyl-α-phenylbenzyl alcohol with a selectivity of 80%.[99,100] (Carboxymethyl)trimethylammonium chloride hydrazide (the Girard reagent T) and lithium tri(*tert*-butoxy)hydroaluminate served as the protecting and reducing agents respectively.

The silica gel-catalysed reduction of aldehydes and ketones by tributyltin hydride is characterised by a high selectivity, but the yields of the corresponding alcohols vary from 69% to 94% under these conditions.[101] According to the authors,[101] the advantages of this method are simplicity, relatively mild conditions, and the absence of the need to neutralise the alkoxide salts, as well as the possibility of the selective reduction of aldehydes in the presence of ketones. One of the most probable mechanisms of the process involves the formation of a six-centre transition state:



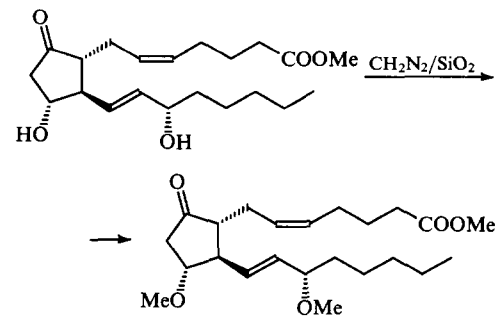
The cyano- and nitro-groups are not reduced by lithium tetrahydroaluminate on silica gel, in contrast to the reaction in the homogeneous system. This feature has been used[102] for the selective reduction of ketones and esters containing the above groups to the corresponding cyano- and nitro-alcohols, which were obtained in 54%–82% yields. Methyl *p*-nitrophenyl sulfoxide was reduced similarly to the nitrosulfide (yield 73%).

The use of lithium tetrahydroaluminate deposited on silica gel for the reduction of aldehydes, ketones, and carboxylic acid chlorides and esters in nonpolar solvents (hexane, benzene) has been considered.[103,104] For the compounds of the first three classes, the process is rapid at room temperature, whereas esters are more inert and their reduction requires the heating of the reaction mixture. Because of these differences in the reactivities, the selective reduction of ketoesters to hydroxyesters is possible (the yields in different syntheses vary from 62% to 100%).

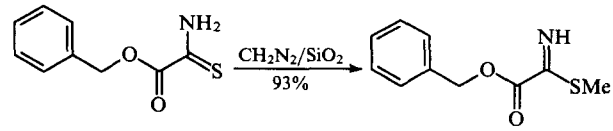
Silica gel treated beforehand with thionyl chloride has been used to reduce sulfoxides to sulfides.[105] The reaction occurred at room temperature for 10 min in CCl_4 or CH_2Cl_2.

4. Alkylation and acylation

In contrast to carboxylic acids, alcohols and phenols are difficult to methylate by diazomethane because of the low acidity of the OH groups. However, following adsorption on inorganic oxides, the acidity of these groups increases appreciably. Because of this, it has been possible to obtain ethers in quantitative yields from aliphatic alcohols and phenols adsorbed on silica gel by treatment of the latter with gaseous diazomethane.[106] The authors showed that, in the methylation of 1-decanol, Al_2O_3, a type NaY zeolite, and other similar carriers exhibit a comparatively weak catalytic effect. Polyhydric alcohols, including prostaglandins and carbohydrates, can also be used as the substrates.[107] For example, treatment of prostaglandins with a large excess of diazomethane makes it possible to obtain the corresponding diesters in quantitative yields.



The methylation of lactams and acyclic amides by diazomethane in the presence of silica gel also proceeds effectively.[108] The thioamide groups are methylated more readily than the amide groups, which may be used to carry out a selective reaction of the type



A simpler procedure has been used for the acetylation of phenols[109] and aliphatic (including secondary and tertiary) alcohols by ketene.[110] Apart from silica gel, aluminium, zinc, and magnesium oxides exhibited a high catalytic activity (the yields of the esters were 70%–91%).

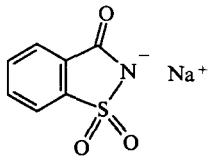
Adsorption on silica gel (and also on aluminium oxide) makes it possible to carry out selectively the monoalkylation of malonic ester anions by 1,5-dibromopentane in the presence of sodium methoxide.[111]

$$CH_2(COOMe)_2 + Br(CH_2)_5Br \xrightarrow{MeONa/SiO_2} Br(CH_2)_5CH(COOMe)_2$$

The reaction takes place at room temperature, but is fairly slow: the attainment of a satisfactory (28%–52%) yield of the product requires up to 13 days.

It has been shown[112] that silica gel is an effective catalyst for the alkylation of phenols by *tert*-butyl bromide. 2-*tert*-Butyl-, 2,6-di-*tert*-butyl-, and 2,4,6-tri-*tert*-butyl-phenols, which are difficult to obtain directly by the Friedel–Crafts reaction, can be synthesised readily by this procedure. $Et(Me_2)CBr$, *p*-$TolCH_2Cl$, $H_2C{=}CH-CHMeCl$, and $MeOCH_2Cl$ can also be used as the alkyl halides; thiophene, benzothiophene, furan, and 1-methylindole can serve as the aromatic substrates. The yields of the alkylation products vary in the range 6%–98% under these conditions.

The alkylation of saccharin



by benzyl, allyl, and hexadecyl bromides, benzyl chloride, and similar reagents has been carried out on silica gel (and also on aluminium oxide) in a microwave oven.[113] Depending on the nature of the alkylating agent, the reaction terminated after 1–10 min and the yields were 21%–91%.

The *N*-alkylation of pyrazoles by alcohols or ethers proceeds effectively on silicon, aluminium, titanium, and zirconium oxides at 200–500 °C.[114] For example, the interaction of 3,5-diphenylpyrazole and methanol results in the formation of 1-methyl-3,5-diphenylpyrazole in 96% yield.

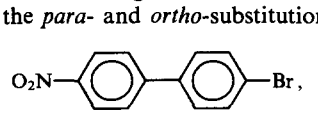
5. Halogenation

According to the results of Stoldt and Turk,[115] when cyclohexene is brominated on silica gel in the absence of solvents, the formation of only *trans*-1,2-dibromocyclohexane is observed. Diethyl fumarate, in which the olefinic function is deactivated, is also effectively brominated under these conditions, the reaction being fully stereospecific and leading exclusively to the *trans*-adduct—*meso*-diethyl 2,3-dibromosuccinate.

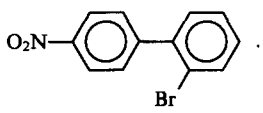
The chlorination of adamantane and other hydrocarbons adsorbed on silica gel by molecular chlorine and sulfuryl chloride has also been studied.[116] In all cases, products involving bridgehead chlorination were obtained in high yields.[116]

Under 'dry' conditions, the process takes place more effectively and selectively than, for example, in the presence of dichloromethane or under homogeneous conditions.

The bromination of biphenyl, 4-bromobiphenyl, and 4-nitrobiphenyl deposited on silica gel by gaseous bromine has been investigated.[117] The ratios of the yields of the products of the *para*- and *ortho*-substitution, for example



and



proved close to those obtained for the reaction carried out in a homogeneous system (~4:1). A control experiment involving biphenyl showed that the reaction does not occur in CCl_4 in the absence of silica gel.

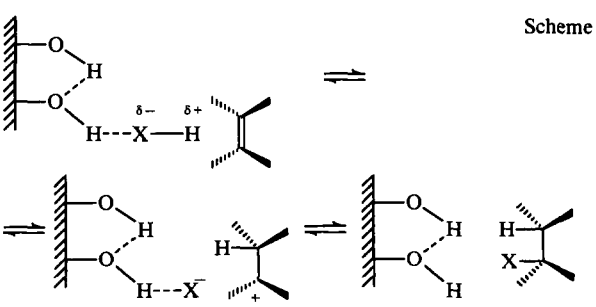
When alkylbenzenes are treated with sulfuryl chloride in the presence of silica gel, preferential substitution in the aromatic ring is observed (whereas in the absence of the catalyst, the chlorination takes place either in the alkyl substituents or does not occur at all).[118] Similar results have been obtained by Yaroslavksy.[119]

A series of studies[120–123] have been devoted to the catalytic introduction of halogen atoms into an aromatic ring. In particular, it has been established[120] that the chlorination of toluene by dichloramine T in the presence of silica gel takes place under very mild conditions (CCl_4, 25 °C) with formation of a mixture of the *o*- and *p*-isomers (65% and 35% respectively). Only fairly acid forms of silicon dioxide, for which the pH of a 10% aqueous suspension did not exceed 5, exhibited catalytic properties in these reactions. The activity increased after preliminary dehydration.[121]

The chlorination of naphthalene by *tert*-butyl hypochlorite (CCl_4, room temperature) leads preferentially to 1-chloronaphthalene (93%), while the chlorination of alkylbenzenes and anisole affords a mixture of the *o*- and *p*-isomers in proportions typical for the usual homogeneous methods of synthesis. Depending on the amount of the brominating agent, the bromination of scatole by *N*-bromosuccinimide (CH_2Cl_2, 30 min) leads to the formation of 2-bromo- or 2,6-dibromoscatole (the substitution in the ring of 2-methyl- and 3-cyanomethylindoles takes place in the same way); the analogous reaction with benzimidazole affords 2-bromo- or 2,5-dibromo-benzimidazole, while the reaction with 2-methylbenzimidazole gives rise to only the 5-bromo-substituted product.[122] The same method has been used to brominate carbazole, where it is possible to introduce up to four bromine atoms into the ring.[123] It is of interest that in the case of *N*-ethylcarbazole the process stops at the stage involving the formation of the tribromo-derivative.

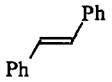
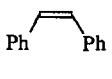
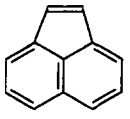
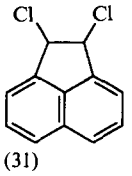
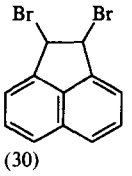
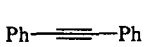
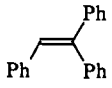
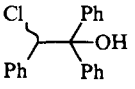
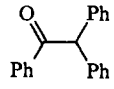
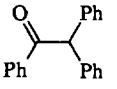
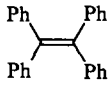
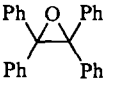
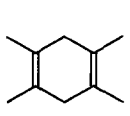
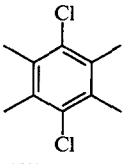
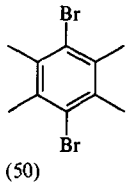
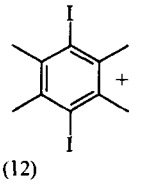
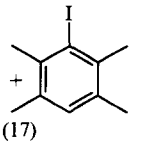
The addition of the hydrogen halides (HCl, HBr, and HI) to alkenes (cycloheptene, oct-1-ene, pinene, etc.), catalysed by silicon and aluminium oxides, has been investigated in detail.[124,125] The best medium for the reactions proved to be methylene dichloride and diethyl ether, the catalysts exhibiting the maximum activity after preliminary exposure to air at 120 °C until the attainment of equilibrium with atmospheric moisture, promoting more complete hydroxylation of the surface. Bearing in mind that the addition reaction results as a rule in the formation of products with the *cis*-configuration, the authors[124,125] proposed the most probable mechanism of the catalytic reaction, according to which the adsorption of the molecules of the hydrogen halide on the acid hydroxy-groups of the surface results in the polarisation of the X–H bond and in the protonation of the alkene with subsequent rapid transfer of the anion X^- (Scheme 1).

Scheme 1



An interesting example of solid-phase tribochemical reactions is the interaction of aryl-substituted alkenes and alkynes with iodosobenzene described by Sohmiya et al.[126] The silica gel with the adsorbed hydrogen halide (HCl, HBr, or HI), the alkene (or alkyne), and iodosobenzene were placed in a mortar and ground with a pestle at room temperature for 5 min. The substrates employed, the products and their yields, are presented in Table 1.

Table 1. The products of the tribochemical reactions of solid alkenes and diphenylethyne with adsorbed hydrogen halides and iodosobenzene (according to the data of Sohmiya et al.[126])

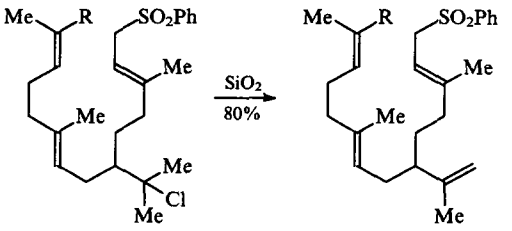
Substrate	Products [yield (%)]		
	HCl	HBr	HI
	 (65)	 (39)	 (>5)
	 (58)	 (58)	[a]
	 (31)	 (30)	[a]
	 (74)	 (51)	 (<6)
	 (66)	 (47)	 (58)
	 (82)	[a]	[a]
	 (60)	 (50)	 (12)
			 (17)

[a] The adducts were absent or their composition had not been established.

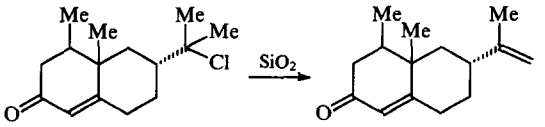
Attempts to carry out the reaction without the mechanochemical treatment were unsuccessful. Having established (for the reaction of *trans*-1,2-diphenyl- and 1,2,3,4-tetraphenylethene with adsorbed HCl) that the presence (absence) of water on the surface hardly affects the halogenation reaction, the authors[126] concluded that the reaction medium is provided directly by the silica gel surface.

6. Elimination

When the chloro-derivatives **20** and **22** are kept in the presence of silica gel, selective dehydrochlorination to give the isopropenyl derivatives **21** and **23** respectively takes place.[127,128]



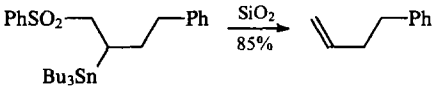
20 **21**



22 **23**

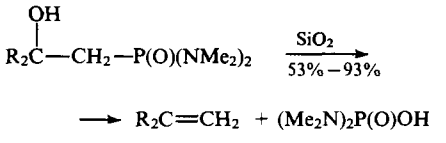
When the elimination reaction is carried out using other reagents, products containing admixtures of the isopropylidene isomers are formed.

The use of silica gel for the removal of trialkylstannyl groups in the last stage of the synthesis of alkenes by the desulfonylation of α,β-unsaturated sulfones has been reported.[129-132]



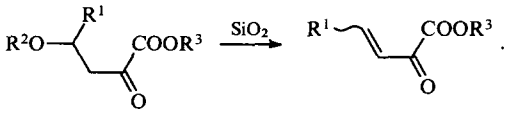
The β-elimination reaction,[129] the vinyl cyclisation of enynes,[130,131] and the methylenation of ketones[132] may serve as examples.

The phosphonamide approach to the synthesis of alkenes[133] includes as the final stage the elimination of phosphoric acid bisdimethylamide from the corresponding amides of β-hydroxyalkylphosphonic acids on refluxing their benzene or toluene solutions in the presence of silica gel.



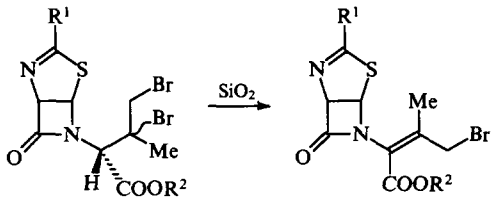
According to the authors,[133] this method is general.

A procedure for the synthesis of β,γ-unsaturated α-ketoesters in accordance with the following scheme has been patented:[134]



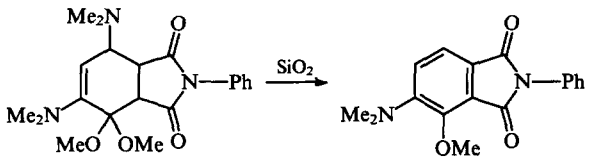
For example, when R^1 = Ph, R^2 = Me, and R^3 = Et, refluxing in benzene for 1 h leads to the corresponding α-ketoester in 92% yield.

The dehydrobromination of the intermediates in the synthesis of derivatives of antibiotics of the cephem group by chromatography on a silica gel column has been reported.[135]

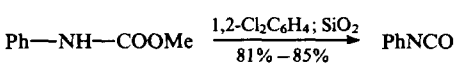


R^1 = $PhOCH_2$, Ph, Bu^t, p-$BrC_6H_4OCH_2$;
R^2 = Me, Ph_2CH.

The silica gel-catalysed elimination of Me_2N and MeO groups described by Gompper and Sobotta[136] required more severe conditions — heating to a temperature >110 °C (the yield was quantitative).

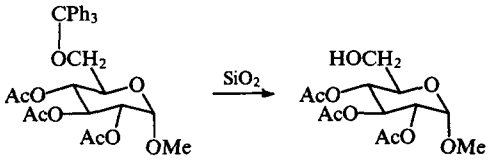


Finally, mention should be made of the synthesis of phenyl isocyanate by the thermal decomposition of methyl *N*-phenylcarbamate (elimination of MeOH).[137]



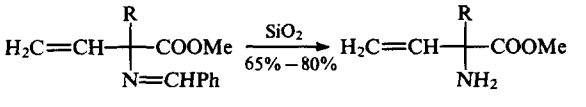
7. Hydrolysis and dehydration

The removal of the trityl protecting group in the synthesis of carbohydrates, reported by Lehrfeld,[138] is virtually the first example of the use of silica gel as a catalyst for hydrolytic processes.

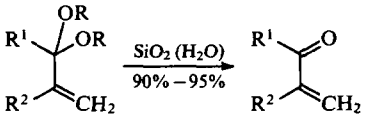


The hydrolysis was carried out by keeping a benzene solution of the initial compound on the chromatographic column for 16 h at room temperature. The yield of the purified detritylated product was 81%.

The hydrolysis of Schiff bases by chromatography on silica gel has been used in the synthesis of α-vinyl-substituted derivatives of valine, serine, histidine, tyrosine, and other aminoacids.[139]

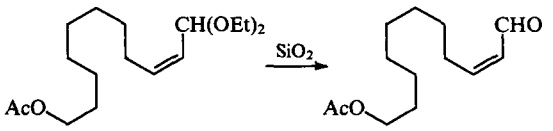


Moist silica gel has been used in the synthesis of alkenes for the removal of the ketal protecting group from the products of the reactions of α-ketoketals with Wittig reagents.[140]



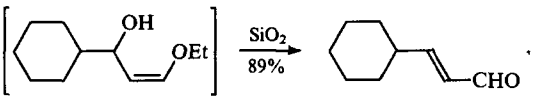
α-Cyclopropylideneketones can be obtained by the same procedure.[141]

The hydrolysis of the diethyl acetals of (*Z*)-α,β-unsaturated aldehydes in the presence of moist silica gel as the catalyst (two days at 23 °C) affords the corresponding (*Z*)-unsaturated aldehydes[142] in 47%–98% yields.

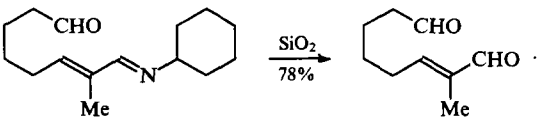


The product usually contains an admixture of the (*E*)-isomer (4%–14%) formed as a result of isomerisation. Other examples of the silica gel-catalysed hydrolysis of acetals have also been described.[143]

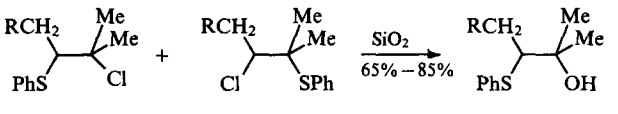
α,β-Unsaturated aldehydes are likewise formed when enol ethers — labile products of the reactions of aldehydes and ketones with (*Z*)-2-ethoxyvinyllithium — are chromatographed on silica gel,[144,145] i.e.



and also when the corresponding aldimines are passed through moist silica gel:[146]

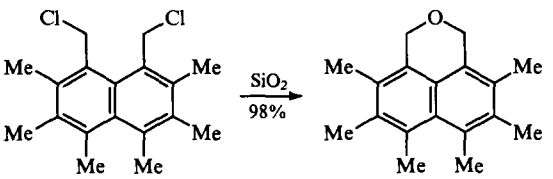


The addition of benzenesulfenyl chloride to isoprenoid compounds at the terminal isopropylidene groups can be used, for example, for the hydroxylation of these substrates. The mixtures of the regioisomers **24** and **25**, formed as intermediates, do not require separation when they are converted into the β-hydroxysulfide **26** in the presence of silica gel.[147]



24 **25** **26**

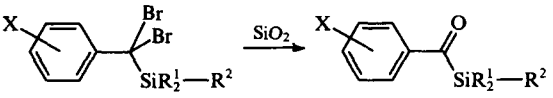
The chromatography of 1,8-di(chloromethyl)-2,3,4,5,6,7-hexamethylnaphthalene **27** on silica gel affords the ether **28** in an almost quantitative yield.[148]



27 **28**

The diether is formed similarly in 84% yield from 1,4,5,8-tetra(chloromethyl)-2,3,6,7-tetramethylnaphthalene.

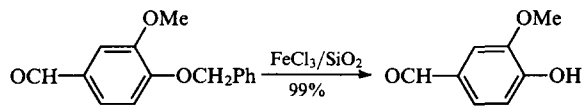
Acylsilanes may be synthesised in high yields by moderate heating (50 °C) of substituted α,α-dibromobenzylsilanes with silica gel in the absence of solvents.[149]



X = H, p-Cl, m-Cl; R^1, R^2 = Me, Ph, m-ClC_6H_4.

The authors[149] noted the importance of the degree of hydration of the silica gel; for example, the reaction was appreciably retarded when the silica gel had been dehydrated beforehand for 48 h at 200 °C. When aluminium oxide was employed, the rate of reaction was also comparatively low.

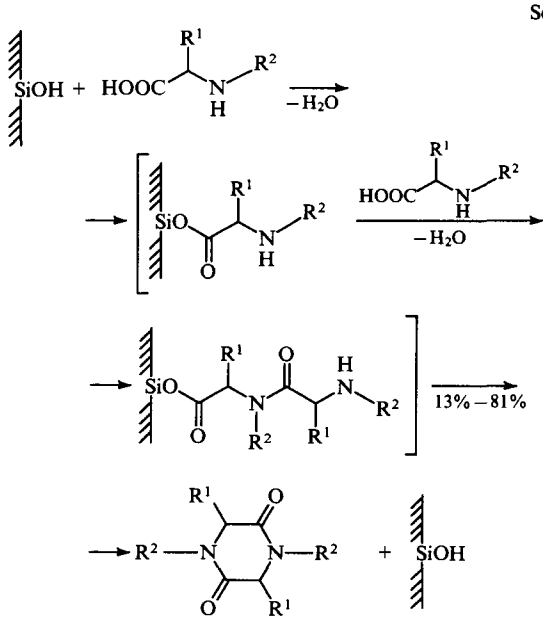
Iron(III) colloids deposited on silica gel can likewise catalyse certain hydrolytic reactions.[84]



The conversion of acetic acid into the amide by treatment with gaseous n-butylamine (200 °C in a stream of nitrogen) may be quoted as the simplest example of SiO_2-catalysed nucleophilic substitution,[150] but the yield of the amide in the presence of silica gel (87%) is lower than in the case where zirconium, titanium, and tin oxides are employed.

It has been established that carboxylic γ-, δ-, and ε-aminoacids are readily cyclodehydrated to the corresponding lactams on refluxing in toluene in the presence of silica gel or aluminium oxide.[151] In most cases their yields exceed 70%, quantitative yields being attained sometimes. For the optically active aminoacids (glutamic acid, lysine, and ornithine), appreciable racemisation is observed. The 'gas–solid phase' synthesis of 2,5-dioxopiperazines from aminoacids is similar in its essential chemical features.[153,152] It has been shown that aliphatic bifunctional aminoacids and proline undergo cyclodimerisation on sublimation in the presence of SiO_2 (170–220 °C) to cyclic dipeptides in 13%–81% yields (silochrome—a silica gel analogue obtained by the hydrothermal treatment of pyrogenic silicon dioxide—was used in the above studies). It has been suggested that the process mechanism involves the condensation of the carboxy-groups of the substrate and the surface silanol groups; the ester-type activated intermediate arising under these conditions is capable of condensing with the next aminoacid molecule attacking from the gas phase. The resulting dipeptide, chemically bound to the silicon dioxide, is readily split off from the surface, affording the corresponding symmetrical 2,5-diketopiperazine (Scheme 2).

Scheme 2

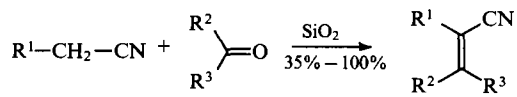


R^1 = H, Me, Bu^s, Pr^i; R^2 = H;
R^1, R^2 = $-(CH_2)_3-$

It is of interest that, despite the fairly severe thermal conditions, appreciable racemisation of the aminoacid residues is not observed. On the grounds that the intermediates are surface-bound dipeptides (see Scheme 2), the authors[154] suggested that simple linear dipeptides can also be used as the initial reactants. Such modification of the 'gas–solid phase' method makes it possible to synthesise both symmetrical and asymmetric diketopeperazines in 40%–82% yields.

The synthesis of lactones with different ring sizes by the intramolecular cyclisation of carboxylic hydroxyacids has been patented.[155]

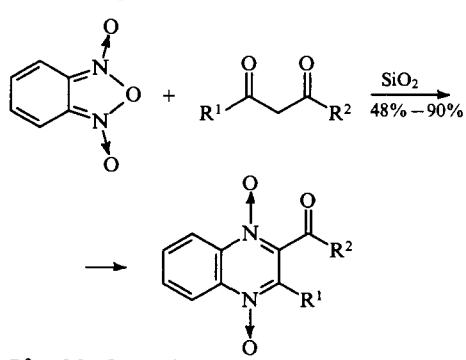
The reactions of carbonyl compounds with substrates containing an activated methylene unit (the Knoevenagel condensation) is accelerated in the presence of silica gel.[156]



R^1 = NC, O_2N, PhCO, *N*-Ac-L-Phe, *N*-Ac-L-Leu-L-Phe, *N*-Ac-L-Leu-D-Phe;
R^2 = H, Me; R^3 = Me, $HOCH_2$, HO(Me)CH, Ph, 4-$MeOC_6H_4$, 4-$Me_2NC_6H_4$, 4-$O_2NC_6H_4$, 2-$HOOCC_6H_4$, 3-MeO(4-HO)C_6H_3;
R^2, R^3 = $-(CH_2)_4-$, $-(CH_2)_5-$.

The interaction takes place when the reactants and the catalyst are mixed in methylene dichloride and lasts from 13 to 72 h. A necessary condition for the success of the synthesis is the presence of two strongly electron-accepting substituents in the methylene component.

The reaction of benzofuroxan with 1,3-dicarbonyl compounds on the silica gel surface leads to the formation of 2,3-disubstituted quinoxaline 1,4-bisoxides.[157]

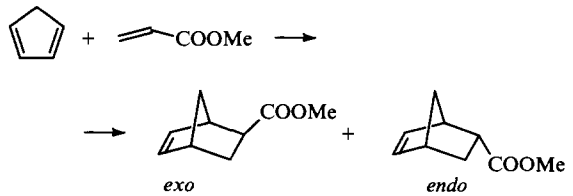


R^1, R^2 = Me, OMe, Ph, etc.

The reaction takes place in the absence of solvents for 1–2 weeks at room temperature. Its effectiveness depends on the acidity of the silica gel: more acid forms have better catalytic properties. The use of aluminium oxide gives rise to less satisfactory results, in particular, the formation of side products is observed.

8. Intermolecular cycloaddition reactions

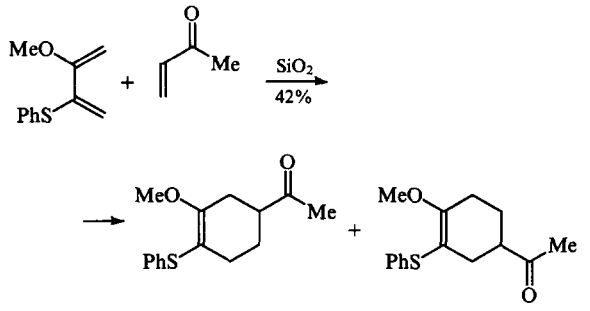
The Diels–Alder addition of the type



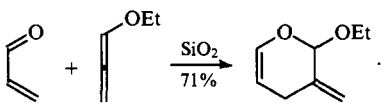
in the absence of a catalyst leads to a ~1 : 3 mixture of the *exo*- and *endo*-adducts. The adsorption of the dienophile on the SiO_2 surface makes it possible to alter their relative yields (10.5% and 87.5%); even better results are achieved when aluminium oxide is employed (2.9% and 93.7%).[158]

The Diels–Alder reaction between 1-acetoxybuta-1,3-diene and tetrafluoro-*p*-benzoquinone with formation of 5-acetoxy-2,3,4a,8a-tetrafluoro-4a,5,8,8a-tetrahydro-1,4-naphthoquinone on a silica gel column takes place at room temperature and is completed after 60 h,[159] whereas in the absence of a catalyst refluxing of the reactants in benzene is needed. The addition of *p*-benzoquinone as the dienophile takes place similarly, but the adduct eliminates acetic acid and the resulting dihydro-intermediate is dehydrogenated by the benzoquinone to 1,4-naphthoquinone (yield 87%).

The adsorption of a mixture of 2-methoxy-3-phenylthiobuta-1,3-diene and methyl vinyl ketone on the silica gel surface without a solvent and subsequent maintenance of the reactants for 24 h at room temperature lead to the formation of a mixture of adducts.[160]

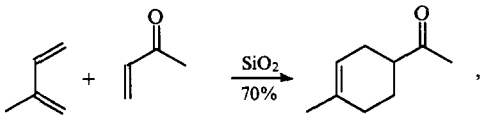


The Diels–Alder cycloaddition of 1-ethoxypropa-1,2-diene to α,β-unsaturated carbonyl compounds proceeds especially effectively on the silica gel surface in the absence of solvents.[161] High yields are attained under relatively mild conditions (50–70 °C, 1–15 h). The following reaction may be quoted as an example:



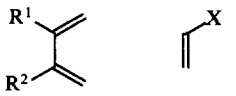
Since the dihydropyrans formed tend to polymerise on the acid centres of the surface of silicon dioxide, the latter was deactivated beforehand by treatment with triethylamine.

A similar approach in carrying out the [4+2]-cycloaddition reaction has been used by Vesselovskii and coworkers.[162,163] Depending on the nature of the diene component (butadienes, cyclopentadiene, furan, etc.) and the dienophile (methyl vinyl ketone, acrolein, methacrolein, crotonaldehyde, and ethyl vinyl ether), the synthesis was carried out at temperatures from −20 to 100 °C and lasted 0.5–14 h. For example, the cycloaddition



took place at room temperature. In an attempt to account for the mechanism of the promotion of the reaction, the authors postulated that adsorption may facilitate the formation (and possibly the stabilisation) of the prereaction complexes between the functional groups firmly fixed on the active surface centres; under these conditions, the absence of a solvent is a favourable factor.

Vesselovskii et al.[164] used chromatographic silica gel, dried beforehand at 200 °C, as the catalyst of the Diels–Alder reactions and other [4+2]-cycloaddition reactions involving substituted butadienes **29**, cyclopentadiene, and cyclohexadiene, as well as the dienophiles **30**.

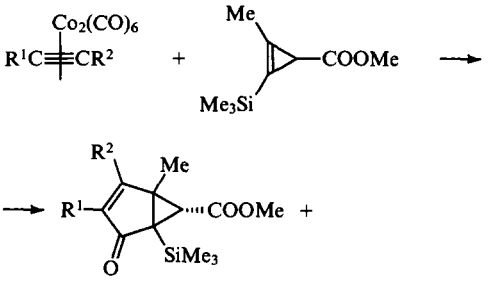


29 **30**

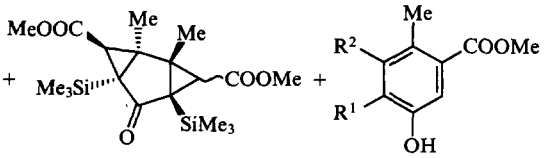
$R^1 = R^2 = H$, Me;
$R^1 = H$, R^2 = Me, $Me_2C{=}CH(CH_2)_2$;
X = CHO, COMe, COOMe.

The adducts were formed stereoselectively with yields up to 92%.

The [2+2+1]-cycloaddition reactions involving cyclopropenes and ethynecobalt hexacarbonyl complexes, described by Kireev et al.,[165] lead to a mixture of three products.



31

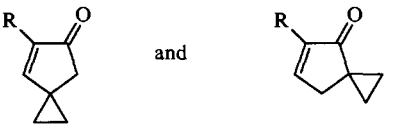


32

$R^1 = R^2 = H$, Me;
R^1 = Ph, R^2 = H.

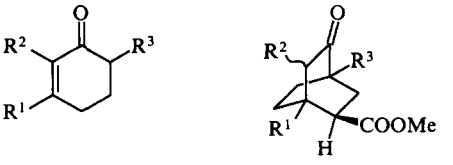
When silica gel was used as the catalyst of this reaction, the product **31** was found to predominate, whereas in the presence of the NaX zeolite mainly compound **32** was formed.

The silicon dioxide-catalysed Khand–Pauson addition[166] of methylenecyclopropane to ethyne and its methyl-, phenyl-, and cyclopropyl-substituted derivatives leads to a mixture of two products, *viz.*



in proportions of (4.4.–6):1. The addition of methylenecyclobutane proceeds similarly.[167]

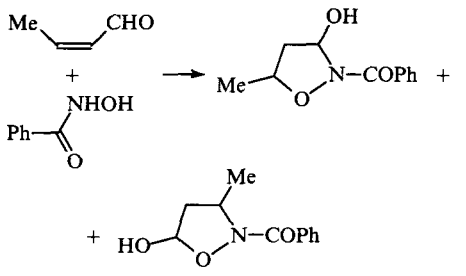
The regio- and stereo-selective Michael addition of methyl acrylate to the cyclohexenone derivatives **33** with subsequent silylation in situ and cyclocondensation in the presence of silica gel at room temperature results in the formation of the bicyclooctanone derivatives **34**.[168,169]



33 **34**

R^1 = H, Me, OMe, Bu, $CH{=}CH_2$;
R^2, R^3 = H, Me.

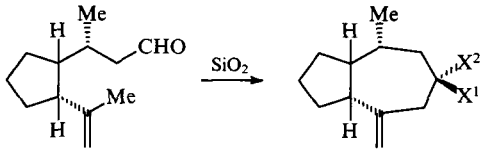
The reaction of phenylhydroxamic acid with crotonaldehyde in methanol leads to a mixture of *N*-substituted 3- and 5-hydroxyisoxazolidines.



The dominant product is the first isomer. The rate of this reaction increases significantly when it is carried out on an adsorbent without a solvent.[170] Best results were obtained when silica gel was employed: the reaction was completed in 30–40 min with the exclusive formation of the 3-hydroxy-derivative (yield 80%–90%).

9. Other cyclisation reactions

Silica gel may serve as an effective catalyst of the cyclisation of unsaturated carbonyl compounds. The cyclisation at atmospheric pressure was investigated in early studies.[171–173] For example, chromatography on a silica gel column proved to be the simplest procedure for the cyclisation of the aldehyde **35** and its stereoisomers to the epimeric bicyclic alcohols **36**,[173] whereas the analogous reaction in a homogeneous system required the treatment of the aldehydes with tin(IV) chloride in benzene.

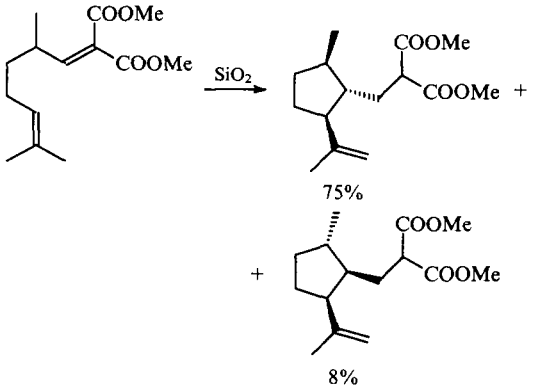


35 **36**

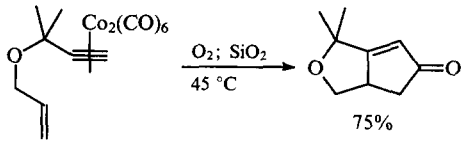
X^1 = H, X^2 = OH (86%);
X^1 = OH, X^2 = H (2%).

It has been shown in the syntheses of a series of five- and six-membered carbocycles that the effectiveness of the process increases significantly when it is carried out under a pressure of 15 kbar (solutions in methylene dichloride, 1.5–53 h, 25–60 °C). In individual instances, a fairly high stereoselectivity was noted.

The thermolysis of the adsorbed substrate in a stream of

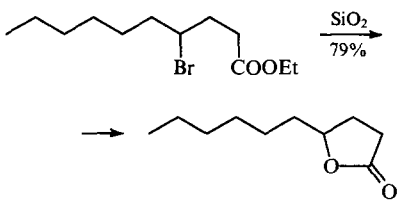


oxygen has been proposed as a general method for the promotion of the Khand–Pauson cyclisation of dicobalt hexacarbonyl complexes of allyl propargyl ethers to derivatives of 3-oxabicyclo[3.3.0]oct-5-en-7-one.[175–177]



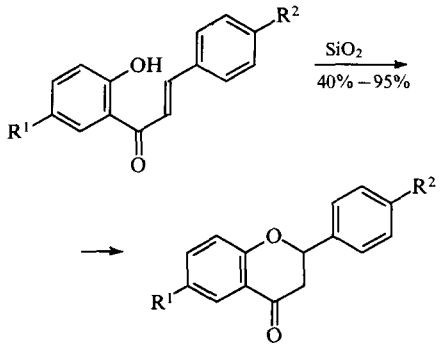
The reactions were completed in 30 min and the yields of the products were 46%–92%. Apart from silica gel, aluminium oxide may be used with different degrees of success and it has therefore been concluded[175–177] that the promoting effect should not be attributed to the specific surface properties of the oxides. The adsorption process itself probably influences the conformation of the initial compound: the attraction of the ether groups to the polar surface centres and the simultaneous repulsion from them of the hydrophobic fragments promote the mutual approach of the latter and a lowering of the entropy barrier.

The lactonisation of γ-haloethers on refluxing them in xylene for 3–15 h has been described (yields greater than 60%).[178]



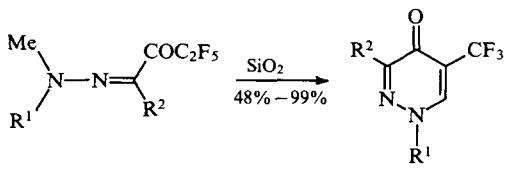
Bis-γ-butyrolactones can also be obtained by this procedure.

The intramolecular cyclisation of 2′-hydroxychalcones in the presence of silica gel (and also of ethylenediamine or the hydrochloride of hydroxylamine) affords flavones.[179]



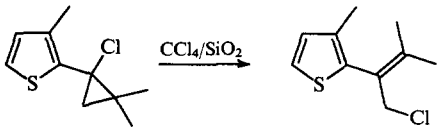
R^1 = H, Me, Cl; R^2 = H, MeO.

The cyclisation of 1,1,1,2,2-pentafluoroalkane-3,4-dione 4-dialkylhydrazones on silica gel (70–90 °C, 6–48 h) is a convenient method of synthesis for 5-(trifluoromethyl)-4-pyridazinones.[180]

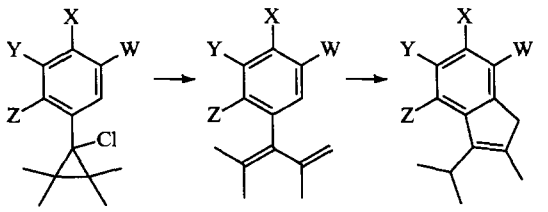


10. The opening of three-membered rings

The opening of the ring in chlorocyclopropanes in the presence of silicon dioxide, leading to the formation of dienes or allyl halides, has been investigated.[181–183]



On the other hand, in the case of 1-aryl-1-chloro-2-methylcyclopropanes **37**, silica gel in carbon tetrachloride catalyses the tandem opening of the three-membered ring accompanied by cyclisation to the indenes **39**.[184]

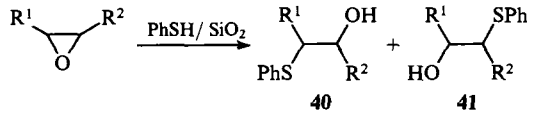


37 **38** **39**

W, X, Y, Z = H, OMe, etc.

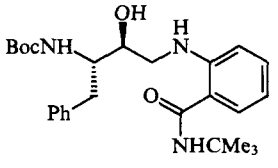
The reaction proceeds at room temperature for 18 h (yields 63%–100%) and in some cases stops at the stage involving the formation of the intermediate dienes **38**, which may be isolated in 33%–90% yields.

The opening of epoxide rings on treatment with thiophenol in the presence of silica gel leads to the α- and β-adducts **40** and **41**.[185–187] In the case of α,β-epoxysilanes, the reaction takes place regioselectively and the isomers **40** are formed in 72%–98% yields.



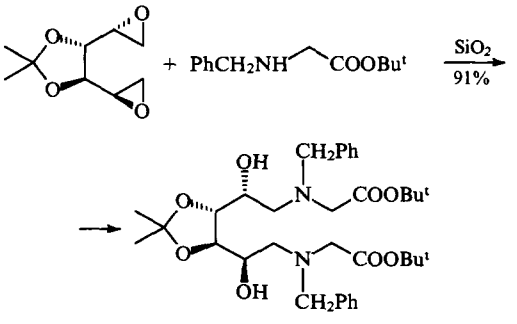
40 **41**

The formation of intermediates of the type



via the silica gel catalysed aminolysis of epoxides by anthranilic acid derivatives was the key stage in the synthesis of new inhibitors of HIV proteases.[188]

The aminolysis of certain epoxides by *tert*-butyl *N*-benzylglycinate in the presence of silica gel as the acid catalyst has been used as a convenient method of synthesis of the corresponding *N*-(β-hydroxyalkyl)glycine esters (in the absence of silica gel, a mixture of regioisomers was isolated).[189]



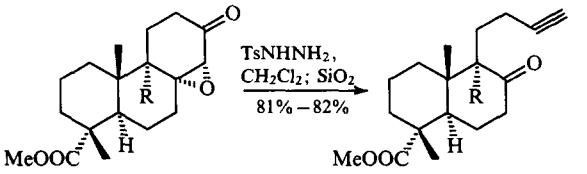
The synthesis was carried out in two ways:

(1) the reactants and the catalyst were kept in methylene dichloride for 1–1½ days under a pressure of 10 kbar and a temperature ranging from room to 65 °C

(2) the reactants were deposited on silica gel and allowed to stand at room temperature for 1–6 days.

Best results were obtained in the second case. According to preliminary data, aliphatic amines may be used as the nucleophiles.

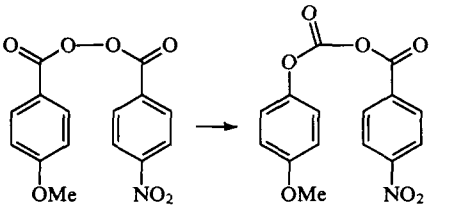
It has been shown that silica gel is an effective catalyst for the opening of the ring in α,β-epoxycycloalkanones by tosylhydrazine (the Eschenmoser reaction).[190] The reaction takes place under fairly mild conditions (at a temperature not exceeding room temperature), high yields (up to 96%) of the products [hept-6-yn-2-ones and 2-(3-butynyl)cycloalkanones] being attained even for relatively unreactive substrates of the type of podocarpanones (R = H, OH).



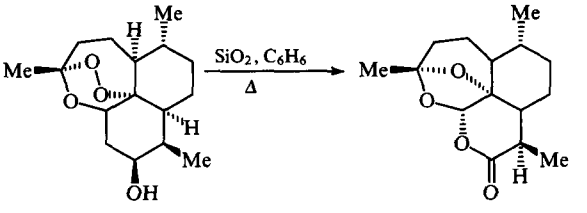
It has been noted that the catalytic effect of silicon dioxide is manifested not only in the formation of the intermediate tosylhydrazone but also in the course of its fragmentation to give the final acetylenic ketone.

11. The decomposition of peroxides

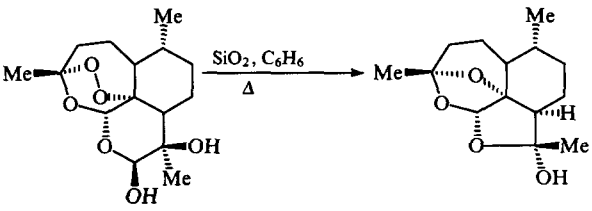
Silica gel is known to catalyse the decomposition of organic peroxides.[191–193] The reaction accelerating factor in the decomposition of di(β-phenylpropionyl), di(β-phenylisovaleroyl), and *p*-nitrobenzoyl β-phenylisovaleroyl peroxides on the silica gel surface reaches 160 relative to the analogous reactions in homogeneous systems. The rate of decomposition of *p*-methoxybenzoyl *p*-nitrobenzoyl peroxide increases by five orders of magnitude in the presence of silica gel.



Interesting reactions of dihydroartemisin **42** and 11β-hydroxy-11-epidihydroartemisinin **44**, leading to the formation of compounds **43** and **45** respectively, have been described.[194] The reactions take place on refluxing in benzene (6 h and 10 min respectively) in the presence of silica gel.



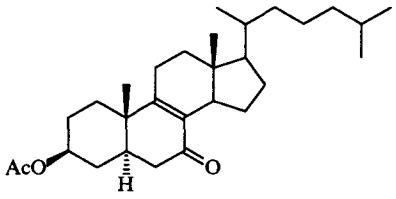
42 **43**



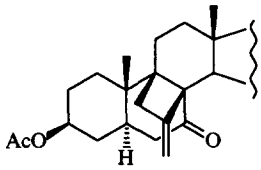
44 **45**

12. Photochemical reactions

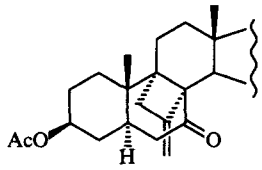
The specific features of the photochemical cycloaddition of enones to allene have been investigated.[195] It was established that, in the case of the steroid enone **46** adsorbed on silica gel, the process is partly displaced towards the more sterically hindered β-addition, leading to the derivative **47**, together with the formation of the α-adducts **48** and **49** and the rearrangement product **50**.



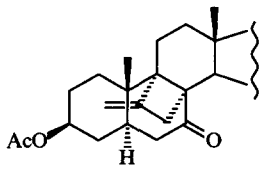
46



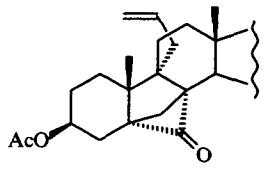
47



48



49

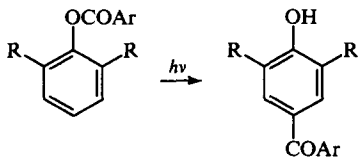


50

For the series of other, simpler examples of the enone – allene photocycloaddition, it was shown that the formation of the β,γ-adducts, which is preferred to homogeneous systems, becomes a minor process on the silica gel surface and the main products are the γ,δ-regioisomers.

The reactions involving the photocycloaddition of alkenes and allene to α,β-unsaturated steroid ketones have been investigated similarly.[196,197] In this case, the adsorption of the ketone on silica gel or aluminium oxide promotes the occurrence of the more sterically hindered β-addition, while α-addition is characteristic of the reaction in homogeneous systems.

The yield of the products of the Fries photorearrangement



R = Me, Pr^i; Ar = Ph, 2,4,6-$Me_3C_6H_2$.

increases from 5%–9% to 23%–70% after the introduction of silica gel into the reaction mixture, best results being attained in the absence of solvents.[198]

Like ozone, the forms of oxygen generated by microwave discharge in oxygen and carbon dioxide atmospheres are effective oxidants for organic compounds.[199,200] At 0 °C, the oxidation of alkenes adsorbed on silica gel affords mainly epoxides and carbonyl compounds, as in homogeneous systems; at temperatures below −60 °C, ozonolysis products are formed. Consequently the microwave discharge in an oxygen atmosphere at low temperatures can be regarded as an oxidation method which is an alternative to dry ozonisation; the comparatively slow formation of ozone, ensuring more selective oxidation, may be included among the advantages of the first method.

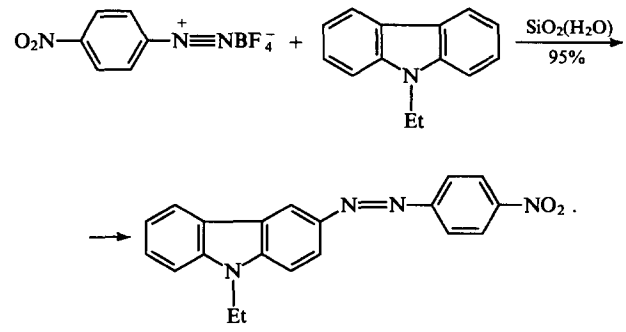
UV irradiation (λ = 350 nm) in the presence of molecular oxygen is also an effective oxidation method. Substituted phenylethenes adsorbed on silica gel are selectively cleaved to ketones or aldehydes under these conditions.[201]

Overall, despite the fact that extensive information has accumulated on the photochemistry of adsorbed molecules (see, for example, the review of de Mayo and Johnston[202]), the experimental data obtained are rarely employed for synthetic purposes.

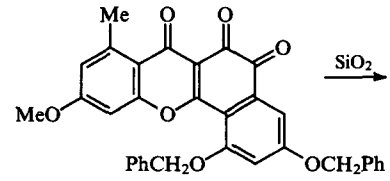
13. Various reactions

The oximes of toluene *p*-sulfonates may be converted into the corresponding amides (the Beckmann rearrangement) by stirring with silica gel at room temperature (yields 45%–90%).[203] The isomerisation of nontosylated aldoximes[204] on silica gel takes place on refluxing in xylene for 52–73 h, the yields amounting to 61%–93% for acetaldehyde derivatives and substituted benzaldehydes.

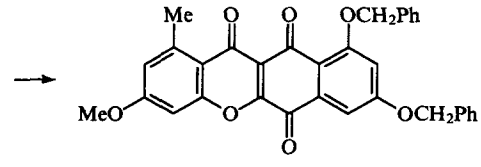
Silica gel facilitates azocoupling,[205] especially in the presence of small amounts of water (4%). The following reaction may serve as an example:



The unusual rearrangement of compound **51** to compound **52**, which takes place almost quantitatively, has been reported.[206]

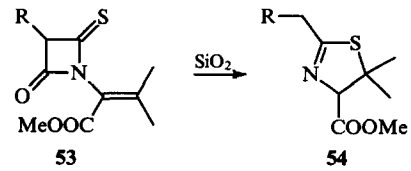


51



52

Treatment of the thiomalonimide **53** with a suspension of silica gel in chloroform gives rise to the thiazoline **54** also in an almost quantitative yield.[207]

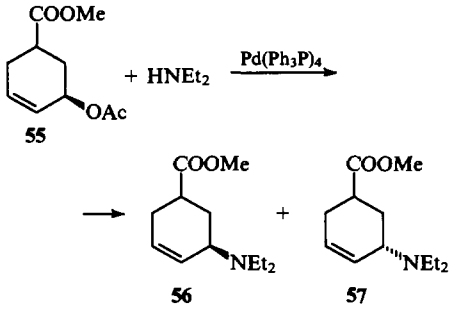


53 **54**

It has been suggested that the first stage of the rearrangement is the hydrolysis of the lactam **53** by the water adsorbed on silica gel.

The instance where silica gel functioning as the carrier for another catalyst nevertheless influences the stereospecificity of the process must be mentioned.[208] The homogeneous reaction of

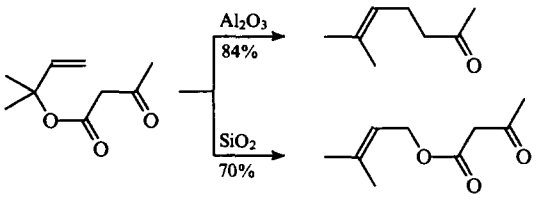
diethylamine with 5-methoxycarbonylcyclohex-3-enyl acetate **55** in the presence of tetrakis(triphenylphosphine)palladium gives a 67 : 33 mixture of the stereoisomers **56** and **57** in 85% yield. On the other hand, when the palladium catalyst is immobilised on silica gel, the only product is compound **56** (yield 72%).



An interesting approach to the creation of stereospecific catalysts has been proposed.[209,210] Chiral cavities, capable of catalysing enantioselective solvolysis (for example, 2,4-dinitrophenolysis) of the mixed anhydride of *N*-benzyloxycarbonyl-L-alanine and benzoic acid, were produced on the silica gel surface with the aid of the optically active *N*-benzoyl-(*N*-α-benzoyloxycarbonyl)-L-alanine amide. This series of studies will not be discussed in detail here because the chiral cavities possess catalytic properties only after the silica gel has been doped with aluminium ions in order to create active Lewis acid centres. Nevertheless, one may expect that this approach may prove applicable to other types of organic reactions catalysed by unmodified silicon dioxide.

Silica gel pretreated with thionyl chloride has been used as an effective catalyst of the thioacetalisation of aldehydes to give 1,3-dithiiranes and 1,3-dithianes (unmodified silica gel did not exhibit an appreciable activity).[211] On treatment with thionyl chloride, the adsorbed water is apparently removed and some of the surface silanol groups are converted into chlorosilyl groups.

In contrast to those cases where the behaviour of silicon and aluminium oxides is in general similar, chromatographic aluminium oxide catalyses the Carroll rearrangement, while the use of silica gel as the catalyst leads to the isomerisation of the alcoholic component of the initial acetoacetic ester.[212]



The last reaction proceeds on heating (60 °C) for 2–5 h.

Silica gel catalyses nucleophilic substitutions with thiocyanates.[213] For example, 1,2-epoxydecane cannot be converted into the corresponding epithio-derivative by treatment with finely ground potassium thiocyanate in toluene at 90 °C, whereas the introduction of silica gel into the reaction mixture ensures a quantitative yield of the thiirane. Best results are achieved in the presence of a small amount of water. Alkyl thiocyanates can be obtained similarly from haloalkanes, but this time preferably in the absence of organic solvents.[214] Silica gel proved to be the most active catalyst among the inorganic oxides investigated by the author.

III. Conclusion

The data examined in the present review show that the presence of chemically unmodified silicon dioxide (usually silica gel) can influence significantly the occurrence of a wide variety of organic reactions. Because of this, it has been frequently used for synthetic purposes in the oxidation (including dry ozonisation), reduction, alkylation and acylation, halogenation, elimination, hydrolytic and dehydration reactions of organic compounds, intermolecular cycloaddition reactions, and other reactions involving the formation of cyclic products as well as the opening of three-membered rings, the decomposition of peroxides, certain photochemical reactions, rearrangements, etc. The studies which have been carried out are largely phenomenological in character; in most cases, the principal or in general the only task was the attainment of the maximum yields of the target products. On the other hand, detailed information on the mechanism of the majority of the heterogeneous processes is not as yet available. Because of this, serious generalisations concerning the characteristic features of the influence of silicon dioxide on the reactions are at present impossible. On the basis of the available data, one can only reach the general conclusion that the silicon dioxide surface can function as a catalyst, as a solid medium for reactions (solid solvent), and/or as a matrix influencing the stereospecificity. In many cases, it is impossible to define clearly the role which the surface plays.

On the other hand, an unambiguous interpretation of the role of silicon dioxide as the catalyst can be found in by no means all publications describing clearly catalytic processes. It has been stated that silicon dioxide exhibits a catalytic activity in the reactions involving the oxidation of organic sulfides by sulfuryl chloride, the formation of sulfides and disulfides on treatment of aromatic compounds with RSCl, $RSCH_2Cl$, and S_2Cl_2, the reduction of aldehydes and ketones by tributyltin hydride, the alkylation and acylation of aromatic alcohols and phenols, the introduction of halogen atoms into an aromatic ring and the addition of hydrogen halides to alkenes, the dehydration of aminoacids, the Knoevenagel condensation, the Diels–Alder addition, cycloaddition and cyclisation, the opening of three-membered rings, the decomposition of peroxides, and certain other reactions.

Attempts to explain the mechanisms of the catalytic processes have been undertaken only for reactions involving the reduction of aldehydes and ketones by tributyltin hydride, the addition of hydrogen halides to double bonds, the cyclodimerisation of aminoacids to cyclic dipeptides, the Diels–Alder addition, and the Khand–Pauson cyclisation. In a number of instances, it has been stated that the degree of hydration of the silicon dioxide influences significantly the effectiveness of the process {for example, the introduction of halogen atoms into an aromatic ring, the addition of hydrogen halides to alkenes, the deketalisation of the products of the reactions of α-ketoketals with Wittig reagents, the hydrolysis of the diethyl acetals of (*Z*)-α,β-unsaturated aldehydes, the synthesis of acylsilanes by heating α,α-dibromobenzylsilanes, and the Diels–Alder reactions [(4 + 2)-cycloaddition], as well as nucleophilic substitution with participation of thiocyanates}. However, no general rules can be traced, since, overall, the state of the surface has different effects on different reactions. Only for the hydrolytic and hydration processes can one reach the unambiguous conclusion that the addition of water to the system should have a positive influence on the hydrolysis and conversely.

In the second case (silicon dioxide as a solid solvent), one may restate briefly that the chemistry of the silicon dioxide surface does not itself exert a significant influence on the course of organic reactions; the decisive factor is that the reactants become concentrated on the adsorbent surface and not the nature of the latter. This has been confirmed by instances of the successful employment of other inorganic oxides (for example Al_2O_3) together with silica gel. Adsorption can apparently facilitate the formation and/or stabilisation of the prereaction complexes between the functional groups of the reactants strongly fixed on the active surface centre; a favourable factor under these conditions is the absence of a liquid solvent.

Similar general considerations may prove legitimate also in the explanation of the role of silicon dioxide as a matrix

influencing stereospecificity. The results of various studies (in particular, on dry ozonisation) make it possible to claim that, by carrying out the reactions in adsorbed monolayers, it is possible in certain cases to increase the regioselectivity by means of the mutual orienting influence of the substrate molecules. Other carriers can apparently be used with equal success; however, unfortunately the limited number of literature data available at present makes it impossible to either confirm or reject the latter hypothesis.

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The interaction of nitriles with electrophiles

I D Gridnev, N A Gridneva

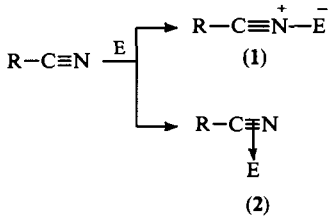
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Abstract. The interactions of organic nitriles with various electrophiles are analysed. It is shown that the numerous processes observed in such reactions are fairly general and are largely controlled by the nucleophilic properties of the nitrile. The bibliography includes 99 references.

I. Introduction

The nucleophilic properties of nitriles are due to the lone pair of the nitrogen atom and the π-electron system of the C≡N triple bond:



This leads to two possible directions of electrophilic attack and the formation of either the *n*-complexes **1** or the π-complexes **2** as the primary products.[1–3] The direction of the primary attack by the electrophile depends on its nature, the structure of the nitrile, and the reaction conditions. For example, quantum-chemical calculations and experimental data obtained by photoelectron and X-ray electronic spectroscopy constitute evidence that the highest occupied orbital of acetonitrile is a molecular π orbital, whilst the orbital occupied by the lone pair is located in a lower position.

I D Gridnev Zelinskii Institute of Organic Chemistry, Russian Academy of Sciences, Leninskii prosp. 47, 113917 Moscow, Russian Federation. Fax (7-095) 135 53 28. Tel (7-095) 135 89 51
N A Gridneva Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, ul. Vavilova 28, 117813 Moscow, Russian Federation. Fax (7-095) 135 50 85

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In the case of benzonitrile, the π orbitals of the benzene ring have the highest energies.[4]

Hence it follows that the primary product of the charge-controlled reaction of acetonitrile with an electrophile should be a π-complex.[5] However, as a result of the influence of a whole series of factors on the populations of the orbitals, such considerations are difficult to generalise and their value is therefore small. Furthermore, only one π-complex of a nitrile with an accurately established structure is known at the present time.[3] Nevertheless, we shall see below that the wide variety of primary products, observed in the interaction of nitriles with electrophiles, can be accounted for only by resorting to the concept of the formation of π-complexes.

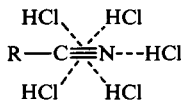
II. Interaction of nitriles with protic acids

Since protic acids catalyse a whole series of reactions of nitriles, the question of the structure of the primary products of the interaction of the latter with protic acids has been widely discussed in the literature.[1–3,6–21] Although it is regarded as generally accepted that nitriles can react with acids to form molecular π-complexes in which the proton retains its linkage with the acid anion, we are aware of only one study in which such interaction has been discussed in detail.[6]

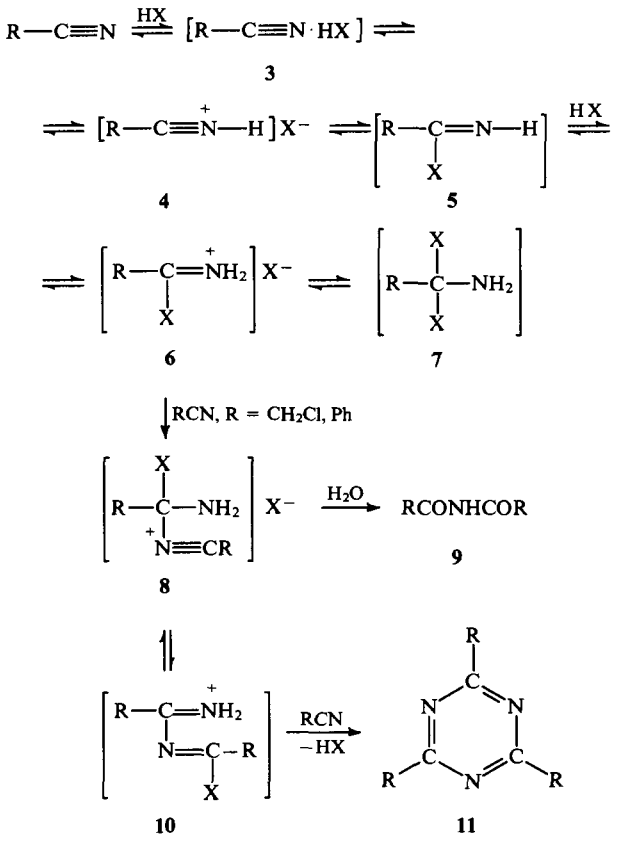
As a result of the study of the fusion diagrams for binary mixtures of hydrogen chloride with acetonitrile, propionitrile, and benzonitrile, it has been shown[6] that these nitriles can form readily fusible molecular compounds RCN·HCl. The authors[6] suggest that the lone pair of the nitrogen atom of the nitrile group participates in the formation of these compounds. The same nitriles can form the molecular compounds RCN·5HCl, RCN·7HCl, and 2RCN·3HCl with lower melting points than the compounds RCN·HCl.

Compound	T_m/°C	Compound	T_m/°C
MeCH·HCl	−63.2	2EtCH·3HCl	−117.0
2MeCN·3HCl	−88.0	EtCN·5HCl	−129.0
MeCN·5HCl	−123.6	PhCN·HCl	−80.6
MeCN·7HCl	−125.0	PhCN·5HCl	−130.0
EtCN·HCl	−97.2	2PhCN·3HCl	−109.0

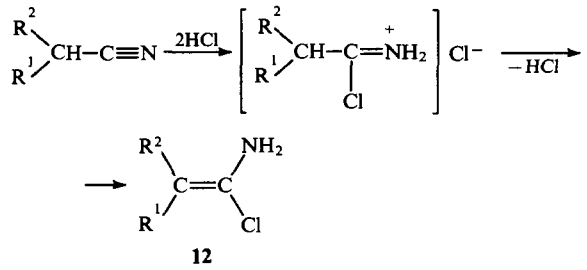
It has been suggested that these compounds are formed as a result of the interaction of HCl with the π-electron system of the nitrile, i.e. they are π-complexes.



At room and higher temperatures, nitriles react with protic acids to form salt-like compounds capable of dissociating in solution into ions, which is indicated by the results of conductimetric measurements[1,7,8] and cryoscopic studies.[9] The information accumulated hitherto makes it possible to represent all the possible products formed in the interaction of nitriles with acids in terms of the following scheme:



Although, as already noted, the formation of type **3** molecular complexes has been discussed in detail only by Murray and Schneider,[6] it is believed that this is the first stage of the interaction of nitriles with any protic acid. The formation of NH-nitrilium salts **4** has been postulated in the study of a series of acid-catalysed reactions of nitriles.[1,10,11] Indeed, in the hydrolysis of nitriles to amides or in the Hoesch reaction (acylation of phenols by nitriles), the intermediate formation of NH-nitrilium salts appears essential. However, low equilibrium concentrations of the salts **4** are sufficient for this purpose and it appears that in the case of nucleophilic anions (Hal^-, OSO_3H^-, $H_2P_2O_7^-$) the anion adds to the nitrile carbon atom with formation of type **5** compounds.[9,12] However, they are extremely unstable and the reports about the synthesis of imidoyl chloride **5** (X = Cl^-) were found to be erroneous.[1,13] The halo- and polyhalo-derivatives of immonium halides **6** (X = Hal^-, Hal_2H^-) have been isolated in a pure state and their structure has been confirmed by elemental analysis and IR spectroscopic data.[12,14,15] The same workers note that the isomeric aminochloro-derivatives **7**, the formation of which has been postulated,[13] cannot be isolated when nitriles interact with HCl. The formation of the neutral compounds **12** in the case where nitriles containing α-protons were introduced into the reaction with HCl [16] showed that the main product present in the mixture of the nitrile and HCl is the immonium halide salt.

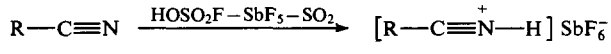


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The reaction of α-halonitriles with acids does not stop at the immonium salt **6** stage. It has been shown[9,11,17–20] that a second nitrile molecule is added with formation of the dimer salts **8** or **10**. A choice between these two structures cannot at present be made, but the formation of the dimer salts has been confirmed by the hydrolysis to the diacylamides **9**. The trimerisation of nitriles with electron-accepting substituents is also possible, leading to the formation of the triazines **11**. However, under the conditions of the interaction of nitriles with protic acids, this reaction proceeds to only an insignificant extent.

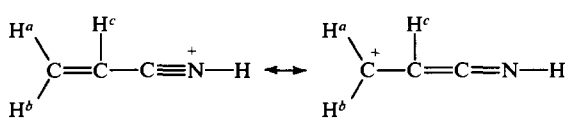
It has been observed in the reaction of fluoro- and bromo-acetonitriles with HCl [21] that, depending on the temperature, both the halo-derivatives of the immonium halides **6** and the dimer salts **8** can be obtained from the same nitriles. The former are formed at temperatures from −50 to −5 °C and the latter at room temperature. Unstable complex compounds are apparently formed initially. At a low temperature, these compounds are stabilised by the addition of a hydrogen halide molecule with formation of a halo-derivative of the immonium halide **6**. At a higher temperature, the unstable molecular complexes decompose, which increases the concentration of the free nitrile and ultimately leads to dimerisation to type **8** salts.[1]

The formation of type **4** NH-nitrilium salts can be observed in superacid media. Olah and Kiovsky[22] investigated protonated nitriles by ^1H, ^{13}C, ^{15}N NMR spectroscopy in solution in $FSO_3H-SbF_5-SO_2$ at lowered temperatures.



The presence of protonated nitriles under the given conditions is indicated by the existence of spin–spin coupling of the proton attached to the nitrogen atom with the protons of the alkyl group in the nitrile. For example, the signal of the methyl group in the protonated acetonitrile is a doublet (δ = 3.25 ppm) with $^4J_{H-H}$ = 2.4 Hz, which is comparable in magnitude to the analogous constant for methyl-ethyne (2.9 Hz). In the ^{13}C NMR spectrum of the protonated [^{13}C]acetonitrile, the signal of the nitrile carbon atom is displaced downfield by 10 ppm relative to the signal of acetonitrile, but the chemical shift nevertheless indicates the retention of *sp* hybridisation of this carbon atom.[22]

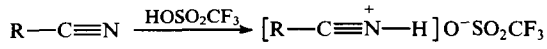
An appreciably greater downfield shift of the H^a and H^b protons than for the H^c proton (1.5 and 0.6 ppm respectively) is observed in the ^1H NMR spectrum of the protonated acrylonitrile. This apparently indicates appreciable delocalisation of the carbonium ion centre in protonated unsaturated nitriles.



It is interesting to note that Olah and Kiovsky[22] were unable to achieve the protonation of nitriles by fluorosulfonic acid, which they attribute to the insufficient acidity of the medium in

the given instant. This fact makes it necessary to treat with caution reports about the preparation of type **4** NH-nitrilium salts by the interaction of nitriles with even weaker acids.

The formation of NH-nitrilium salts on dissolution of trifluoromethanesulfonic acid in nitriles has been reported.[11]



4a

R = Me, Pr, Ph.

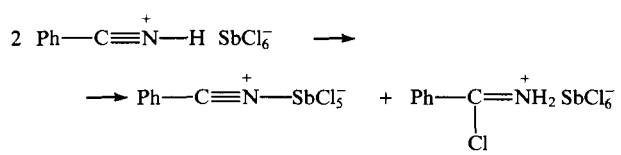
Nitrilium trifluoromethanesulfonates **4a** were isolated from solution in the form of a red oil. The IR spectra of these compounds show a 50 cm^{-1} hypsochromic shift of the $\nu(C\equiv N)$ vibrational frequency compared with the free nitriles, which led the authors[2] to attribute to them the structure of the nitrilium salts **4**. However, other data confirming this hypothesis are not quoted. Solutions of trifluoromethanesulfonic acid in nitriles are able to interact with phenols and their ethers via a reaction analogous to the Hoesch reaction.[11] After 20–30 days, the yields reach 70%–80% and acylation takes place in the *para*-position.



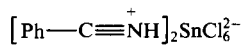
R = Alk, Ph; R′ = Me, Pr.

Halonitriles dimerise on treatment with CF_3SO_3H, which indicates the fundamentally similar nature of the interaction of nitriles with various protic acids.

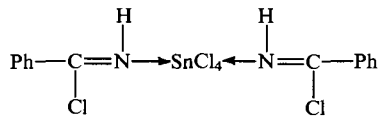
It is also essential to mention the NH-nitrilium salts with complex anions. The synthesis of such compounds has been reported in a number of communications.[1,12,14] The most detailed study[12] showed that the formation of the nitrilium salt **4** ($X = SbCl_6^-$) is not observed in the interaction of HCl with the complex $PhCN-SbCl_5$, which the authors attribute to the instantaneous disproportionation of the salt.



The only NH-nitrilium salt which it has been possible to isolate is apparently compound **13**. It has been shown by conductimetric measurements that it is not the donor–acceptor complex **14**.[12]



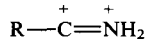
13



14

However, the salt **13** also disproportionates above 50 °C.

A recent investigation of the Houben–Hoesch reaction showed[23] that the most probable species undergoing acylation is the dication



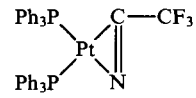
This hypothesis has been confirmed by the fact that the monocationic reagent *N*-methylbenzonitrilium triflate reacts with benzene only in the presence of an acid as strong as the $CF_3SO_3H-SbF_5$ mixture, whereas trifluoroacetic acid does not catalyse the process at all. Trifluoromethanesulfonic acid without added SbF_5 has only a slight catalytic effect.

It is also of interest to note that the complexes of nitriles with $FeCl_3$ and $AlCl_3$ do not react with HCl at all even at temperatures above 120 °C.

Thus the principal types of interaction of nitriles with protic acids are the formation of the immonium salts **6** in the case of aliphatic nitriles and the formation of the dimer salts **8** in the case of aromatic and α-halo-substituted nitriles. The formation of NH-nitrilium salts **4** can be detected only in superacid media for aliphatic nitriles.

III. Coordination of nitriles to transition metals

It has been suggested that in the complexes of nitriles with transition metals there is a possibility of interaction of the acceptor (the metal ion) both with the π-electron system of the triple bond of the nitrile and with the lone pair of the nitrogen atom.[3] In the IR spectrum of compound **15**, the frequency $\nu(C\equiv N)$ is 1780 cm^{-1}, which is 350 cm^{-1} lower than in the initial nitrile.

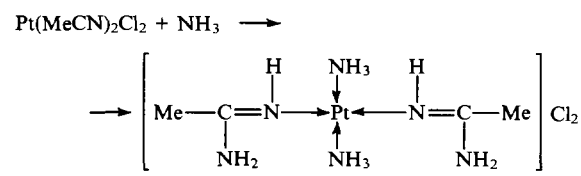


15

Such a low stretching vibrational frequency has been attributed to the formation of a π-complex with the platinum atom.

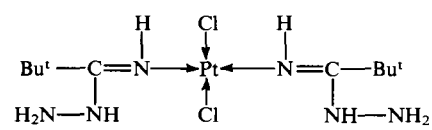
For the majority of the complexes between nitriles and transition metals, X-ray diffraction studies have shown that the MNC angle is close to 180°, whilst the length of the $C\equiv N$ bond diminishes on coordination to the metal atom,[24] i.e. its strength increases. The frequency $\nu(C\equiv N)$ increases under these conditions by 50–300 cm^{-1}.[4,25,26] However, despite this, the coordinated nitriles have enhanced electrophilic properties, which is reflected in a number of reactions.

For example, coordinated nitriles interact much more readily with amines and other nitrogen bases than the free nitriles. The nitrile complexes are converted quantitatively into amidine complexes at room temperature.[27]



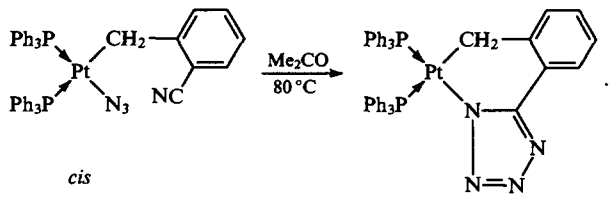
Similar reactions have been observed for the complexes $Re(RCN)_2Cl_4$ (R = Me, Ph) and a series of aromatic amines.[27]

It has been shown[28] that nitriles may be converted into amidines on treatment with hydrazine. The interaction of *trans*-$Pt(Bu^tCN)_2Cl_2$ with hydrazine hydrate in solution in ethanol leads to the formation of complex **16**.



16

An interesting example of intramolecular cyclisation has also been observed:[29]



cis

Such cyclisation does not occur when the initial complex is the *trans*-isomer.

The catalytic effect of transition metal ions on the rate of hydrolysis of nitriles, noted in a number of investigations,[29-31] has been attributed to the intermediate formation of nitrile complexes with subsequent conversion of the inner-sphere nitriles into the amides of the corresponding acids.[3] It is also believed that the facilitation of the reactions with nucleophiles when the nitrile is coordinated to a transition metal atom is associated with the decrease in the electron density on the nitrile carbon atom as a consequence of its displacement towards the central atom.[3,32]

It has been noted[4,33] that the introduction of strongly electron-accepting substituents into the nitrile molecule may alter the nature of its participation in complex formation, transforming it from an electron-donating to an electron-accepting component. For example, in the formation of complexes between nitriles and electron acceptors containing a central metal atom with populated *d* orbitals (Rh, Ru, Co, Mo), the transfer of electron density from the nitrile group to the metal may be accompanied by the additional formation of a donor–acceptor bond as a result of the interaction of the electrons of the metal *d* orbitals and the unoccupied π^* orbitals of the nitrile.[4] The participation of the π MO of the nitrile in the η^5-cyclopentadienylmanganese dicarbonyl and phosphine-molybdenum dicarbonyl complexes of nitriles has been demonstrated by electronic spectroscopic methods.[34,35] The intense charge-transfer band at $\lambda \approx 500$ nm, observed in the electronic spectra of these compounds, constitutes, according to Michurin et al.,[4] definite confirmation of the manifestation of π-electron-accepting properties by the nitrile in these complexes.

The π-electron-accepting properties of nitriles are exhibited also in complexes of the type Et_3N-SO_2-RCN, where $R = CCl_3$ or p-$NO_2C_6H_4$. The appreciable bathochromic shift of $\nu(C\equiv N)$ (by 20–30 cm^{-1}) in the IR spectra of these compounds indicates the transfer of electron density to the antibonding π MO of the nitrile.[36]

IV. Interaction of nitriles with Lewis acids

Nitriles are extremely effective electron donors in complex formation with Lewis acids.[4] The formation of complexes can be detected even for weak Lewis acids such as the halogens and interhalogen compounds.[37-39] It was shown in the above studies by UV spectroscopy that the equilibrium constants for the complex formation reactions between nitriles and the halogens increase in the sequence $Br_2 < I_2 <$ IBr < ICl. An increase in the equilibrium constant is favoured also by an increase in the electron-donating capacity of the hydrocarbon group in the nitrile.[37-39]

The complexes of nitriles with metal halides have been thoroughly investigated. They are formed on simple mixing of the reactants and can be readily isolated in a pure form and characterised. Table 1 shows that the hypsochromic shift of the $\nu(C\equiv N)$ vibrational frequency is observed in all the complexes of nitriles with metal halides, which is a common phenomenon for all the complexes of nitriles whose formation involves the lone pair of the nitrogen atom.[4]

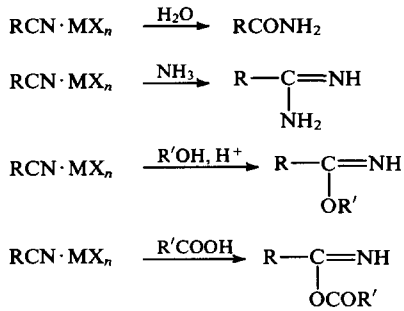
Table 1. The quantities $\nu(C\equiv N)$ and $\Delta\nu$ for the complexes of nitriles with Lewis acids.

Composition of complex	$\nu(C\equiv N)/cm^{-1}$	$\Delta\nu/cm^{-1}$	Ref.
$MeCN\cdot BF_3$	2359	111	40
$MeCN\cdot BCl_3$	2328	81	41
$PhCN\cdot BCl_3$	2304	75	41
$MeCN\cdot AlCl_3$	2330	77	42
$MeCN\cdot AlBr_3$	2335	82	42
$2\,MeCN\cdot ZnCl_2$	2306	44	43
$2\,MeCN\cdot SnCl_4$	2300	38	44
$PhCN\cdot SnCl_4$	2258	27	45
$2\,MeCN\cdot NiCl_2$	2286	41	46
$2\,PhCN\cdot TiCl_4$	2269	38	47
$4\,EtCN\cdot NiBr_2$	2290	42	48
$4\,MeCN\cdot RuCl_2$	2270	29	49
$H_2C{=}CHCN\cdot NbCl_5$	2264	36	50
$H_2C{=}CHCN\cdot FeCl_2$	2257	29	51
$H_2C{=}CHCN\cdot CoCl_2$	2260	32	51
$2\,MeCN\cdot ReCl_4$	2310	59	52
$2\,MeCN\cdot TiCl_4$	2280	26	53

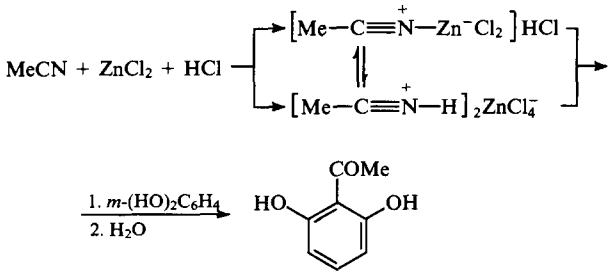
The causes of such increase in the vibrational frequency of the C≡N bond have not been fully elucidated. Initially, this phenomenon was attributed to the increasing charge separation and hence to a larger dipole moment of the C≡N bond in the complexes.[54] In a later study,[55] it was shown that one of the causes may be the kinematic interaction between the stretching vibration of the N–B and C–B bonds with the normal C≡N mode in the complexes $MeCN\cdot BX_3$ (X = Cl, F, Br). However, according to the results of Bittie and Gilson,[56] the observed increase in $\nu(C\equiv N)$ cannot be accounted for solely by the kinematic effect, since calculation yields a shift of 25 cm^{-1}, whilst the observed experimental values are 70–100 cm^{-1}. Nevertheless the shift of the $\nu(C\equiv N)$ vibrational frequency is regarded as a reliable criterion of the formation of complexes of nitriles via the lone pair of the nitrogen atom.[1,2,4]

This conclusion has been confirmed by X-ray diffraction for a series of complexes of acetonitrile with Lewis acids.[11,44,57] A linear $Me-C\equiv N-MX_n$ coordination and a shortening of the C≡N bond (1.10–1.15 Å) were observed in all these investigations.

The chemical properties of the nitrile–Lewis acid complexes are characterised by a greater ease of nucleophilic attack on the nitrile carbon atom compared with the free nitrile. This is manifested in their interactions with water, organic acids, alcohols, and nitrogen bases. In fact, all these reactions proceed smoothly only in the presence of Lewis acids.[1-3]

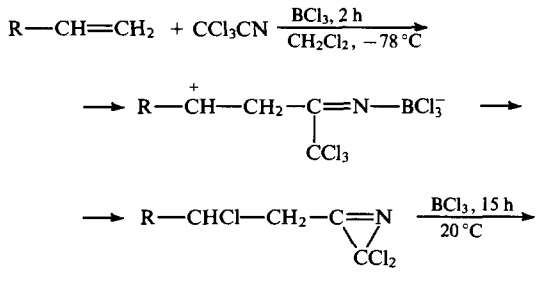


The Hoesch reaction, which was already known at the beginning of the century, also proceeds in the presence of a Lewis acid — $ZnCl_2$.[11]

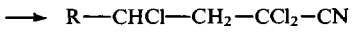


The recently discovered reaction of complexes of nitriles containing electrophilic substituents with BCl_3 and BBr_3 is of the greatest synthetic interest.[57-59] Japanese investigators[57,58] observed that, in the presence of BCl_3, trichloroacetonitrile interacts with a wide range of alkenes, affording the products of the electrophilic attack by the nitrile on the double bond of the unsaturated compound. The mode of the reaction then depends significantly on the structure of the unsaturated compound.

Thus, it has been shown that the interaction of α-alkenes with trichloroacetonitrile in the presence of BCl_3 in methylene chloride at −78 °C leads to satisfactory yields of dichloroaziridines **16**, which may be converted into the corresponding dichloronitriles.[57]



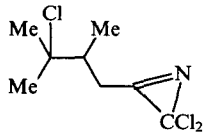
16



17

R	Yield (%)	
	16	**17**
n-C_6H_{13}	90	60
Bu^n	90	66
Bu^{iso}	90	77
$EtMe_2C$	92	59
Bu^t	68	65
$PhCH_2$	44	19

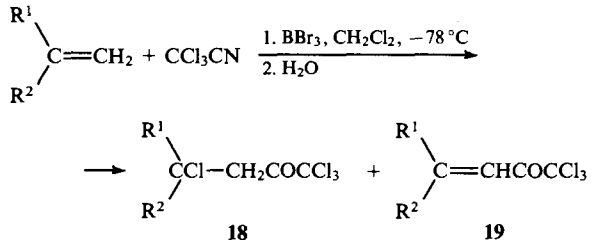
In the case of compound **16** (R = Bu^t, $PhCH_2$), the reaction lasted 15 h and in the case where R = Bu^t the compound



was isolated as a side product in 28% yield.

The use of BBr_3 as the catalyst in this reaction leads to the formation of the same product, which shows that the carbonium ion is stabilised by a chlorine atom in trichloroacetonitrile.[57]

A different mode of reaction has been observed for 1,1-disubstituted alkenes — aziridines are not formed and the stabilisation of the carbonium ion is achieved either by the 'abstraction' of a halide ion from the catalyst or as a result of the elimination of an α-proton. A different origin of the halogen from that in the preceding reaction is indicated by the formation of a bromoketone when BBr_3 is employed as the catalyst.[57]



18 **19**

In the case of *tert*-butyl(methyl)ethene, an increase of the reaction temperature to room temperature leads to the formation of rearrangement products (Table 2).

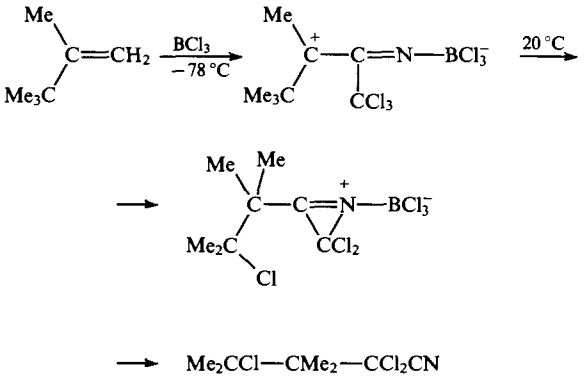
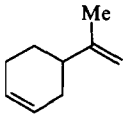
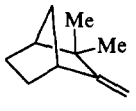


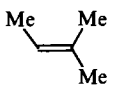
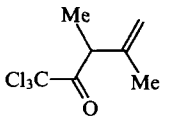
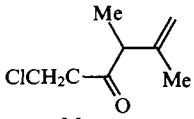
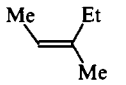
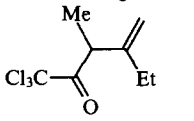
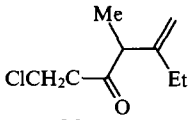
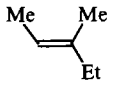
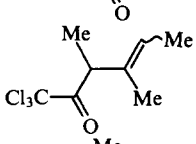
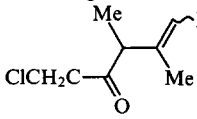
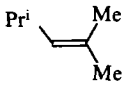
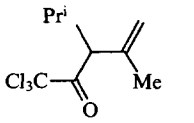
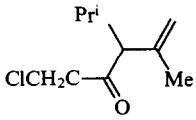
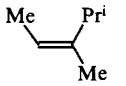
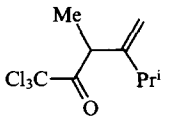
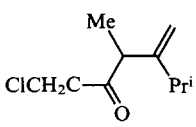
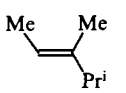
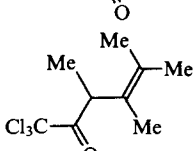
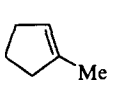
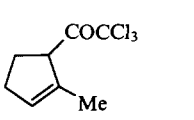
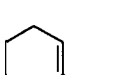
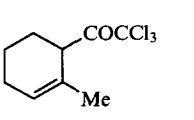
Table 2. The yields and ratios of the products **18** and **19**.

Alkene	Overall yield (%)	Compound **18**: compound **19**
	92	80:20
	90	80:20
	91	86:14
	95	0:100
	89	0:100
	75	0:100

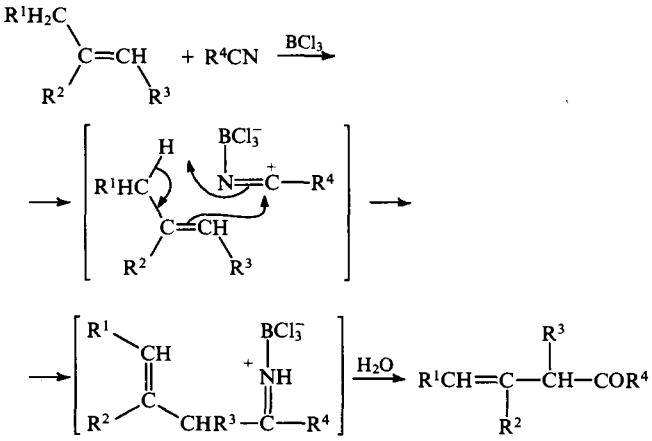
The causes of the different modes of reaction for different alkenes are not discussed in the communication of Hamana and Sugasawa.[57] It is noted that only BCl_3 and BBr_3 are suitable as catalysts. When $AlCl_3$, $TiCl_4$, or $BF_3.OEt_2$ and nitriles with less strongly electron-accepting substituents than CCl_3 are employed, the reaction does not occur.

A different mode of reaction occurs for trisubstituted alkenes. β,γ-Unsaturated ketones are formed exclusively in this instance. It is believed[58] that the reaction proceeds via the 'ene' mechanism.

Table 3. Conditions in the preparation and yields of the β, γ-unsaturated ketones **20**.

Alkene	Nitrile	Product	Yield (%)
	Cl_3CCN		70
	H_2CClCN		74
	Cl_3CCN		76
	H_2CClCN		70
	Cl_3CCN		74
	H_2CClCN		70
	Cl_3CCN		74
	H_2CClCN		71
	Cl_3CCN		74
	H_2CClCN		71
	Cl_3CCN		45
	Cl_3CCN[a]		90
	Cl_3CCN[a]		90

Note. When CCl_3CN was used, the reaction was carried out at −78 °C for 2 h, whereas in the case of $ClCH_2CN$ it was carried out at 20 °C for 20 h.
[a] The reaction time 5 h.

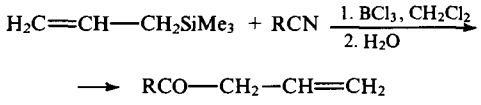


20

Table 3 shows clearly the difference between the reactivities of trichloroacetonitrile and chloroacetonitrile. In the latter case, the reaction requires room temperature and a time longer by a factor of 10.

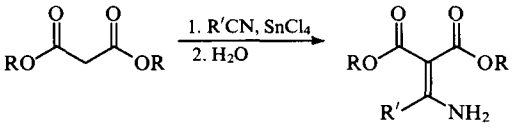
The concerted reaction mechanism of the 'ene' type is confirmed by the rigorous regiospecificity of the reaction. When two possible modes of reaction are possible, the proton is abstracted from the alkyl group located in the *cis*-position relative to the vinyl proton.

In the interaction of trichloroacetonitrile and chloroacetonitrile with allyltrimethylsilane in the presence of BCl_3, allylketones are formed.[59]



R = CCl_3, CH_2Cl.

It has been also observed recently that the complexes of nitriles with tin tetrachloride may be alkylated by malonic acid esters, which leads to the formation of derivatives of α,β-dehydroaminoacids in 20%–60% yields.[60]

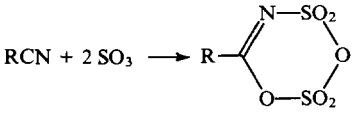


R′ = Me, Et, Ph, CH=CHPh, CH=CHMe.

Thus, although numerous studies were devoted to the investigation of the structures and physicochemical properties of complexes of nitriles with Lewis acids already in the 1960–1970s, the study of their synthetic possibilities as acylating agents is only just beginning.

V. Interaction of nitriles with sulfur trioxide

The interaction of nitriles with sulfur trioxide has been described in detail in the communications of Bodrikov, Michurin, and coworkers.[61,62] Thus it has been shown that the reaction with SO_3, leading to the formation of 1,3,2,4,5-dioxadithiazine 2,2,4,4-tetroxides **21**, is a general reaction of nitriles (Table 4).



21

Table 4. Some characteristics of 1,3,2,4,5-dioxadithiazine 2,2,4,4-tetroxides **21**.

R	Yield (%)	T_m/°C	ν(C≡N)/cm^{-1}
Me	96	40–42	1665
Et	97	46–48	1662
Bu^t	92	57–59	1660
H_2C=C(Me)	95	45–48	1636
CCl_3	98	46–48	1670
CBr_3	92	76–78	1668
$CHCl_2$	97	54–56	1672
Ph	98	81–83	1645
p-MeC_6H_4	97	165–167	1642
p-ClC_6H_4	99	132–134	1650
m-$O_2NC_6H_4$	95	193	1658
p-$O_2NC_6H_4$	96	177–180	1657
3,5-$(O_2N)_2C_6H_3$	98	140–142	1665

For alkylnitriles and nitriles with unsaturated substituents, the reaction temperature varies from −75 to −60 °C, whilst for halonitriles and aromatic nitriles it varies from −40 to −25 °C. The structure of compound **21** has been confirmed by X-ray diffraction.[63]

However, it has been found[64] that 1,3,2,4,5-dioxadithiazine 2,2,4,4-tetroxides are not the primary products of the interaction of SO_3 with nitriles. This is indicated by the hypsochromic shift of ν(C≡N) when nitriles are mixed with SO_3 in CCl_4. The absorption frequencies of the cyano-group of the nitriles (ν) and their mixtures with SO_3 in CCl_4 (ν') are given below.

R	ν(C≡N)/cm^{-1}	ν'(C≡N)/cm^{-1}
Me	2255	2285
Et	2251	2282
Bu^t	2239	2283
H_2C=C(Me)	2232	2262
Ph	2231	2261
p-MeC_6H_4	2231	2260
p-ClC_6H_4	2234	2267
m-$O_2NC_6H_4$	2238	2270
p-$O_2NC_6H_4$	2238	2270
m-MeC_6H_4	2232	2259
p-$MeOC_6H_4$	2229	2258

For nitriles with strongly electron-accepting substituents [R = CCl_3, CBr_3, 3,5-$(NO_2)_2C_6H_3$], the presence of SO_3 does not induce a hypsochromic shift of ν(C≡N) in the IR spectrum but gives rise to a decrease in the intensity of this band.

It has been suggested[64] that the observed changes in the IR spectra of nitriles in the presence of SO_3 should be regarded as the result of the formation of the donor–acceptor complexes **22**.

The initial formation of the donor–acceptor complexes on mixing nitriles with SO_3 has also been confirmed by the observed kinetic features in the formation of the tetroxide **21**. These features are consistent with a two-stage mechanism.[65]

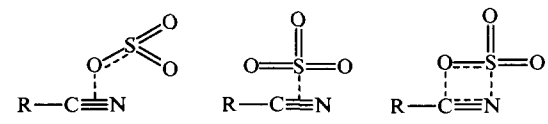
$$RCN + SO_3 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} RCN\cdot SO_3$$

22

$$RCN\cdot SO_3 + SO_3 \xrightarrow{k_2} \mathbf{21}$$

$k_2 > k_1$.

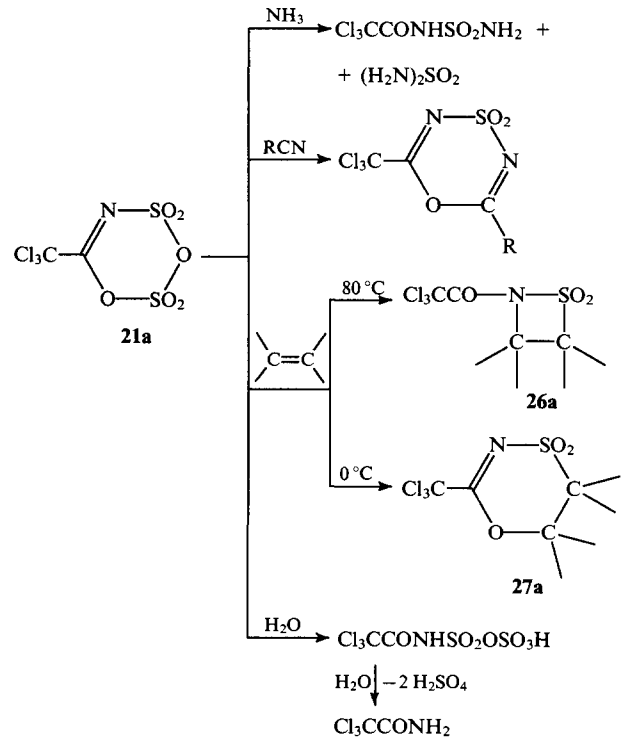
Quantum-chemical analysis of the possible forms of the donor–acceptor complexes of nitriles with SO_3 has shown that the most probable form of the complexes of nitriles having strongly electron-accepting substituents with SO_3 is form **23**, whilst for the remaining nitriles forms **24** and **25** are equally probable.



23 **24** **25**

The chemical properties of 1,3,2,4,5-dioxadithiazine 2,2,4,4-tetroxides depend on the structure of the group R in the nitrile entering into the composition of the tetroxide. Tetroxides having strongly electron-accepting substituents interact with nucleophiles with retention of the C–O bond in the tetroxide (Scheme 1).[6]

Scheme 1



In the interaction of nitriles having strongly electron-accepting substituents with tertiary amines, the dipolar compounds **29** are formed. Their structure has been demonstrated by X-ray diffraction.[67]

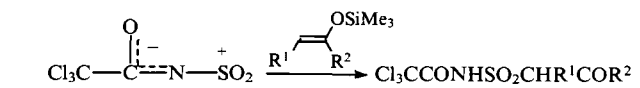
$$\mathbf{21} + NEt_3 \xrightarrow[-SO_3\cdot NEt_3]{} R{-}C(=O){-}N^{+}{-}SO_2^{-}$$

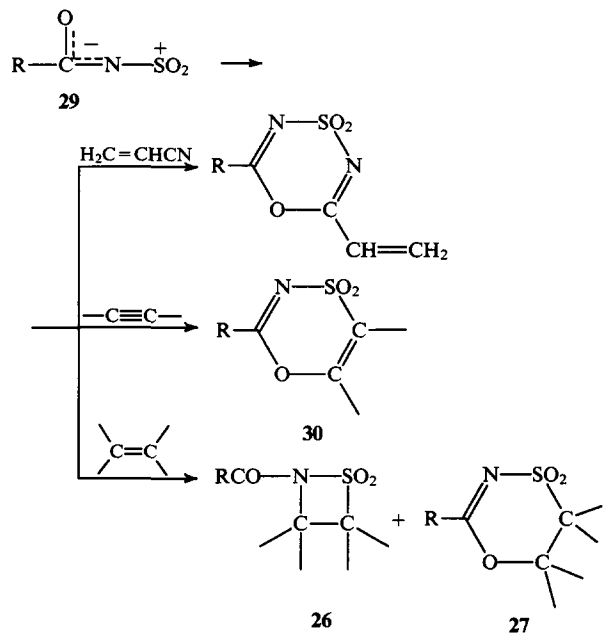
29

R = CCl_3, CBr_3, 3,5-$(O_2N)_2C_6H_3$.

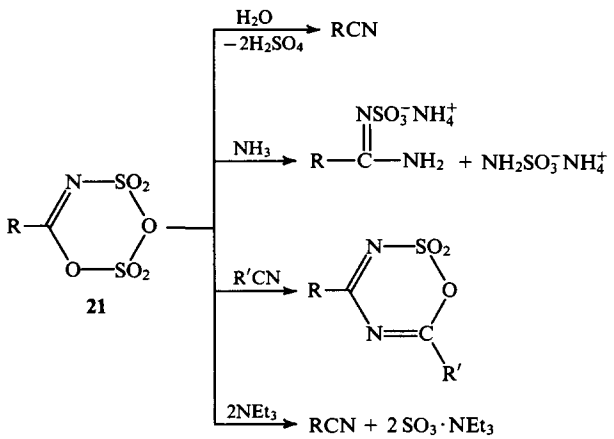
Like the tetroxides **21**, compound **29** reacts with unsaturated compounds.[68]

The formation of compounds **26** may be detected only when trimethylethene or styrene is used as the substrate. In all the remaining cases (in the reactions with allyl chloride, allylbenzene, *p*-methylallylbenzene, *p*,β-dimethylstyrene, isoprene, phenylethyne, diphenylethyne, and *tert*-butylethyne), the [4+2]-cycloaddition reaction takes place with formation of compound **27** or **30** respectively.[69] The interaction of compounds **29** with the trimethylsilyl ethers of enols proceeds with formation of 2-oxosulfonamides.

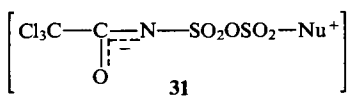




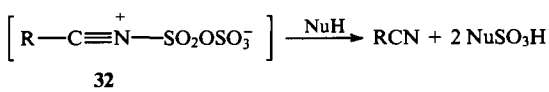
On the other hand, tetroxides containing electron-donating and weakly electron-accepting substituents react with nucleophiles with dissociation of the C–O bond.[63–65]



It has been suggested[65] that the observed differences in the behaviour of tetroxides **21** with strongly electron-accepting substituents and with electron-donating or weakly electron-accepting substituents are due to the fact that in the former case the reaction proceeds via the relatively stabilised intermediate **31**.



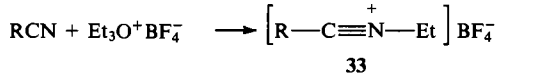
On the other hand, in the case of electron-donating substituents, the formation of the azacarbenium type intermediate **32**, the decomposition of which affords the initial nitrile, proves to be favourable.[65]



VI. Alkylation of nitriles. Alkylnitrilium salts

Meerwein et al.[69] reported in 1956 the synthesis of a large number of alkylnitrilium salts for nitriles and various alkylating agents. This study still remains the main source of information about alkylnitrilium salts.

Alkylnitrilium salts may be obtained by the reaction of nitriles with triethyloxonium tetrafluoroborate followed by the removal of ether (Table 5).[70]

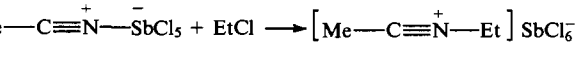


Nitrilium tetrafluoroborates and tetrachloroaluminates are extremely hygroscopic, deliquesceing in air almost instantaneously. The composition of the compounds obtained has been confirmed by elemental analysis for the halogen.

Table 5. The alkylnitrilium salts obtained by alkylating nitriles with triethyloxonium salts.

Alkylnitrilium salt	T_{decomp}/°C	Yield (%)
$[MeC{\equiv}N^+Et]BF_4^-$	—	89
$[EtC{\equiv}N^+Et]BF_4^-$	68–75	70
$[PhC{\equiv}N^+Et]BF_4^-$	92–98	64
$[PhC{\equiv}N^+Et]SbCl_6^-$	170–172	64
$[PhC{\equiv}N^+Et]AlCl_4^-$	—	36

Nitrilium salts can also be obtained from complexes of nitriles with Lewis acids and alkyl halides.[69]



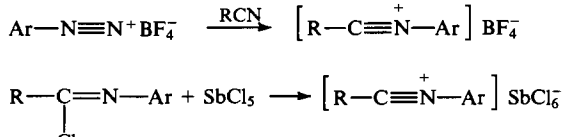
The alkylation time then depends on the ease of the formation of the carbonium ion from the alkyl halide (Table 6).

Table 6. Conditions in the alkylation of the complex $PhCN^+ - SbCl_5^-$.

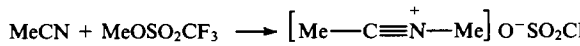
Alkyl chloride	Nitrilium salt	PhCN : RCl	Time	Yield (%)
EtCl	$PhCN^+ - Et\,SbCl_6^-$	1 : 12	1 month	75
Pr^iCl	$PhCN^+ - Pr^i\,SbCl_6^-$	1 : 10	1 month	83
Bu^tCl	$PhCN^+ - Bu^t\,SbCl_6^-$	1 : 2.2	1 min	90

This method of synthesis of alkylnitrilium salts is extremely convenient and is widely used on the preparative scale.

The methods described above are not suitable for the synthesis of *N*-arylnitrilium salts, and the latter are therefore synthesised by the interaction of nitriles with arenediazonium salts or by treating iminohalo-derivatives with Lewis acids.[70]

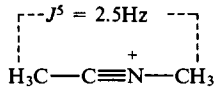


The synthesis of alkylnitrilium triflates by the interaction of nitriles with methyl triflate has been reported:[70]



The structure of alkylnitrilium salts has been investigated by IR and NMR spectroscopy. The IR spectra of alkylnitrilium

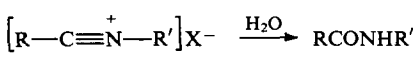
salts, like those of the protonated nitriles and their complexes with Lewis acids,[21,70,71] exhibit an 80–100 cm^{-1} hypsochromic shift of $\nu(C\equiv N)$. It has been suggested that this finding indicates unambiguously that the main contribution to the structure of the nitrilium salts comes from the form with the charge localised on the nitrogen atom.[71] The ^1H NMR spectra of the nitrilium salts indicate the existence of spin–spin coupling between the alkyl group at the nitrogen atom and the α-protons of the nitrile.[21]



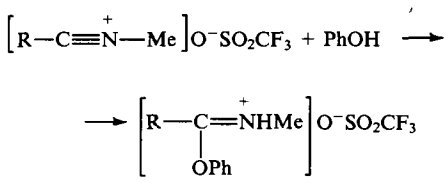
δ = 2.67 ppm δ = 3.66 ppm

The linear structure of the alkylnitrilium ions has been confirmed by an X-ray diffraction study of *N*-(2,6-dimethylphenyl)acetonitrilium tetrafluoroborate.[72]

N-Alkyl- and *N*-aryl-nitrilium salts interact with nucleophiles at the nitrile carbon atom. For example, their hydrolysis leads to *N*-alkylamides.[69]

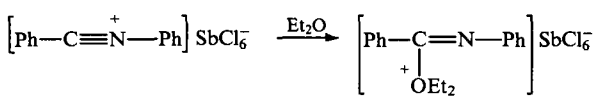


Nitrilium salts react similarly with phenol.[70]

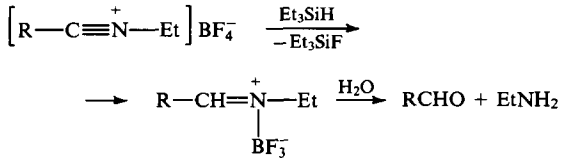


R = Me, Ph.

An unstable compound of an *N*-arylnitrilium salt with ether has been obtained.[69]

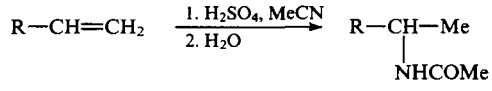


The interaction of *N*-alkylnitrilium salts with triethylsilane leads to the formation of aldehydes and amines.[73]

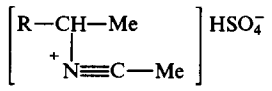


VII. The Ritter reaction

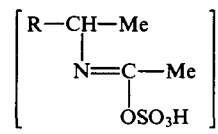
The classical version of the Ritter reaction involves the alkylation of nitriles by the carbonium ions generated in an acid medium from alkenes and alcohols with subsequent hydrolysis, which leads to *N*-alkylamides.[74,75]



The reaction mechanism presupposes the intermediate formation of the alkylnitrilium salt **34**.



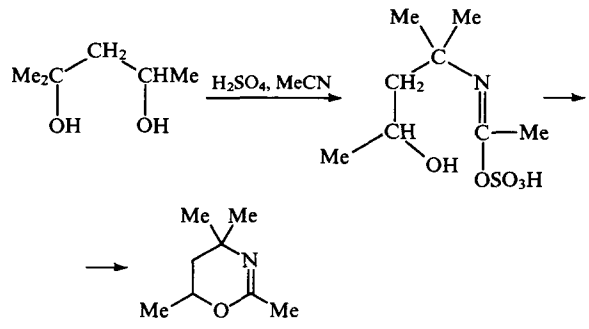
34



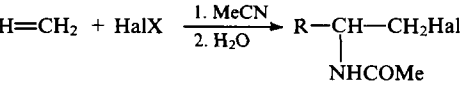
35

However, the direct detection of such intermediates in the Ritter reaction has not so far been reported in the literature. Bearing in mind the complexity of the chemical behaviour of nitriles in acid media (see Section I), it is fairly difficult to imagine the true reaction mechanism. The majority of investigators, including Ritter himself, prefer to represent the intermediate by formula **35** with a covalently bound anion.

The development of the synthetic possibilities of the Ritter reaction arose primarily from its use in the reaction of the nitrile with molecules having a variety of functional groups. Thus heterocyclic compounds may be synthesised by the Ritter reaction.[76,77]

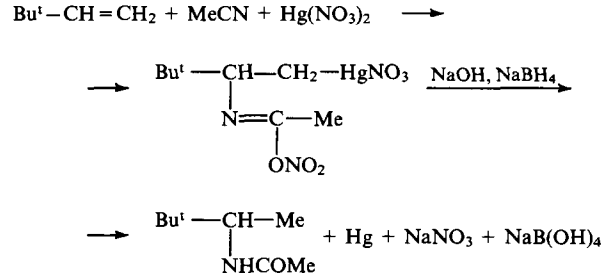


Another direction in the synthetic development of the Ritter reaction involved the employment of electrophiles other than the proton. For example, the halogens have been used as the electrophiles.[78–80]

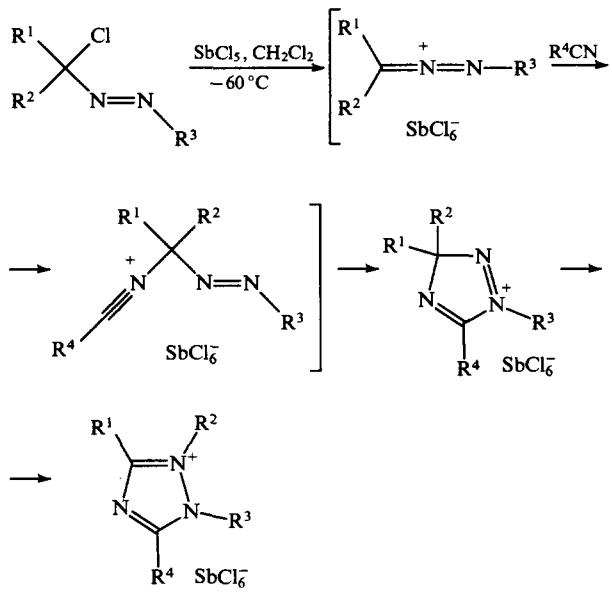


Hal = Cl, Br; X = Cl, Br, OH, N_3, HCONH, ClNCOOEt.

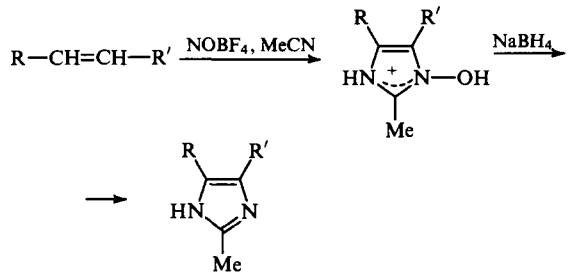
The use of mercury(II) nitrate and acetonitrile leads ultimately to the same products as the Ritter reaction, but makes it possible to avoid acid conditions. The value of this approach has been demonstrated in the reaction of acetonitrile with *tert*-butylethene, which occurs without a skeletal rearrangement.[81]



The diversity of the carbonium ions capable of allylating nitriles is well illustrated by their reactions with 1-aza-2-azonioallene salts.[82]

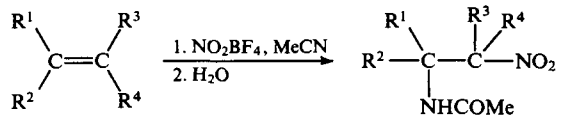


An interesting example of a modified Ritter reaction is the interaction of nitrosonium[83] and nitronium[84,85] tetrafluoroborates with alkenes. The yield of the imidazole derivatives depends on the structure of the alkene.

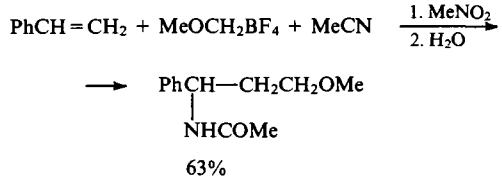


R = Me, R′ = H (80%); R = R′ = Me (80%);
R = Ph, R′ = H (50%); R + R′ = $(CH_2)_4$ (50%).

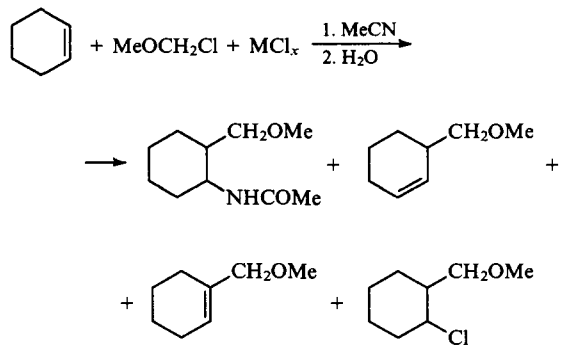
Nitronium tetrafluoroborate interacts with alkenes in acetonitrile, giving rise to β-*N*-acylaminonitro-derivatives after hydrolysis.[84,85] The best yields in this reaction (80%–90%) have been obtained for substituted styrenes.[85]



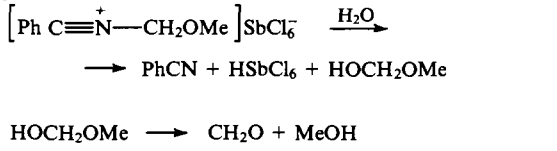
The reaction involving the coupled formation of C–C and C–N bonds is of special interest. It was first described[86] in relation to styrene.



The possibility of the employment of the chloromethoxymethane–Lewis acid–acetonitrile system for this reaction was investigated in a later study,[87] but the yields of the target products do not exceed 40% in this instance and the formation of side products is observed.



It is interesting to note that, according to Meerwein's data, alkylnitrilium salts of the type $[Me-C\equiv N-CH_2.OMe]^+X^-$ should be formed under the conditions of the last two reactions. However, in contrast to the remaining known nitrilium salts, their interaction with a nucleophile (in the given instance with an alkene) involves an alkyl and not the nitrile carbon atom. This finding agrees well with Meerwein's data for the interaction of a similar alkylnitrilium salt with water. This was the only instance in which he observed that hydrolysis entailed the formation of the initial nitrile and not an *N*-alkylamide.[69]

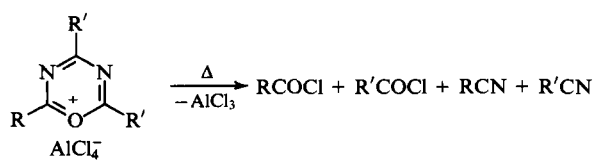


VIII. Acylation of nitriles. Acylnitrilium salts

The syntheses of a series of acylnitrilium salts via the acylation of a series of complexes of nitriles with Lewis acids by acyl halides have been described in Meerwein's classical paper.[69] The compositions of the reaction products were confirmed by elemental analysis for the halogen.

PhCN·$PhCOZnCl_3$ (**36**),
2 PhCN·$PhCOAlCl_4$ (**37**),
2 PhCN·$PhCOSbCl_6$ (**38**),
2 MeCN·$MeCOSbCl_6$ (**39**),
2 PhCN·$PhSO_2SbCl_6$ (**40**),
3 PhCN·$MeCOSbCl_6$ (**41**),
3 PhCN·$(PhCO)_2SnCl_4$ (**42**),
3 PhCN·$MeCOAlCl_4$ (**43**).

Meerwein et al.[69] believe that the acylnitrilium salt PhCN.$PhCOZnCl_3$ **36** constitutes benzonitrile acylated at the nitrogen atom. They attribute the structure of the diazapyrylium salts **44** to the salts **37**–**40**, which has been confirmed by their thermal decomposition, in which exchange of substituent groups is observed.

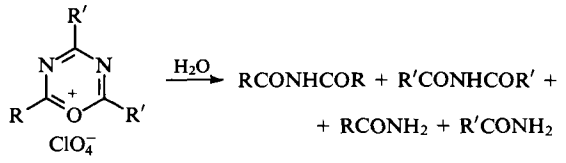


44

For complexes **41**–**43**, the authors consider the structure of acylated triazines, but they present no data whatever to confirm this hypothesis.

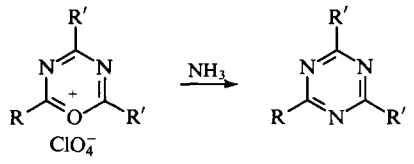
In Schmidt's study,[88] the structure of aryldiazapyrylium salts obtained by Meerwein's method, involving the heating of the

benzonitrile–Lewis acid complex with an acyl halide, was confirmed by a series of chemical reactions. Thus their hydrolysis leads to a mixture of two amides and two acylamides.



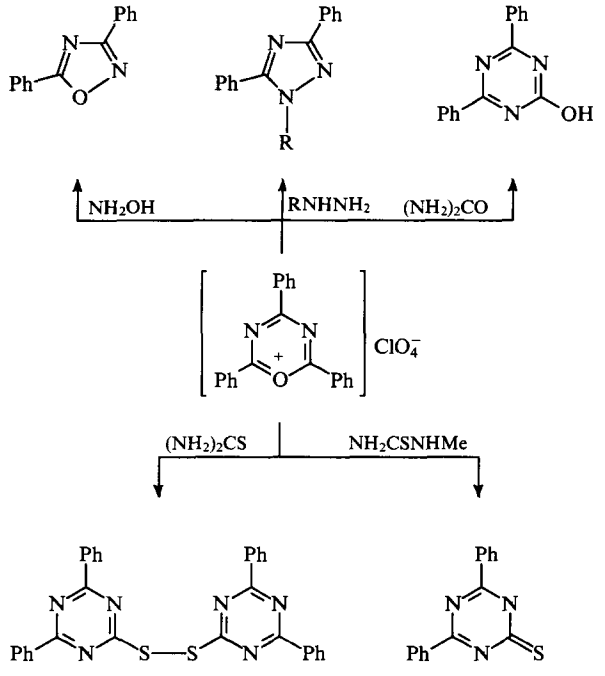
R, R′ = Ar.

Reaction with ammonia converts the diazapyrylium salts into triazines.

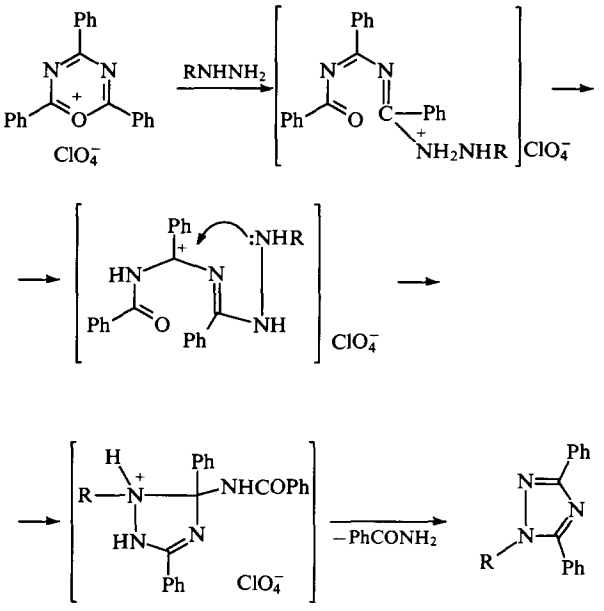


R, R′ = Ar.

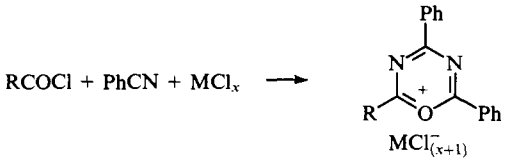
Schmidt also observed a series of reactions of triphenyldiazapyrylium perchlorate, which take place with elimination of benzamide.



Apparently the primary attack by the nucleophile is directed to the nitrile carbon atom linked to oxygen.



The IR spectra of a series of diazapyrylium salts synthesised by the interaction of acyl halides with Lewis acids and benzonitrile in nitrobenzene, dichloroethane, or without a solvent have been investigated.[89]

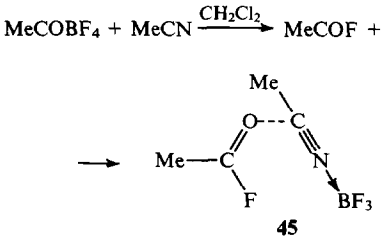


R = Me, Ph, CH_2Cl; MCl_x = $SbCl_5$, $SbCl_3$, $SnCl_4$.

It is of interest to note the differences between the conditions in the synthesis of the diazapyrylium salts mentioned by Sumarokova et al.[89] Thus the reaction of the complex $PhCN.SbCl_5$ with acyl halides takes place rapidly at room temperature, whereas the synthesis of the diazapyrylium salts involving the use of $SnCl_4$ or $SbCl_3$ as the Lewis acid requires prolonged maintenance at 80 °C and the yields of the target products are in this case lower.

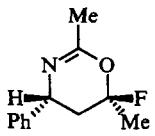
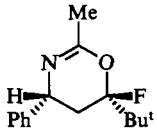
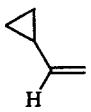
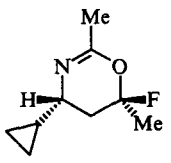
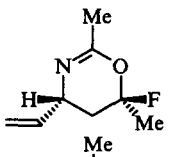
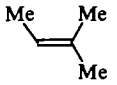
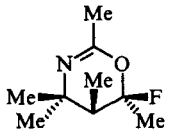
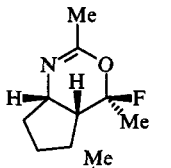
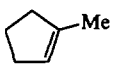
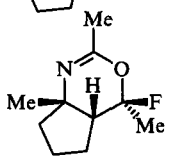
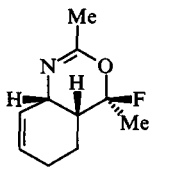
The diazapyrylium salts have been obtained in the form of yellow or orange crystals; their structure has been confirmed by measurements of the molecular mass (by the cryoscopic method), by elemental analysis, and by IR spectroscopy. The IR spectra of the diazapyrylium salts contain no absorption bands above 1650 cm^{-1}, but they do contain a group of bands in the region 1540–1640 cm^{-1}, which Sumarkova et al.[89] assigned to the diazapyrylium ring vibrations.

The interaction of acetyl tetrafluoroborate with acetonitrile in methylene chloride has been studied in detail.[90] It was shown by NMR spectroscopy that this interaction involves the transfer of boron trifluoride from acetyl fluoride to acetonitrile, which leads to the reformation of complex **45**, in which the oxygen atom of the acetyl fluoride is coordinated to the electrophilic carbon atom of the complex $MeCN.BF_3$.

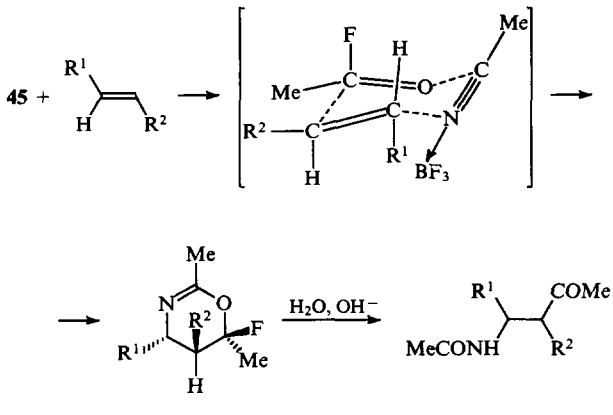


45

Table 7. The structure of the fluorooxazines obtained by the acylamidation reaction.

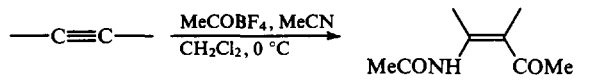
Reagent	T/°C	Product	Yield (%)
	0		62
	0		52
	−10		35
	−10		33
	0		57
	0		48[a]
	0		66[a]
	−20		25[b]

[a] Approximately 20% of the corresponding 3-acetylcyclopentene was isolated. [b] The low yield is due to the polymerisation of the product.

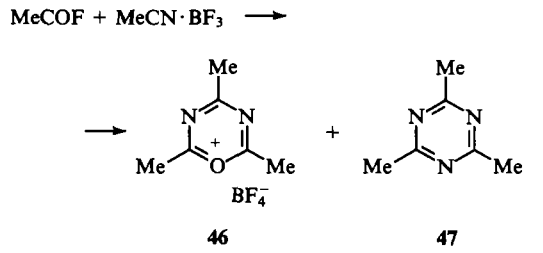


The formation of complex **45** is confirmed by the fact that, when an unsaturated hydrocarbon is added to the MeCOF–MeCN–BF_3 system, the acylamidation reaction, leading to the *syn*-stereospecific formation of the corresponding 6-fluoro-5,6-dihydro-1,3-oxazines, takes place (Table 7).[90–94]

The reactions with ethynes, which give stereospecifically products of the *syn*-acylamidation of the triple bond, take place similarly (Table 8).[95]

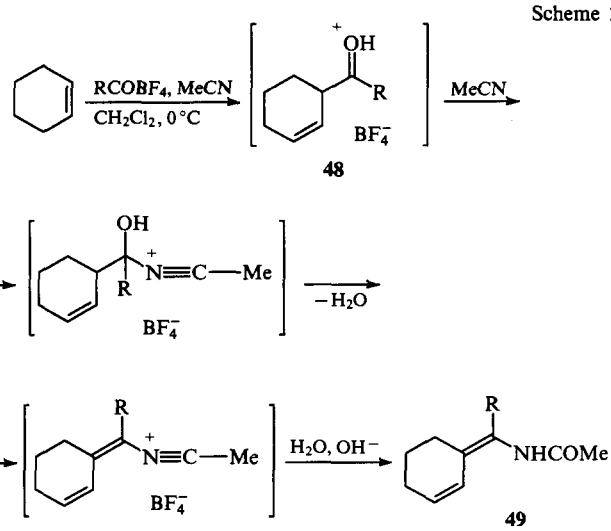


When the MeCOF–MeCN–BF_3 system is kept for a long time in a sealed tube, the formation of a dark-red solution, containing the diazapyrylium salt **46** and the triazine **47**, is observed. This solution does not interact with unsaturated hydrocarbons.[90]



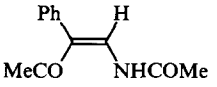
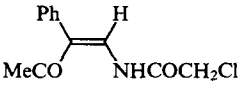
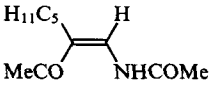
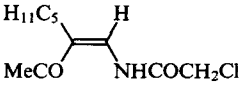
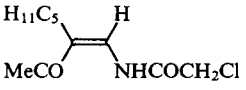
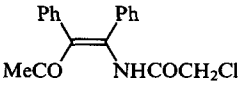
The complexity of the processes occurring in the acyl fluoride–nitrile–boron trifluoride system is indicated by the results of a study of the influence of the structure of the unsaturated substrate on the nature of the acylamidation reaction.[96–98] For example, in contrast to cyclopentene, cyclohexene does not afford 1,2-adducts on interaction with the MeCOF–MeCN–BF_3 system. The diene amide **49**, isolated in this reaction (Scheme 2), is formed via the interaction of the protonated unsaturated ketone **48** with the nitrile.[96] Thus in certain cases complex **45** can function also as an acylating agent.

Scheme 2



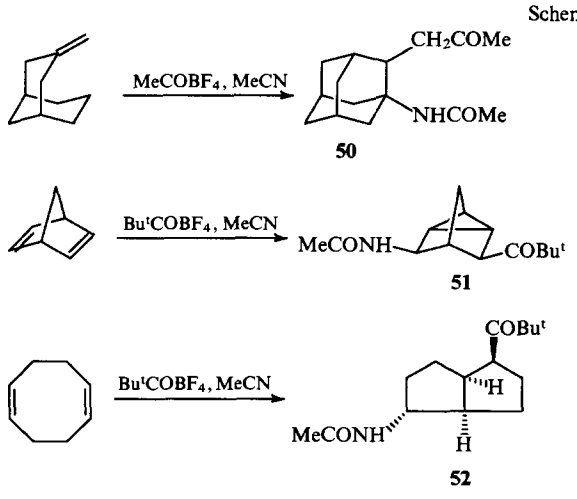
Nonconjugated cyclic dienes interact with the acyl fluoride–nitrile–boron trifluoride system to form the polycyclic amides **50–52**, which are the products of transannular cyclisation (Scheme 3).[97,98] The acylating properties of complex **45** are apparently also manifested in these reactions, but the unusually high stereospecificity observed in these reactions[98,99] may be evidence that in this case too the nitrile does not behave simply as an external nucleophile, participating in some way in the transition state of the reaction.[98]

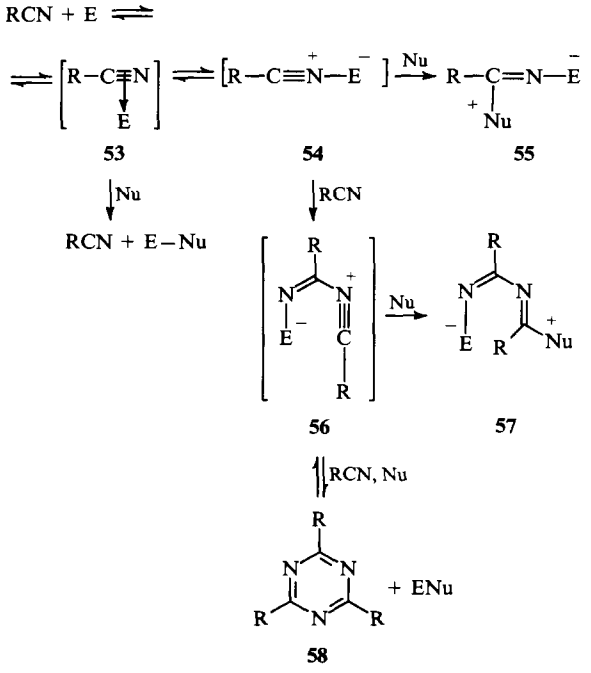
Table 8. The acylamidation of ethynes.

Ethyne	Nitrile	Conditions		Product	Yield (%)
		T/°C	time/h		
Ph–C≡CH	MeCN	20	1		35
Ph–C≡CH	$ClCH_2CN$	0	1		41
n-C_5H_{11}–C≡CH	MeCN	20	1		45
n-C_5H_{11}–C≡CH	$ClCH_2CN$	0	1		39
Ph–C≡C–Ph	MeCN	42[a]	—		0
		42[a]	—		44

[a] The reaction was carried out by refluxing in CH_2Cl_2.

Scheme 3





IX. Conclusion

In conclusion of the consideration of the reactions of nitriles with electrophiles, mention should be made of the fact that they are common to different electrophiles.

The majority of investigators believe that the primary products of the interaction of nitriles with electrophiles are donor–acceptor complexes **53**. A sufficiently strong interaction between the nitrile and the electrophile has not yet been manifested in these π-complexes, so that their treatment with nucleophiles leads to the regeneration of the nitrile. Under appropriate conditions (usually at higher temperatures), the π-complexes **53** are converted into the n-complexes **54**. The n-complexes **54** have a linear structure, their C≡N bond is shortened, and attack by the nucleophile is directed to the nitrile carbon atom with formation of type **55** compounds.

Under favourable conditions (usually in those cases where R is a fairly strong electron-accepting substituent), the second nitrile molecule behaves as the nucleophile and the dimeric salts **56** are formed. These may be stabilised by interaction with the former electrophile, affording compounds having the general formula **57**. Attack by the nucleophile in its interaction with compound **57** is usually directed to the nitrile carbon atom of the second nitrile molecule. Finally, the triazine **58** may be formed; this reaction path is also favoured by electron-accepting substituents R.

The understanding of the by no means simple pattern in the interaction of nitriles with electrophiles, achieved only recently, makes it possible to seek new reactions of nitriles, which will undoubtedly enrich synthetic organic chemistry.

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Dendritic polymers obtained by a single-stage synthesis

M N Bochkarev, M A Katkova

Contents

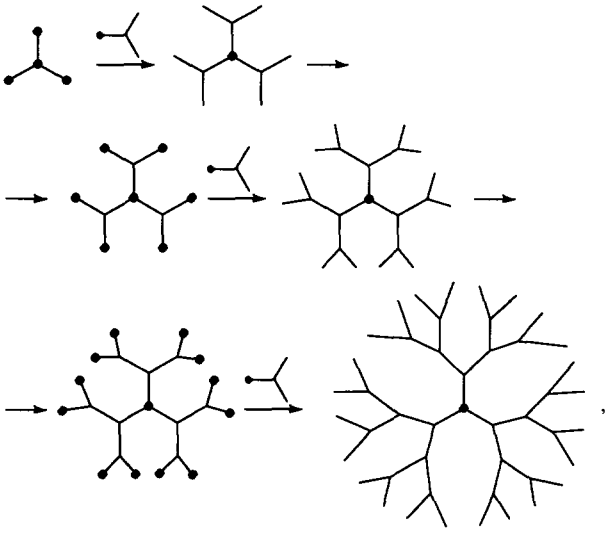
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Abstract. The methods of synthesis, the structure, and properties of the dendritic polymers formed under the conditions of uncontrolled single-stage synthesis are surveyed. The bibliography includes 69 references.

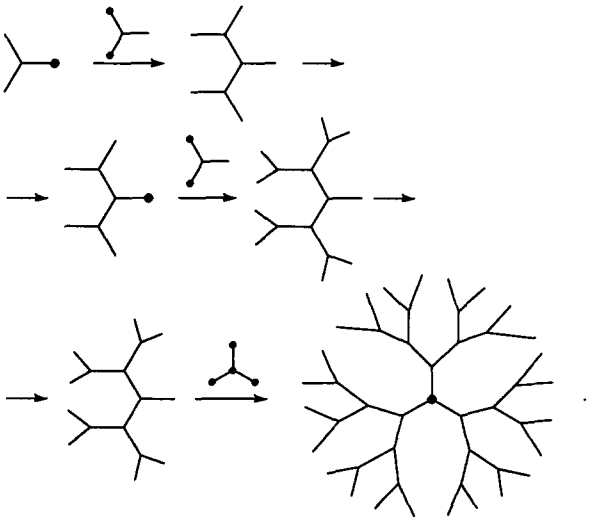
I. Introduction

Studies on polymeric compounds of a fundamentally new type have become one of the most promising and rapidly developing aspects of modern chemistry during the last decade. Their macromolecules have a specific (largely spherical) close-packed shape and the three-dimensional close-packed framework of each molecule consists of concentric layers of branching elementary units. The objects which are studied in this chemical field are so unusual and so difficult to describe within the framework of the IUPAC nomenclature that a new terminology for their designation had to be developed. At the present time, this process is not yet complete and many of the terms, designations, and symbols employed still cannot be regarded as generally accepted. The only firmly established name for the compounds of this class themselves is 'dendrimers' or 'starburst dendrimers' proposed by Tomalia et al.[1] The terms 'arborols' (proposed by Newkome et al.[2]) and 'cascade compounds' are used to a lesser extent. More general designations such as nanomolecules and nanoscopic objects are also employed. The choice of terminology is dictated by the structure of the macrochains, which resembles that of the crown of a tree [dendron (Greek), arbor (Latin) = tree] or a cascade of repeating structural elements, and by the average dimensions of the molecules of these substances (1 – 100 nm). The terms hyperbranched and highly branched polymers have begun to be used recently for the group of dendrimers distinguished by a smaller degree of order in the molecular framework. These objects are in fact the subject of the present review.

One of the fundamental differences between the classical dendrimers and the highly branched polymers is the method of their synthesis. The former are obtained by many repetitions of the chosen sequence of reactions, which makes it possible to grow gradually new generations of layers of elementary fragments around the central atom (or molecule) called the initiator core of the dendritic molecule (divergent scheme), i.e.



or the reverse procedure is employed: the formation of the molecule begins from its periphery and proceeds with increase at each stage in the size of the intermediate dendrons, having a conventional conical shape, the dendrons becoming attached to the core only in the last stage to form the final dendritic macromolecule (convergent scheme), i.e.



M N Bochkarev, M A Katkova Polynuclear Organometallic Compounds Laboratory, Institute of Organometallic Chemistry, Russian Academy of Sciences, ul. Tropinina 49, 603600 Nizhnii Novgorod, Russian Federation
Tel. (7-831) 266 67 95 (M N Bochkarev)

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In both cases, the formation of each generation normally includes at least two reactions (for example, the addition of the initial monomer with protected functional groups to the growing molecule and the removal of the protection from the functional groups). Thus both approaches are not only multistep but also multistage. The combination of these methods, i.e. the formation of giant molecules by the addition of monomer molecules or dendrons to the dendrimer molecule previosly synthesised by the divergent or convergent methods, should also be noted. This procedure makes it possible to synthesise heterolayered dendrimers with a high molecular mass.[3]

In contrast to this, highly branched polymers are obtained under the conditions of uncontrolled single-stage synthesis in which the initial monomers employed are compounds of the type $A-R-B_x$ ($x \geqslant 2$), where A and B are functional groups of two types, which under certain conditions enter into a polycondensation or polyaddition reaction with formation of A–B bonds. Such continuous processes and their possible products have in fact been used as models in the theoretical studies of Flory[4] and Stockmayer,[5] whose communications were the first on the subject of hyperbranched formations with a hierarchical architecture of the molecular framework. However, the first specific synthesis of such compounds, achieved 30 years later by Vögtle and coworkers,[6] were carried out according to a multistep divergent scheme. This strategy of the synthesis, i.e. numerous repetitions of the selected reaction sequence, was adhered to by the vast majority of investigators in the field of dendrimers and cascade compounds.[7–10]

The monodispersity of the polymers obtained under these conditions and the predictability of the architecture of the framework, of the number of functional groups on the surface of macromolecules, and of their shape, size, and molecular mass give incontrovertible advantages to the stepwise method. This procedure has been used for the synthesis of diverse dendrimers, such as polyamidoamine dendrimers,[11] compounds with a carbochain skeleton,[12] including optically active,[15] carbosilane,[13] and carbosiloxane[15] compounds, dendrimers with ferrocenyl end-groups,[16] dendrimers with fullerene as the core,[17] dendrimers with coordinated cobalt[18] and ruthenium[19] atoms, carbaboranyl,[20] phenoxy-,[21] phenylethynyl,[22] phosphino-,[23] phosphonio,[24] phenylene,[25] and high-spin polyradical[26] dendrimers, cascade crown-ethers,[27] tetrathiofulvalene dendrimers,[28] etc.

At the same time, together with the above advantages, the stepwise strategy suffers from a series of disadvantages, the most serious of which is the considerable amount of labour involved due to the need for numerous repetition of the operations. Furthermore, the use of large excesses of the reactants creates problems in the isolation and purification of the dendrimers (intermediate generations and target products). Owing to these difficulties, the dendrimers obtained by the multistep synthesis belong to the category of fairly expensive substances which are difficult to obtain.

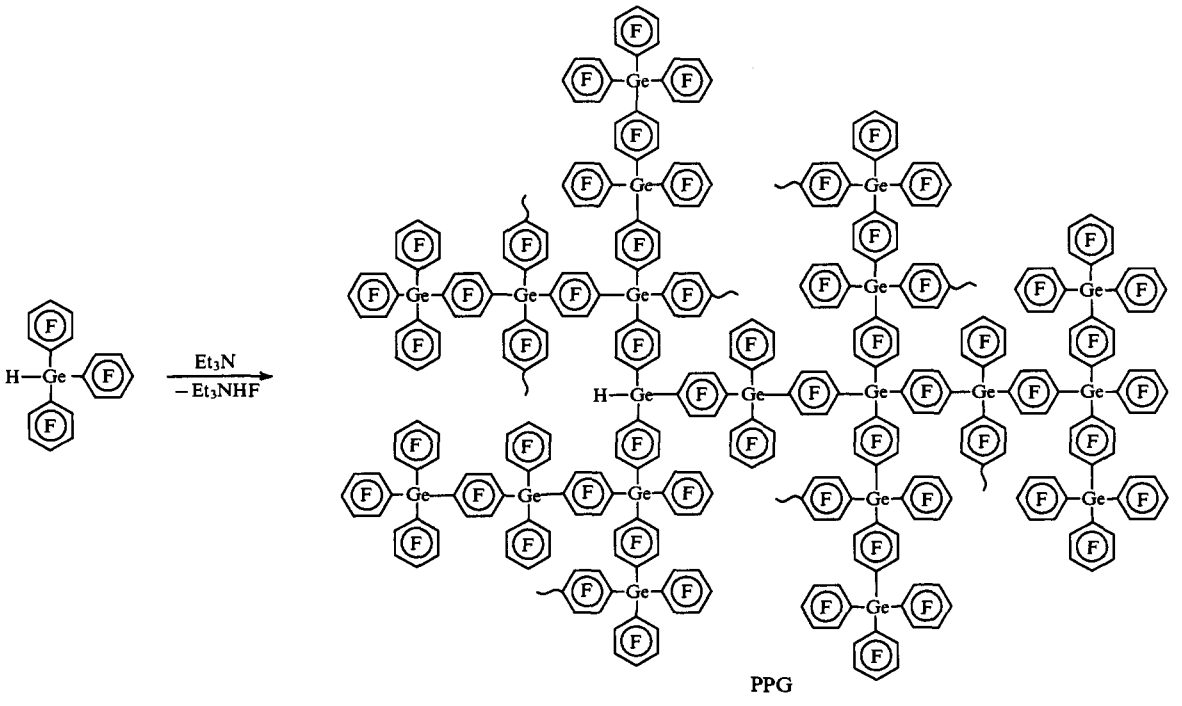
The single-stage method of synthesis of analogous derivatives is free from this disadvantage.

II. Single-stage methods of synthesis and types of dendrimers

As is frequently the case, the invention of compounds with a branched but not cross-linked molecular framework is due to nature, which employs this principle for the formation of glycogen, amylopectin, certain other polysaccharides, and proteins.[29–31]

The first mention of the artificial compounds formed on polycondensation of monomers of the type $A-R-B_x$ and having a cascade structure of the macrochain dates back to the 1920s[32] when the reaction between 2,4,6-trihalophenols and alkali metals with subsequent polycondensation of the resulting phenoxide 2,4,6-$X_3C_6H_2OM$ was carried out. One may assume that weakly ordered dendritic polymers had been obtained even earlier by the Friedel–Crafts polycondensation of benzyl halide derivatives under mild conditions.[33,34] However, in none of these instances were the products considered from the standpoint of the possible organisation of the macromolecules and their belonging to a new class of substances. The same approach to the products, treated as the usual branched polymers without consideration of the specific features of their structure, was also employed in a later study by Kricheldorf et al.,[35] who achieved the cocondensation of 3-(trimethylsiloxy)benzoyl chloride with a small amount of 3,5-bis(trimethylsiloxy)benzoyl chloride. As will be shown below, 3,5-bis(trimethylsiloxy)benzoyl chloride was used subsequently also by other investigators to obtain dendritic polyesters.

Scheme 1



The first specific synthesis of a dendrimeric compound by a single-stage method was achieved by the present authors on the basis of tris(pentafluorophenyl) derivatives of germanium $(C_6F_5)_3GeX$ (X = H, Br, GeR_3).[36-38] The synthesis was based on the earlier observations of the formation of disubstituted tetrafluorophenyl derivatives *p*-MC_6F_4M in the reactions of the organogermanes $(C_6F_5)_3GeX$ with electropositive metals and their organic derivatives.[39-41] A reinvestigation of these reactions and of the substances formed established that in all cases the main organogermanium product is a dendritic polymer — perfluorinated polyphenylgermane (PPG) with the formula $[(C_6F_5)_2.Ge(C_6F_4)]_n$. The best results were obtained when the reaction of the hydride $(C_6F_5)_3GeH$ with triethylamine in tetrahydrofuran (THF) was employed. Synthesis of PPG includes two stages occurring simultaneously: the formation of the anions $(C_6F_5)_3Ge^-$ and their polycondensation as a result of the nucleophilic substitution of the fluorine atoms in the *para*-positions (Scheme 1).

This mechanism of the synthesis of PPG has been confirmed indirectly by the formation of the mercurate complex $\{[(C_6F_5)_3Ge]_3Hg\}^-[(Me_3Si)_2NH_2]^+$ on interaction of $(C_6F_5)_3.GeH$ with $(Me_3Si)_2NH$ in the presence of $[(C_6F_5)_3Ge]_2Hg$ [40] and by the formation of the cross-linked insoluble perfluoropolyphenylenegermanes $[(C_6F_5)_2Ge]_n$ and $[(C_6F_5)_2GeGe(C_6F_5)_3]_n$ from the dihydride $(C_6F_5)_2GeH_2$ and the dihydrodigermane $(C_6F_5)_2Ge(H)-Ge(H)(C_6F_5)_2$.[42] It is interesting to note that the closest analogues of tris(perfluorophenyl)germane $(C_6F_5)_3EH$ (E = C, Si, Sn) as well as the germanol $(C_6F_5)_3GeOH$ do not undergo self-condensation in the presence of amines even on heating.[43] The tin-containing dendritic polymer $[(C_6F_5)_2Sn(C_6F_4)]_n$ was obtained in a low yield by heating $(C_6F_5)_3SnBr$ with alkali metals in THF. The condensation of tris(pentafluorophenyl)silane under the same conditions is accompanied by the elimination of pentafluorophenyl groups.

Side reactions, which lower the yield of the polymer and lead to significant disturbances of the cascade structure of the macromolecules, have been noted also in the polycondensation of the asymmetric digermane $(C_6F_5)_3GeGe(C_6F_5)_2H$ (Scheme 2).[44]

In this case not only the C–F bond but also the Ge–Ge group is subject to attack.

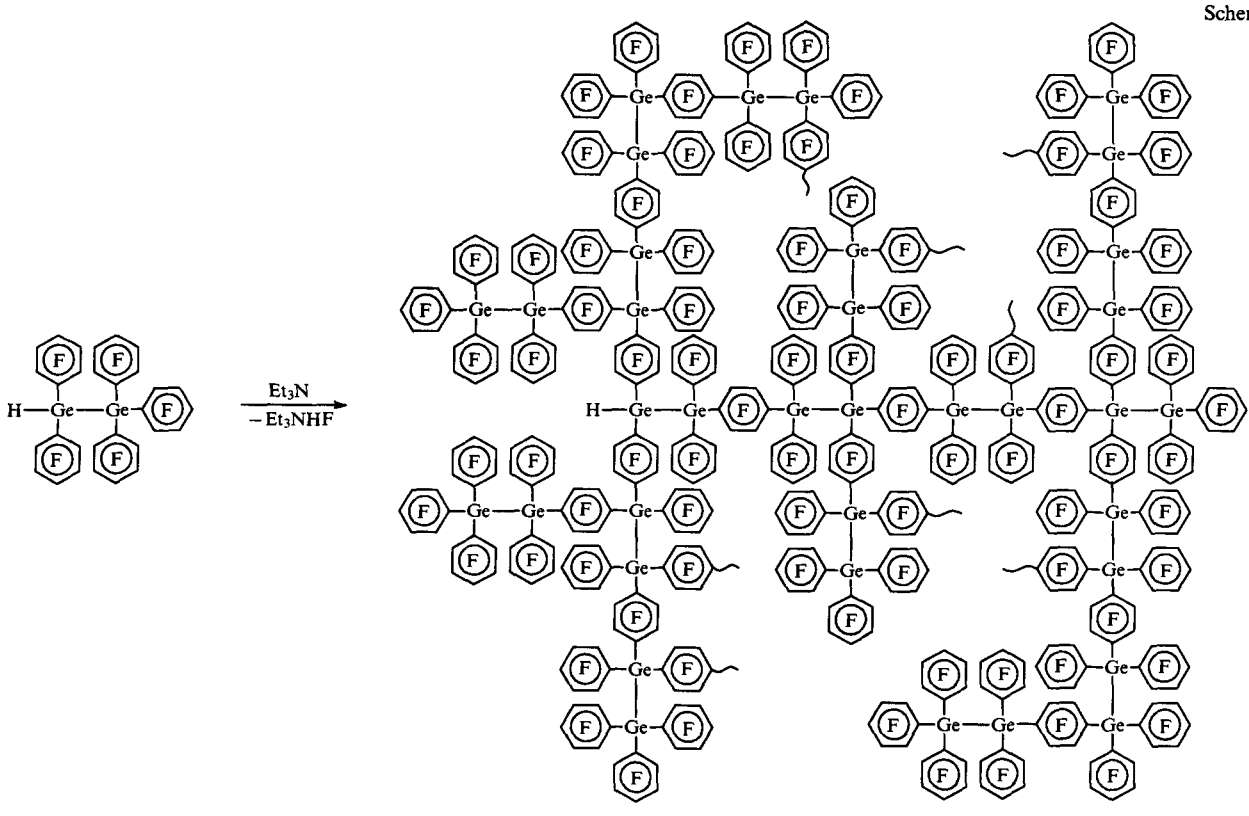
An attempt has been made to synthesise perfluoropolyphenylenegermane from the trihydride $C_6F_5GeH_3$.[45] It might have been expected that the condensation of this monomer in accordance with Scheme 1 would lead to the formation of a dendrimer resembling PPG but having on the surface of the macromolecules the hydride functional groups GeH_3 instead of $(C_6F_5)_3Ge$. The synthesis of such a polyhydrogermane appeared especially attractive, since the high reactivity of the Ge–H group promised to impart to the new polymer properties which would expand its synthetic possibilities. However, in contrast to other pentafluorophenylhydrogermanes, $C_6F_5GeH_3$ does not interact with amines and its reactions with derivatives of reactive metals (RMgX, $C_{10}H_8Na$) lead to linear insoluble polymers $[(C_6F_4)GeH_2]_n$ which are complicated by the elimination of the C_6F_5 groups.

Two brief communications concerning the synthesis of highly branched polyphenylenes by the polycondensation of $3,5\text{-}Br_2C_6H_3MgBr$ (on heating) and $3,5\text{-}Br_2C_6H_3B(OH)_2$ (under catalytic conditions) appeared simultaneously with the first publication on the synthesis of PPG.[46,47] The latter reaction was subsequently investigated in greater detail.[25] The condensation was carried out in an organic solvent–water mixture in the presence of sodium carbonate and $Pd(PPh_3)_4$ (Scheme 3). The mobility of the terminal Br atoms made it possible to employ the dendrimer **1** for the synthesis from it of a series of modified polymeric substances (see Section IV).

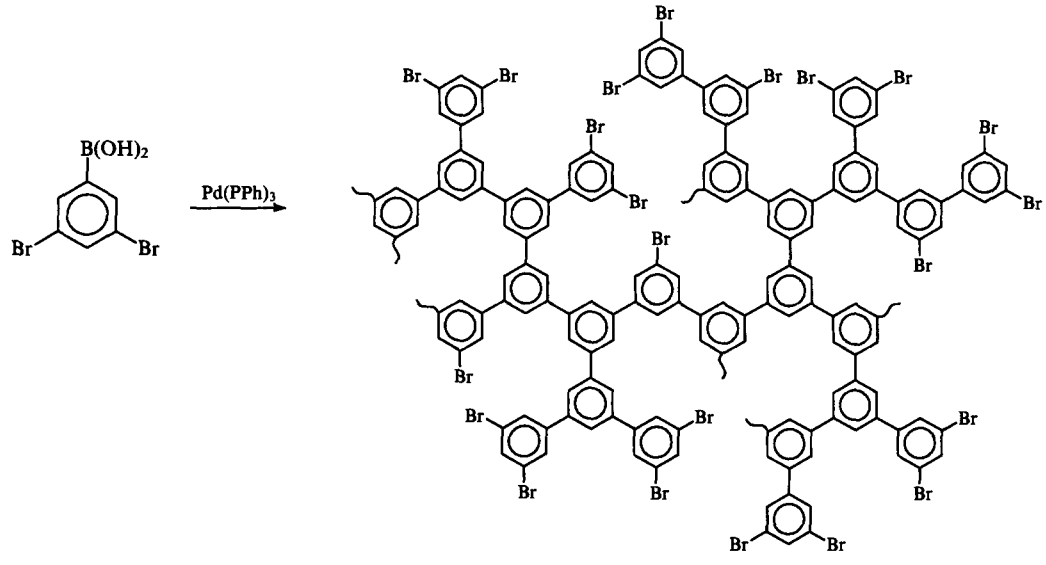
The polycondensation of 3,5-bis(trimethylsiloxy)benzoyl chloride, mentioned above, on heating to 250 °C leads to the formation of a low-molecular-mass and weakly branched polyester in a low yield.[35] By carrying out this reaction with the monomer purified beforehand by distillation, Frechet and coworkers[48] obtained the dendritic polyester **2** in up to 96% yield and a degree of branching of 55%–60%† (Scheme 4).

† The degree of branching is understood as the percentage ratio of the sum of the number of terminal units and the number of units with branching points to the total number of units of the polymer [(see C J Hawker, R Lee, J M J Frechet *J. Am. Chem. Soc.* **113** 4583 (1991)].

Scheme 2

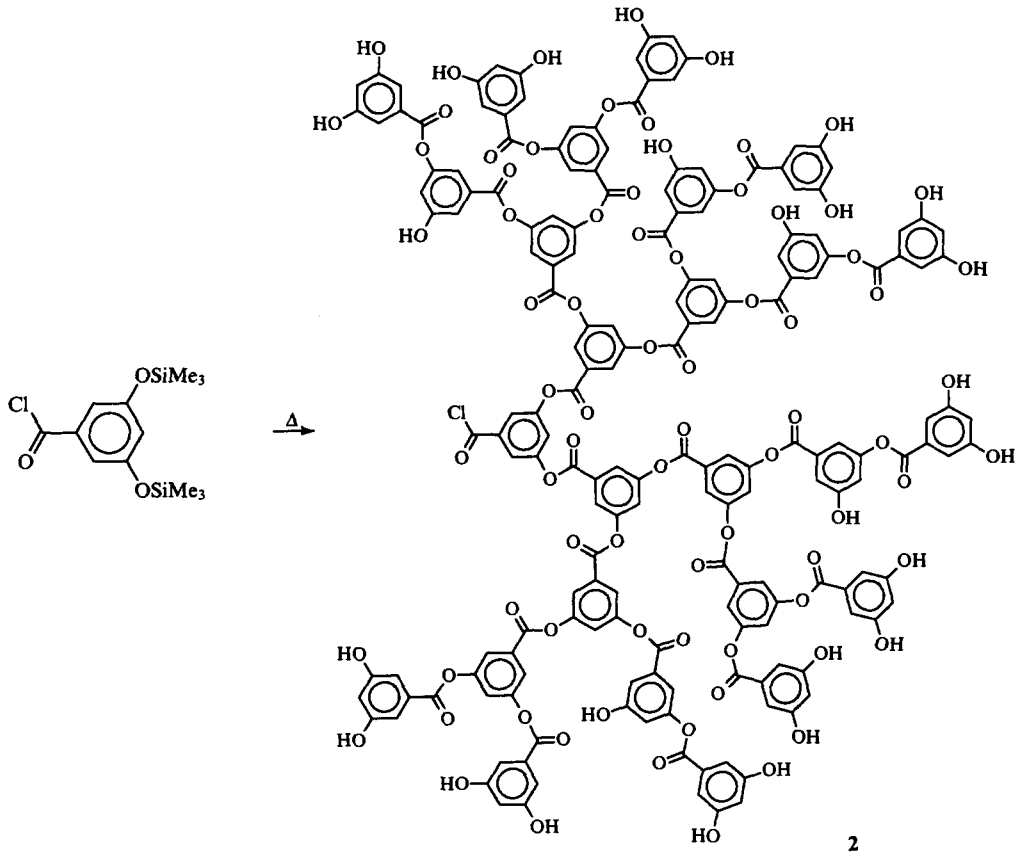


Scheme 3



1

Scheme 4



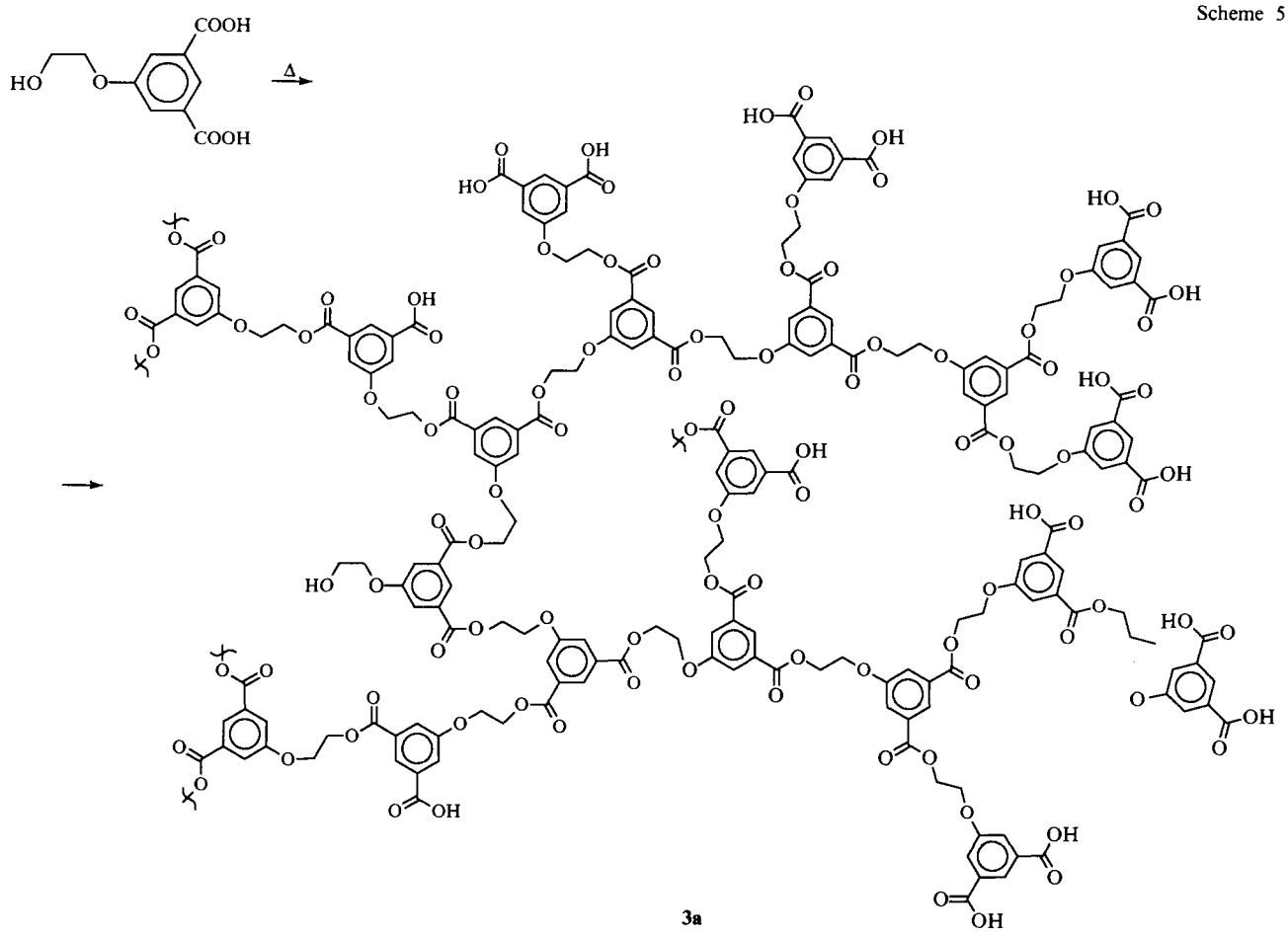
2

Apart from $3,5\text{-}(Me_3SiO)_2C_6H_3COCl$, 3,5-diacetoxybenzoic,[49] 5-(2-hydroxyethoxy)isophthalic, and 5-acetoxyisophthalic acids[50,51] have been used to obtain similar polyesters. The reactions were carried out in the monomer melt without a catalyst or in the presence of ammonium salts. The polycondensation of the hydroxyethoxy-derivative takes place at 180 °C in the presence of catalytic amounts of $Bu_2Sn(OCOMe)_2$ (Scheme 5).

The condensation of 5-acetoxyisophthalic acid requires heating to 250 °C, which promotes dehydration of the carboxy-groups and the formation of the cross-linked insoluble polymer **3a**, which is readily converted into the soluble dendrimer **3b** with acid end-groups on refluxing in a THF–water mixture. The COOH end-groups in the polymers **3a, b** were protected by converting them into ester of amide groups. The cocondensation of 5-acetoxyisophthalic acid with 3-(4-acetoxyphenyl)propionic acid, which occurs under similar conditions, leads to dendritic copolymers with different contents of linear fragments.[51]

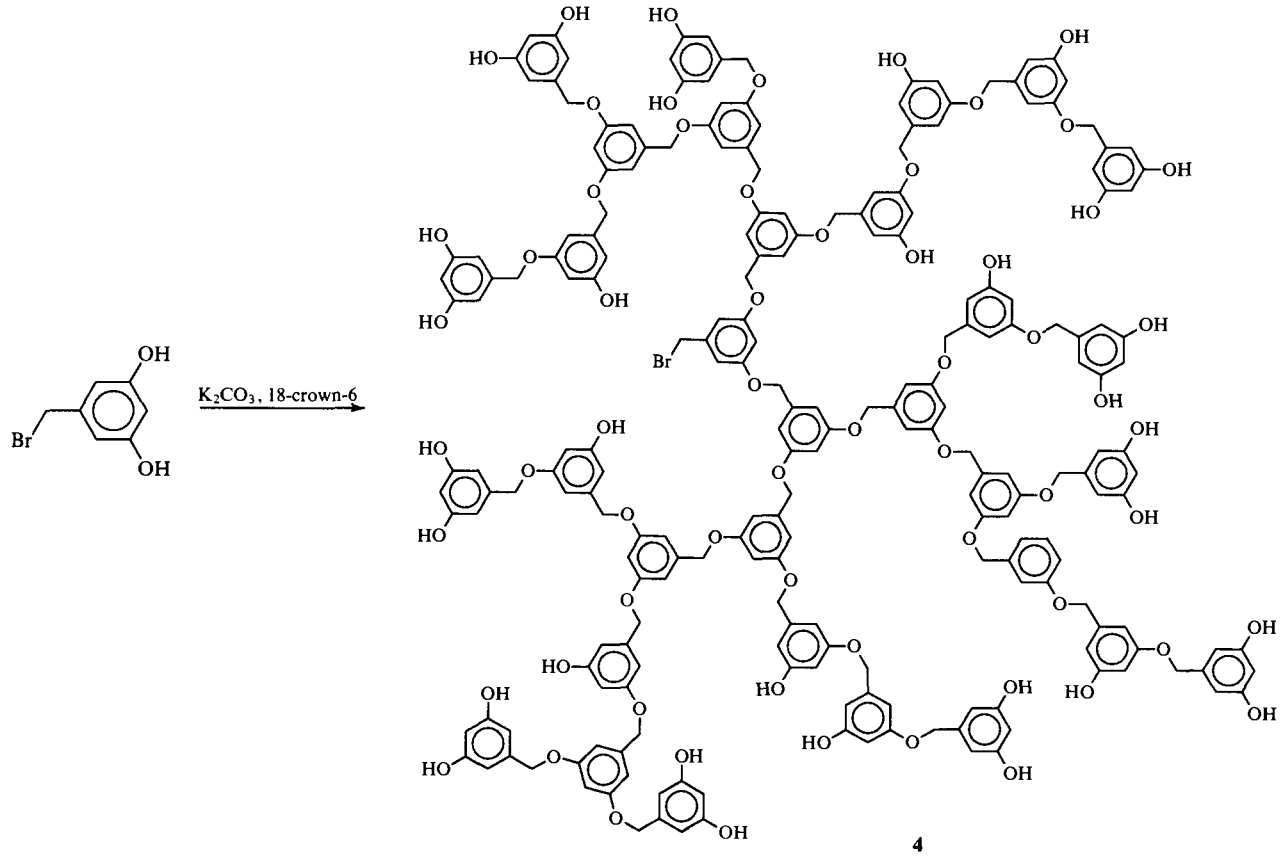
The polyester **4**, based on 3,5-dihydroxybenzyl bromide and having a cascade structure, is synthesised by treatment with K_2CO_3 (Scheme 6).[52,53] Polymer specimens in which the phenolic

Scheme 5



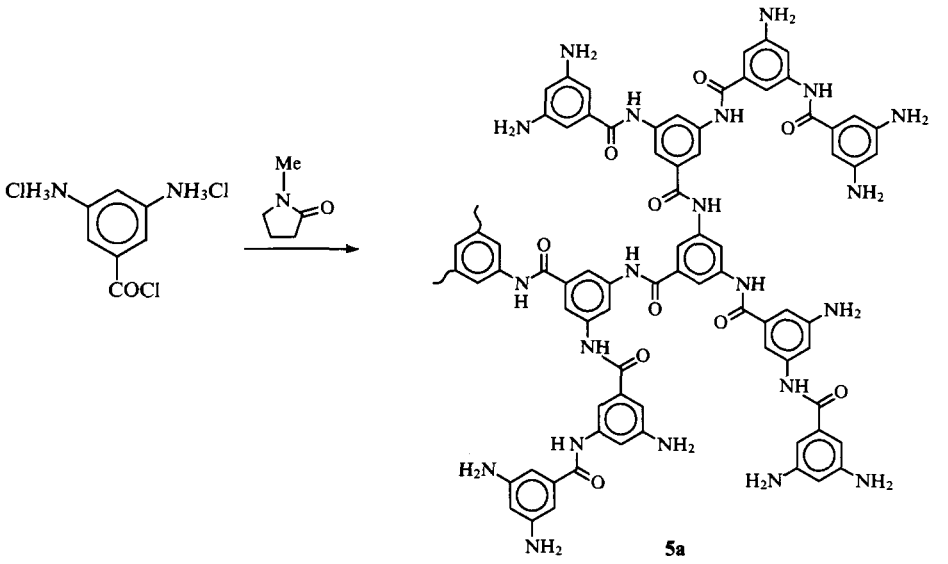
3a

Scheme 6

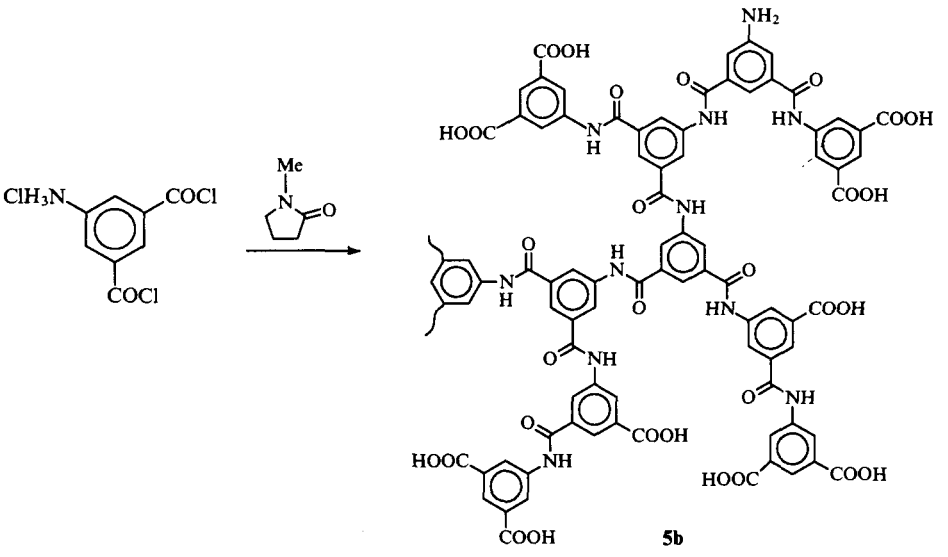


4

Scheme 7



5a



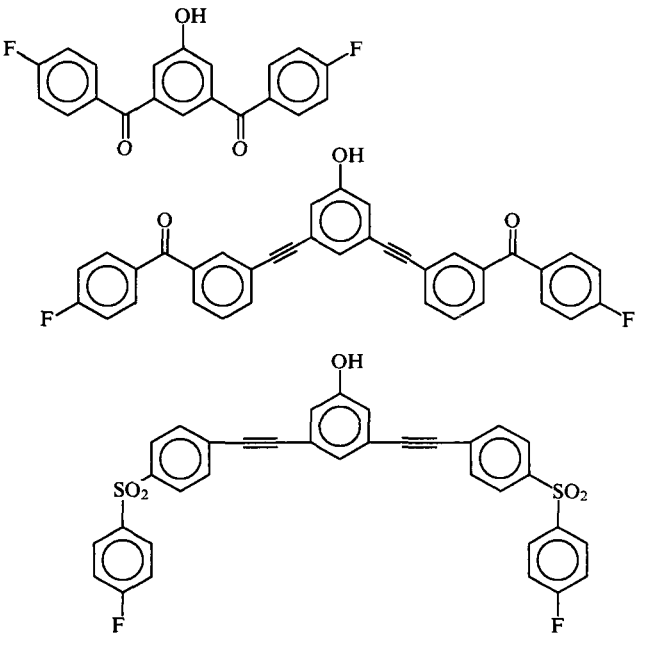
5b

end-groups had been replaced by the inert benzyl groups as a result of the reaction with benzyl bromide were used for subsequent investigations and measurements. The solvent exerts a significant influence on the yield and the molecular mass of the product in this instance: in dichloroethane, the yield does not exceed 38% and $\overline{M}_n$ = 2800, whereas in acetone the yield reaches 73% with $\overline{M}_n$ = 14700. According to ^{1}H NMR data, the polymers formed contain 20%–30% of *C*-alkylated fragments, which are a result of C–C condensation in a side reaction.

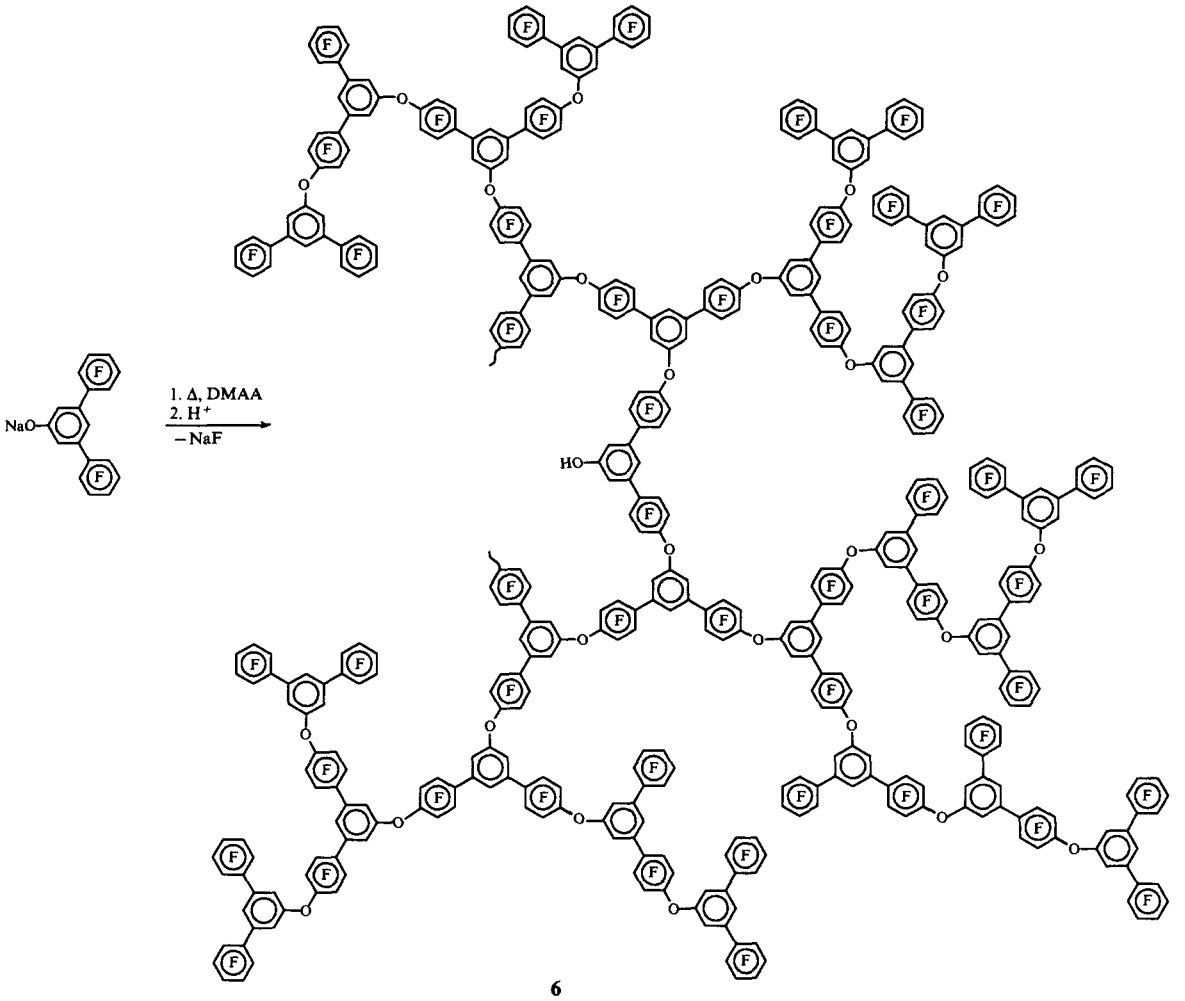
The dendritic aromatic polyamides **5a, b** were obtained from 1,3,5-trisubstituted benzenes in two ways: by the neutralisation of the hydrochloride with subsequent condensation of the resulting free amine (Scheme 7) and by the hydrolysis of the chloride of the sulfinylaminoacid 3,5-$(OSN)_2C_6H_3COCl$ [or 3,5-$(ClCO)_2C_6H_3NSO$].[54]

The dendritic analogues of the well known and widely used linear poly(phenylene oxides) are formed on polycondensation of phenoxides containing pentafluorophenyl or *p*-fluorophenyl substituents in the 3- and 5-positions (Scheme 8).[55]

Other dendrimers of this group were obtained under the same conditions from their monomers



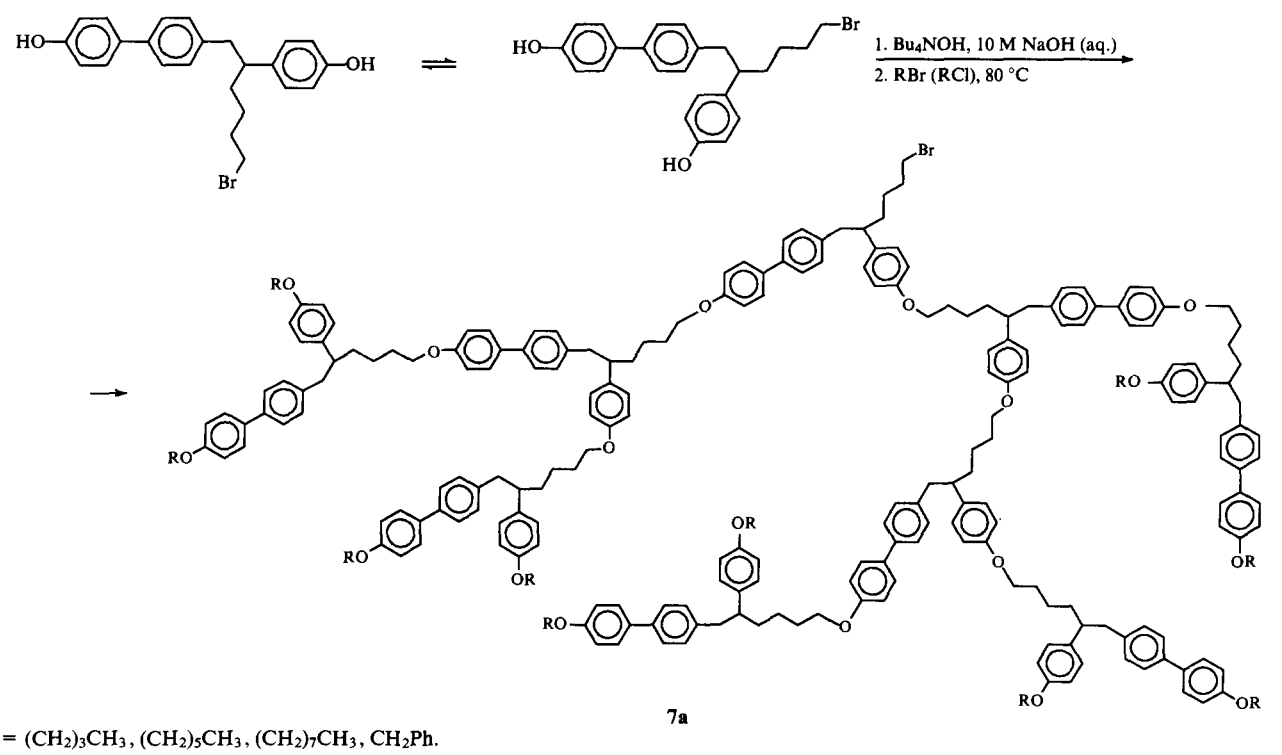
Scheme 8



6

DMAA = *N*,*N*-dimethylacetamide.

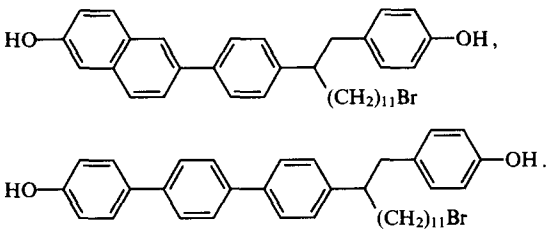
Scheme 9



7a

R = $(CH_2)_3CH_3$, $(CH_2)_5CH_3$, $(CH_2)_7CH_3$, CH_2Ph.

The dendritic polymers **7** of the unusual 'willow-like' type have been synthesised recently from 6-bromo-1-(4-hydroxy-4'-biphenyl)-2-(4-hydroxyphenyl)hexane **7a** and the corresponding decane **7b**.[56,57] The polyesterification was carried out under the conditions of phase transfer catalysis in the presence of tetrabutylammonium hydrogen sulfate with subsequent alkylation of the terminal hydroxy-groups (Scheme 9). Similar polymers have been obtained[57] from the diols

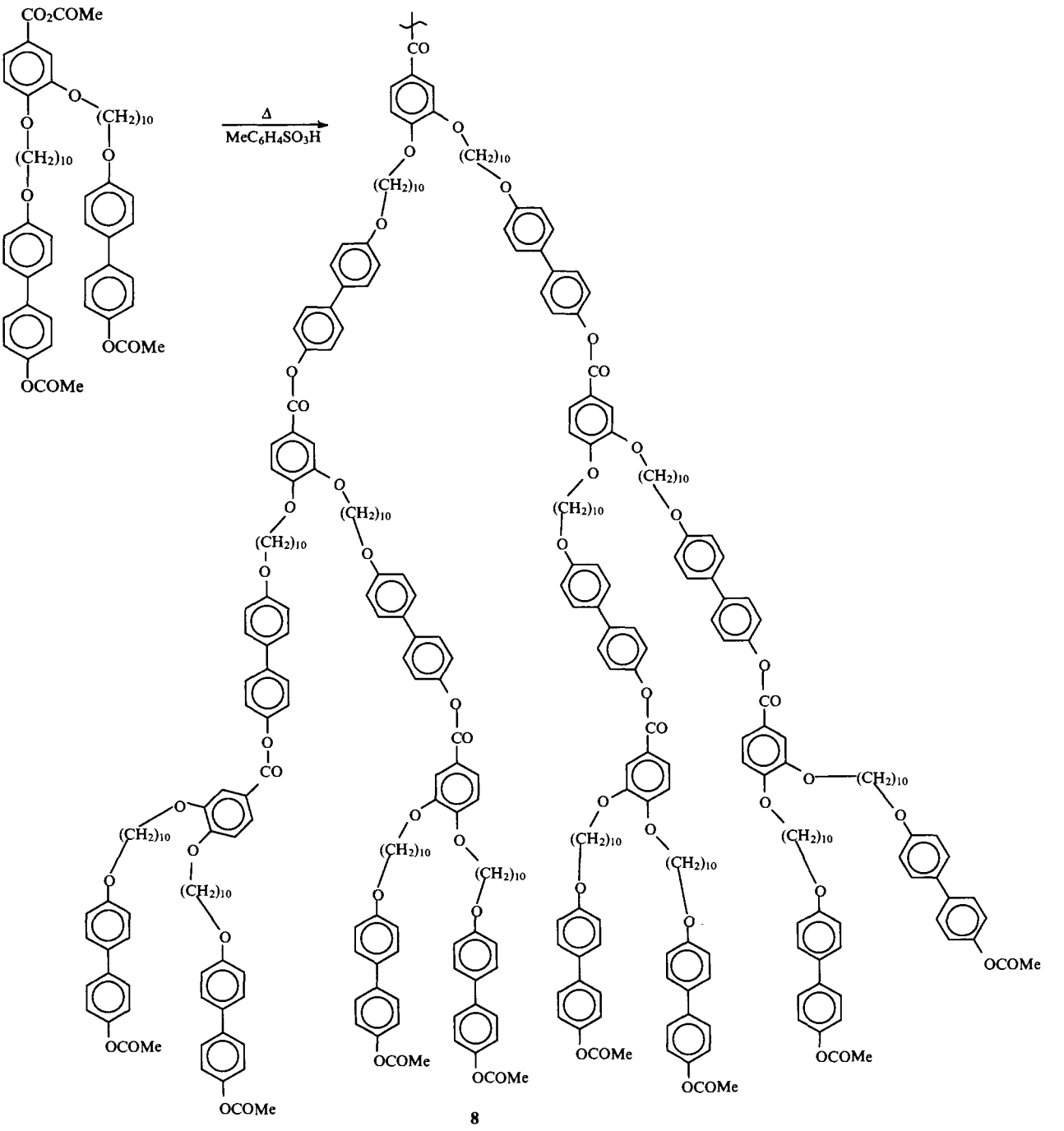


The choice of the monomers for these syntheses was dictated by their mesogenic nature, which permitted the hope that liquid crystal properties might appear in the products.

This was also the aim in the synthesis of the polyester **8** by heating a melt of the monomer at 240 °C in the presence of toluene-*p*-sulfonic acid (Scheme 10).[58] After the polycondensation had been completed, the end-groups were functionalised by adding to the mixture the chloride of a substituted benzoic acid with asymmetric substituents.

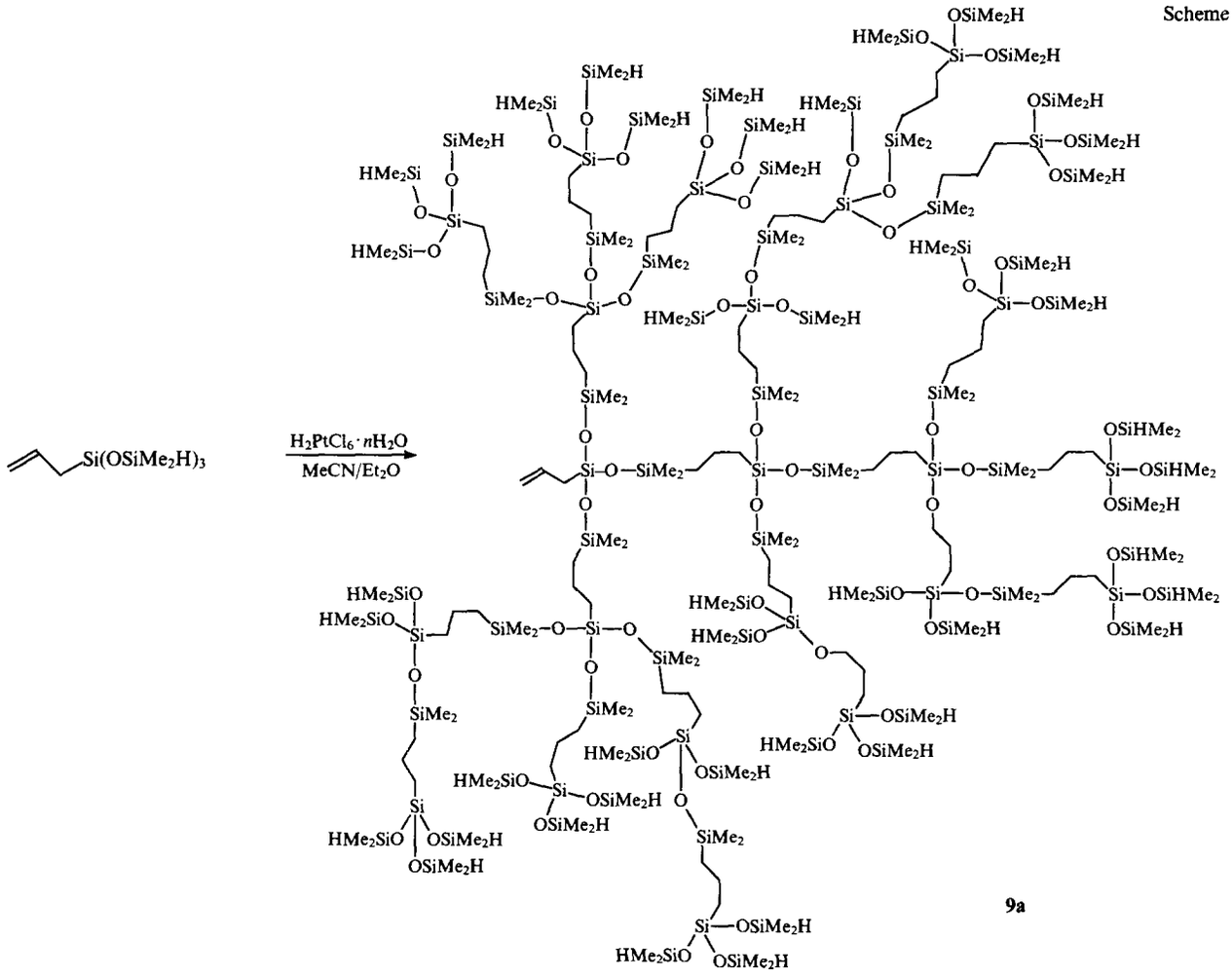
In order to obtain the dendritic polycarbosiloxanes **9a, b**, the allyl(siloxy)silanes $CH_2=CHCH_2Si(OSiMe_2H)_3$ and $CH_2=CHCH_2SiMe(OSiMe_2H)_2$ were synthesised by the cohydrolysis of chlorodimethylsilane with allyldichlorosilane and allyldichloro(methyl)silane respectively.[59,60] The subsequent polymerisation of these monomers in the presence of a platinum catalyst at 52 °C led to dendrimers containing 3–4 layers of monomer units (Scheme 11). In order to prevent intermolecular

Scheme 10

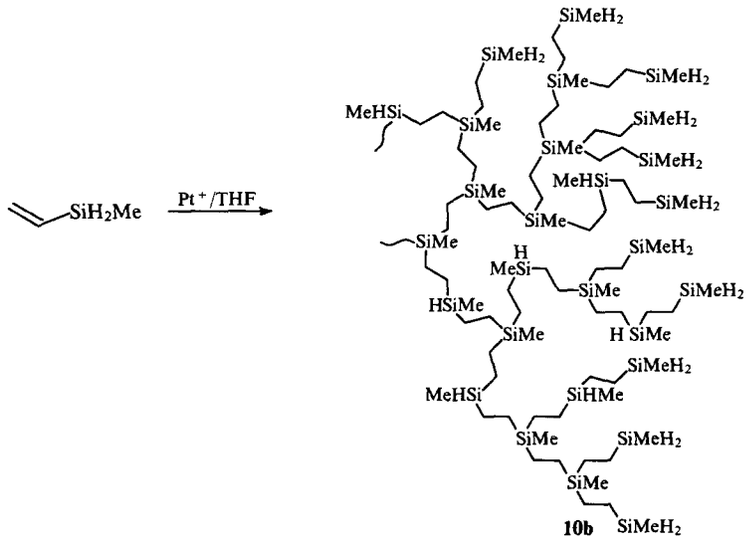


8

Scheme 11



Scheme 12



cross-linking as a consequence of the oxidation of the Si–H end groups and the formation of Si–O–Si bridges, leading to a decrease in the solubility of the polymers, the freshly prepared polysiloxanes **9a**, **b** were treated with allyl phenyl ether. As a result of the addition of the latter, the reactive Si–H groups were replaced by the inert ether end-groups Si–$CH_2CH_2CH_2OPh$.

The same reaction, i.e. catalytic hydrosilylation, was used to obtain the group of dendritic polycarbosilanes **10a–d** from the allyl- and vinyl-silanes $(CH_2{=}CHCH_2)_2MeSiH$, $(CH_2{=}CHCH_2)_3SiH$, $CH_2{=}CH(Me)SiH_2$, and $(CH_2{=}CH)_2{=}MeSiH$ (Scheme 12).[61] All the reactions come to an end after several hours (at 85 °C) and afford high yields of dendritic polymers in the form of viscous transparent liquids. Derivatives with allyl end-groups were then used to obtain modified carbosilanes.

III. The molecular mass, shape, and structure of the macromolecules

In considering the theoretically ideal polycondensation reaction of type $A-R-B_x$ monomers, de Gennes and Hervet [62] concluded that such a reaction should lead to the maximum possible molecular mass, i.e. to a polymer the molecular mass of which is determined solely by the amount of the monomer introduced into the reaction. However, studies have shown that all real processes give rise to dendrimers with a limited molecular mass and size of the macromolecules. The addition in this instance of the initial monomer to the reaction mixture after the completion of the process leads neither to an increase in the molecular mass nor to the appearance of a new fraction of the polymer with a new value of $\overline{M}$.[25,36,61] This finding cannot be rigorously explained, because the molecules of all the dendrimers described above contain on their surface active functional groups capable of combining with additional monomer molecules and hence of giving rise to new generations of layers.

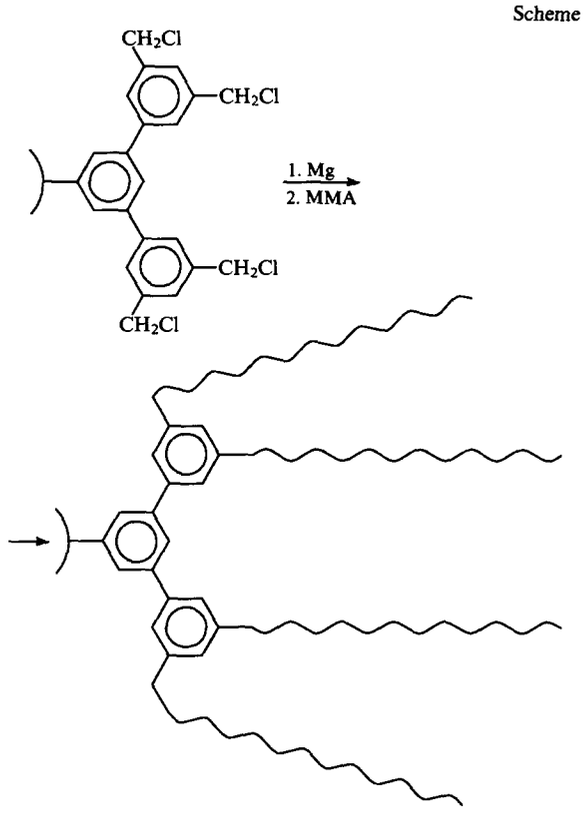
The limitation of the molecular mass of the polymers in real processes has been attributed [25,59,60,63] to steric hindrance, which increases with increase in the size of the macromolecule, or to the formation of an intramolecular ring incorporating group A in the growing dendron $A-[R]_n-B_y$. Apparently this explanation is valid for the convergent mechanism of the formation of the dendritic molecule. However, there are grounds for the hypothesis that, under the conditions of the uncontrolled single-stage synthesis, all versions of the growth occur—convergent, divergent, and their combinations. All three mechanisms are then equally probable in the initial stages. The contributions of the convergent and combined mechanisms ensure a rapid growth of the molecule up to a definite critical size, after the attainment of which the divergent mechanism becomes dominant (as a result of the decreased shielding of the active centres), which leads to a sharp retardation of the increase in $\overline{M}$. (In this respect, there is no doubt about the influence of steric factors.) Hence it follows that the observed limiting values of $\overline{M}$ for all types of dendritic polymers obtained via a single-stage synthesis are only apparent. The introduction of an additional amount of the monomer into the reaction mixture should lead not only to the formation of a new portion of molecules with the 'standard' size but also to some increase in the molecular mass ($\Delta\overline{M}$) of the molecules already present. However, this increase is readily masked against the background of the increase in the overall mass of the polymer.

An indirect confirmation of this hypothesis is provided by the procedure discovered for the rapid increase in the molecular mass of PPG,[36] in which the least soluble fraction and hence the fraction with the highest molecular mass, isolated beforehand from the standard polymer, is introduced into the reaction with a fresh portion of the monomer, where it plays the role of a giant initiator core. The sixfold repetition of this operation made it possible to obtain PPG with a molecular size in excess of 2200 Å for an initial diameter of 50–55 Å. On the other hand, in the synthesis of PPG in the presence of $(C_6F_5)_4Ge$, which plays the role of a kind of inhibitor of the convergent path, a polymer with a lower molecular mass was obtained.[43]

The same principle, i.e. the use of dendritic molecules as the starting compounds, was used in the synthesis of star polymers based on the polyphenylene dendrimer **1** (Scheme 13)[63] and the carbosilane dendrimer **10a**.[61]

The degree of polymerisation n in real cascade compounds obtained in a single stage synthesis varies from 9–15 (for dendrimer **7a**)[56] to 200–300 (for PPG and the polymers **6a–d**).[55] Evidently the type of the monomer and not the rate of reaction exerts a decisive influence under these conditions. Thus, the dendrimer **1** with $n = 25-30$ and PPG with $n = 300$ are formed equally rapidly at room temperature, whereas the triphenylene polymer **6a** ($n \approx 330$) is formed on heating for 0.5–2.0 h.

Scheme 13



The conditions under which the synthesis is carried out affects the degree of polymerisation to a lesser extent. However, in a number of instances a change of the solvent, of the monomer concentration, of the temperature, and of the reaction time entails a change in the degree of polymerisation by a factor of 2–3.[48,55]

The polydispersity of the dendritic polymers obtained by a single stage synthesis does not exceed three in most cases. M_w/M_n exceeds 4 only for certain specimens of the polymers **6a–d** and is up to 10 for the dendrimer **3b**. In the case of the polymer **3b**, the molecular mass distribution of the product is polymodal.[51]

One of the most important characteristics of dendrimers is the shape and linear dimensions of the macromolecules. The construction of three-dimensional models of dendrimers showed that after only 3 generations the molecules approach a spherical shape and become regularly spherical following a further increase in the number of generations. The spherical form of the cascade compounds is apparently in fact responsible for their antifriction properties.[64]

Another characteristic feature of the dendrimer molecules is the presence of cavities, the size of which depends on the geometrical characteristics of the elementary unit.[25,43] In the dendrimers **1** and in PPG, the size of the cavities is 5–6 Å. The presence of unoccupied cavities in the molecules of the dendrimers makes it possible to employ them in compositions of the 'guest–host' type. Such complexes have been obtained for the polyphenylene–*p*-toluidine system.[25]

In the case of PPG,[36–38,43] the molecular diameter was determined by small angle laser scattering (SLS), small angle X-ray scattering, electron microscopy, and the calibrated filter method. The first two methods give rise to a significant scatter. For a PPG specimen with a molecular mass of $(1-1.5) \times 10^5$, which corresponds to $n = 180-270$ and a number of generations $G = 4-5$, it was found that the diameter of the macromolecules is 130–140 Å. Spherical particles with a similar diameter (~200 Å) have been observed by electron microscopy for the same specimen. PPG with a molecular mass of 400 000 has particles of the same size. However, repeated measurements on a standard PPG specimen demonstrated a significantly smaller

average diameter, namely 50–55 Å.[43] The unduly large molecular dimensions obtained from measurements by small angle laser and X-ray scattering are evidently associated with the low accuracy of these methods.

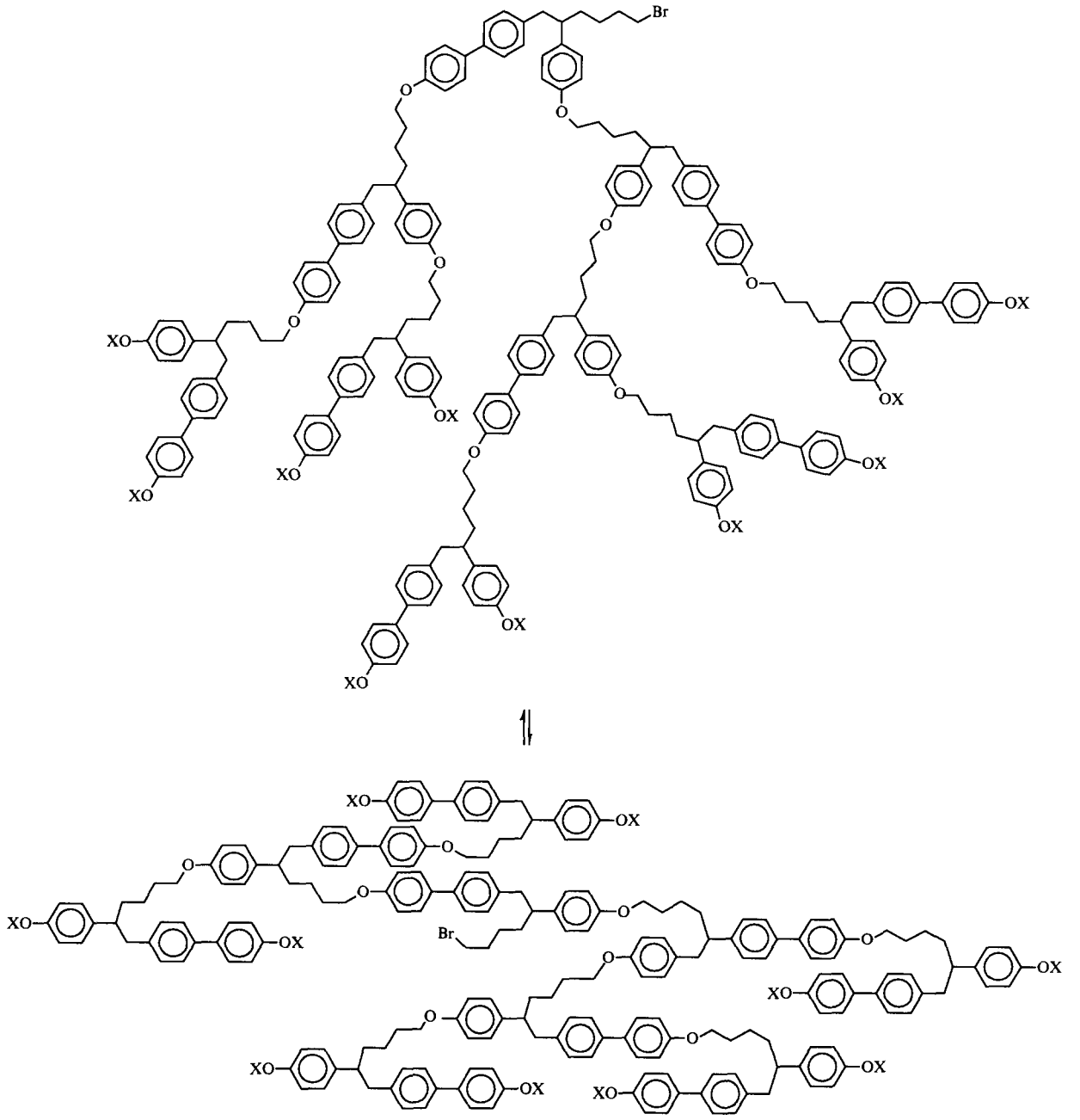
Computer modelling showed that PPG molecules have a diameter of 52.9 Å for $G = 4$ and 63.2 Å for $G = 5$. The calculated molecular masses of the polymer (for a 100% degree of branching) with $G = 4$ and 5 are respectively 90 000 and 270 000. Taking into account the smaller degree of branching in the real polymer, the agreement of the values of $\overline{M}$ obtained with the experimental value of 100 000–150 000 may be regarded as satisfactory.

It has been found for the dendritic polyphenylene **1**[25] and the polyester **2**,[48] in which the multiplicity of the monomer unit is 2, that the degree of branching of these polymers (according to NMR spectroscopic data) does not exceed 60%–70%. In addition, one should take into account the fact that, when the molecule is formed under the conditions of uncontrolled synthesis, the role of initiator core may be assumed not only by the $A-R-B_x$ monomer with a blocked functional group A but also by the ring $[-A-R-B_x-]_n$ formed in the initial stage via intramolecular condensation. As a result of this, the deviation from the ideal dendritic structure is inevitably reflected in the molecular mass and linear dimensions of the macromolecules obtained. It has been suggested that a decrease in the monomer concentration in the initial reaction mixture promotes the formation of intramolecular rings.[55]

IV. Properties

Like the usual flexible-chain polymers, the dendrimers obtained by a single-stage synthesis are viscous liquids, amorphous white powders, or vitreous colourless or pale-yellow substances. Many of them are capable of forming film coatings, but their mechanical properties (for example, their tensile strength) are significantly inferior to those of the usual polymers. However, their employment as modifying additives to rubber compositions based on siloxane raw rubbers leads to a significant increase in the tensile strength of the latter.[61]

Scheme 14



All dendritic polymers are readily soluble in organic solvents such as toluene, chloroform, acetone, and THF. Compared with the linear polymers formed from isotypical elementary units, the solubility of dendrimers is higher. It has been suggested that this is associated with the spherical shape of the molecules, which prevents the close packing of the polymer segments.[48] The peripheral functional groups also exert a considerable influence on the solubility: thus the introduction of alkyl terminal substituents tends to increase the solubility of the polymers in hydrocarbons, whilst the use of carboxylate, hydroxy-, or hydrochloroammonio-end-groups solubilises previously insoluble dendrimers.[25,54,63]

One of the characteristic properties of all dendrimers, including cascade polymers, is a low viscosity of their solutions [the viscosity of PPG solutions is four orders of magnitude lower than that of the solutions of poly(butyl methacrylate) with a similar molecular mass].[65] The molecular mass and concentration of the solutions exert little influence on their viscosity.[36,51,65] In terms of their rheological properties, these substances are closer to suspensions than to solutions of flexible-chain polymers. It is of interest to note that, when a small amount of the dendrimer is added to the normal polymer, the viscosity of the melt of the mixture is significantly reduced.[63]

The spatially fractal nature of the macromolecular framework of dendrimers indicates their possible crystallinity. However, the deviations in the spatial disposition of the elementary units from the ideal sites as well as the reduced degree of branching in the real specimens make it possible to obtain crystals only for first and second generation dendritic compounds.[66] All the remaining polymers of this class are amorphous, which is indicated by the absence of melting points and crystallisation temperatures in these compounds.[55,67] The glass points of isotypical polymers depend little on the molecular mass, but change markedly when the end-groups are altered.

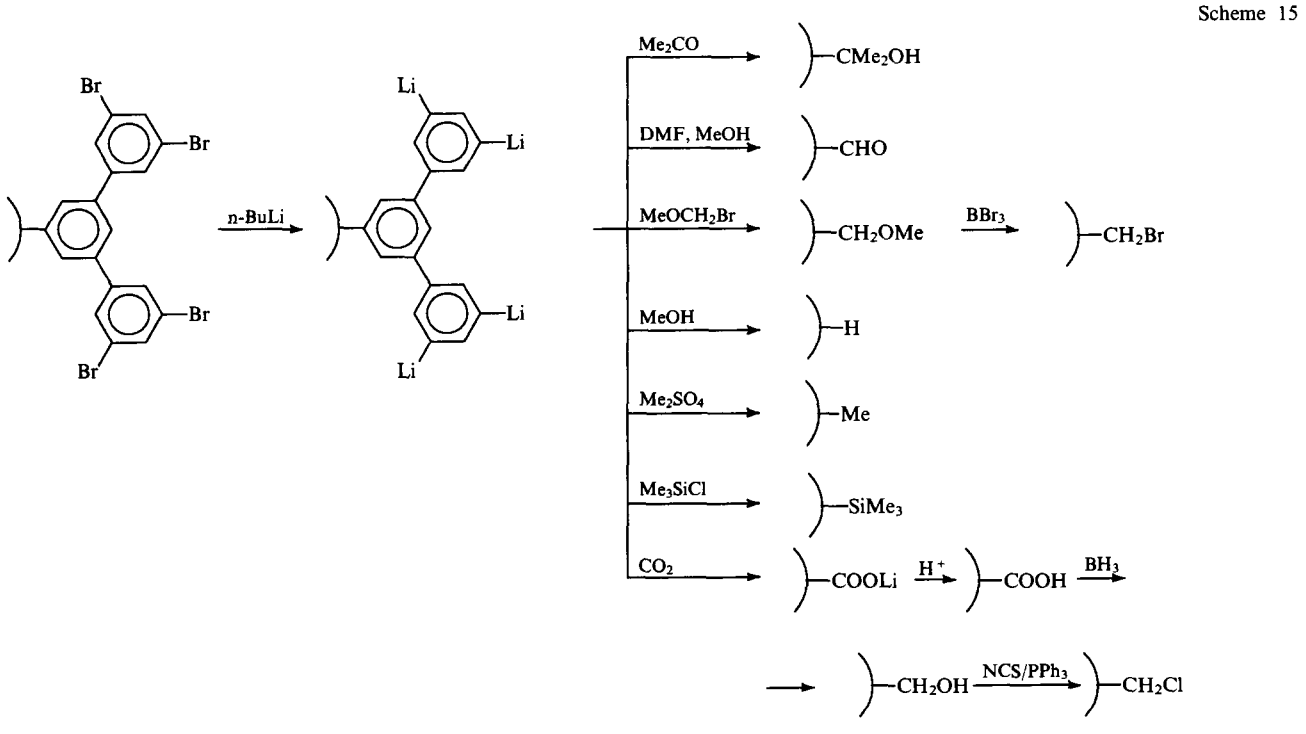
The 'willow-like' dendrimers **7**, obtained by Percec and Kawasumi[56,57] from monomers having mesogenic properties by virtue of their conformational isomerism, are thermotropic liquid crystal substances. It has been suggested that, both in the isotropic phase and in solution, these substances contain mesogenic elementary units in the *gauche*-conformation (or in a *gauche*–*anti* dynamic equilibrium). Such conformation of the units gives rise to the hierarchical architecture of the molecular framework characteristic of dendrimers. On decrease in temperature, the elementary units pass to the *anti*-conformation, which entails a change in the tree-like macromolecular skeleton. They acquire a compact form, corresponding to the nematic mesophase of the polymer (Scheme 14). The transition has been noted in the temperature range from 20 to 40 °C depending on the length and nature of the end-groups of the macrochains.

The existence of a liquid-crystal phase at room temperature has also been noted in a study of solutions of the polymers **5a, b** in amides.[54] For the dendritic polyester **8**, the formation of the cholesteric mesophase has been noted in the temperature range 60–148 °C.[58] By virtue of the presence of chiral end-groups, the same polymer is optically active.

The study of the temperature dependence of the heat capacity of PPG over a wide temperature range (0–550 K) showed that the specific features of the molecular structure of the dendrimer and the molecular shape are hardly reflected in the thermodynamic characteristics of the polymer.[67]

The thermal stability of dendritic polymers is as a rule higher than that of their linear analogues and the corresponding monomeric compounds.[46,48,55,63,68] The polyphenylene dendrimers **1** and **6** belong to the class of the most thermally stable polymeric substances. They begin to decompose in air on heating above 500–550 °C.[55,63] PPG is almost as stable.[68] When PPG is heated at 420 °C for 1.5 h, it loses 4.5% of its mass, the elimination of C_6F_5H and C_6F_6 molecules and partial cross-linking of the macromolecules being noted under these conditions. Among other thermal decomposition products, fluorine and the digermane $[(C_6F_5)_3Ge]_2C_6F_4$ were noted. Decomposition at 580 °C leads to the formation of carbon and germanium. It has been found that the addition of small amounts of dendrimers to the usual polymeric substances frequently increases the thermal stability of the latter.[63,68,69] It has been observed for PPG that the temperature range in which the dendritic polymer exhibits a stabilising activity coincides with the temperature range of its decomposition. This suggests that the substances responsible for the stabilising effect are not the dendrimers themselves but the low-molecular-mass products of their decomposition.[69]

Scheme 15



The possibility of modifying polymers **1** and **4** by replacing the peripheral functional groups has been investigated.[47,52,63] It has been found that the bromine atoms and the phenolic groups in the dendrimer **1** can be replaced by alkyl, aryl, carboxy-, carboxylate, haloalkyl, ethynyl, etc. groups (Scheme 15).

During the modification, 70% – 80% of the functional groups of the initial polymer are as a rule exchanged. It has been noted that a polymer with partially substituted functional groups enters more readily into the subsequent substitution reaction. This property, which has been observed also in relation to other examples,[3] is apparently common to all the dendritic formations. It has been suggested that this may be caused by the local polarisation of the functional groups. Thus the replacement of the functional end-groups, accompanied by significant changes in the solubility and glass point, permits the deliberate alteration of the characteristics of dendritic materials and leads to prospects for the synthesis of micellar and lyotropic systems.

The high reactivity of the peripheral functional groups in the dendrimer **1a** and its derivatives has been used to synthesise polymers of a new type, the so-called star polymers. The macromolecule of such a compound, obtained from compound **1**, closely resembles the shape of the sea urchin.[63] Its 'body' comprises the molecule of the initial dendrimer and the outgoing 'rays (needles)' consist of the linear oligomer and polymer chains. These molecules were synthesised by the successive Br/Li/$SiMe_2R$ (R = CH_3, C_8H_{17}, $C_{18}H_{17}$, $C_{30}H_{61}$) substitution of functional groups or by growing linear polymer chains [of polypropiolactone and poly(methyl methacrylate)] on the surfaces of the spherical molecules, where the dendrimer molecule plays the role of the initiator core.

Thus, one may conclude that, despite the low organisation of the molecular architecture of the dendritic polymers obtained by a single-stage synthesis, their physicochemical properties differ little from those of the dendrimers obtained by the multistep method. Taking into account the advantages of a single-stage synthesis of the dendrimers and the highly promising practically useful properties of such substances, one may confidently predict a vigorous development of this aspect of modern chemistry in the immediate future.

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The synthesis and biological activity of 4-[bis(2-chloroethyl)amino]-DL-, L-, and D-phenylalanine amides and peptides

V P Krasnov, E A Zhdanova, L I Smirnova

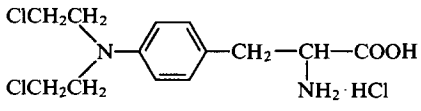
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Abstract. The review is devoted to the synthesis and biological properties of the amides and peptides containing the stereoisomers of 4-[bis(2-chloroethyl)amino]phenylalanine. The approaches to the selection of the structures of the compounds indicated, ensuring an increase in the selectivity of their antitumour activity, are examined. The bibliography includes 131 references.

I. Introduction

Sarcolysine (Sarc) or 4-[bis(2-chloroethyl)amino]-DL-phenylalanine hydrochloride **1** and melphalan (Mel) or 4-[bis(2-chloroethyl)amino]-L-phenylalanine hydrochloride **2**, which are antitumour preparations widely used at the present time, have been synthesised and investigated independently and simultaneously by two groups of investigators in the USSR and England.



1–3

Continuing the idea of L F Larionov concerning the use of essential metabolites, in particular aminoacids, as carriers for the alkylating group, sarcolysine[1] and its enantiomers based on L- and D-phenylalanines have been synthesised in the Soviet Union. The D-enantiomer **3** [medphalan (Med)] was synthesised in England under Bergel's supervision.[2,3]

V P Krasnov, E A Zhdanova Aminoacid Chemistry Laboratory, Institute of Organic Synthesis, The Urals Branch of the Russian Academy of Sciences, ul. S Kovalevskoi 20, 620219 Ekaterinburg, Russian Federation.
Fax (7-343) 244 59 54. Tel. (7-343) 249 30 57.
L I Smirnova The Oncological Scientific Centre, Russian Academy of Medical Sciences, Kashirskoe shosse 24, 115478 Moscow, Russian Federation. Fax (7-095) 230 34 50. Tel. (7-095) 111 82 95.

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On the basis of experimental data, the authors[2,4] established that the L-form **2** is more active than the D-form **3**. This is probably associated with the difference in the transport of the stereoisomers, their chemical transformation in the organism (medphalan is deaminated by D-aminooxidase much faster than melphalan), and the nature of the tumours.[5]

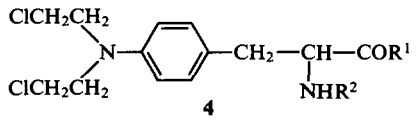
It was established that the transport of melphalan to the tumour cell takes place with the aid of two transferring systems: the L system, which transports leucine, phenylalanine, tryptophan, and valine, and a system similar to ASC, which transports alanine, serine, and cysteine.[6–8] The pharmacokinetics of ^{14}C-labelled sarcolysine and melphalan have been considered in a review[9] and in another communication.[10] Melphalan has been used clinically for the treatment of the same tumours as sarcolysine.[11]

The high activities of sarcolysine and melphalan and their successful clinical application stimulated the development of a new aspect of the chemotherapy of cancer — the synthesis and study of the derivatives of these compounds, as well as the synthesis of the cytotoxic derivatives of other aminoacids. Aminoacids and peptides are known to pass through the membranes of tumour cells 4–5 times more readily than through those of normal cells[12] and there is therefore a possibility of their accumulation in the cancer cell. On this basis, aminoacids and peptides have been frequently used as 'transporters' of alkylating agents.

II. *N*-Acyl derivatives of 4-[bis(2-chloroethyl)-amino]phenylalanine and their esters, amides, and salts

Some information about the chemistry of alkylating preparations, including the chemistry of sarcolysine peptides, has been surveyed in earlier reviews[13,14] and in the review of Giller et al.[12] Since sarcolysine has a toxic side effect in relation to hematopoiesis, attempts were made to increase the selectivity of its transport into tumour cells by synthesising a wide variety of *N*-acyl derivatives; esters, amides, and hydrazides. A large series of derivatives **4**, synthesised after sarcolysine had been obtained, have been described in a review.[5]

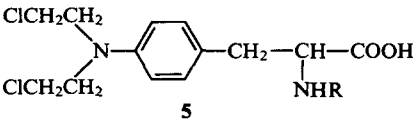
A series of compounds with other aliphatic and aromatic acyl groups as well as urethane and sulfonamide analogues of sarcolysine **5** were obtained later.[15]



4

R^1 = OH, OCH_3, OC_2H_5, $OCH_2C_6H_5$, OC_3H_7-iso, NH_2, NHC_2H_5, NHC_6H_{11}-cyclo, $NHNH_2$ etc.;

R^2 = H, CHO, CH_3CO, CH_3CH_2CO, $CH_3(CH_2)_2CO$, $CH_3(CH_2)_3CO$, $CH_3(CH_2)_{14}CO$, $CH_3(CH_2)_{16}CO$, $HOOC(CH_2)_2CO$, $ClCH_2CO$, ICH_2CO, p-$(ClCH_2CH_2)_2NC_6H_4CH_2CO$, nicotinoyl, tetracyclinylmethylene, hydroxytetracyclinylmethylene, etc.

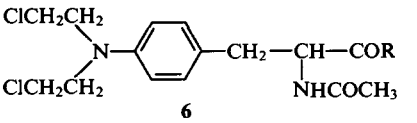


5

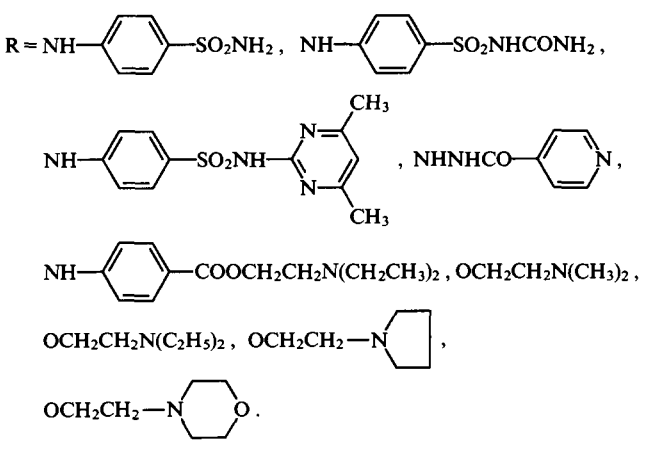
R = CH_3CO, $C_5H_{11}CO$, $C_8H_{17}CO$, $C_{11}H_{23}CO$, $C_6H_5CH_2CO$, C_6H_5CO, sec-C_4H_9OCO, C_6H_5OCO, p-$CH_3C_6H_4SO_2$.

The compounds were used in biological tests in the form of salts with ethanolamine. They are all characterised by a lower toxicity than sarcolysine. *N*-Acetylsarcolysine **5** (R = CH_3CO) possesses the highest antitumour activity. There is no clear-cut correlation between the physicochemical and biological properties of the compounds. The capacity for metabolic transformations is apparently very important. It may be that the antitumour activity is shown to a greater extent the easier the deacylation of the preparation in vivo.

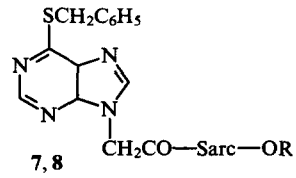
In order to investigate the antitumour properties, a large number of sarcolysine amides were synthesised, for example the *N*-acetylsarcolysine derivative **6** containing streptocide, urosulfan, sulfadimesine, tubazid, and novocaine residues, as well as the dialkylaminoalkyl esters of *N*-acetylsarcolysine.[16]



6



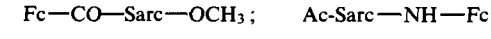
The 6-benzylthio-9*H*-purin-9-ylacetic acid residue was used as the agent for the transfer of sarcolysine into the tumour cell. The derivative **7** was obtained by alkylating 6-benzylthiopurine with the ethyl ester of *N*-(bromoacetyl)sarcolysine. The alkaline hydrolysis of the derivative **7** leads to compound **8**.[17]



7, 8

R = C_2H_5 (**7**), H (**8**).

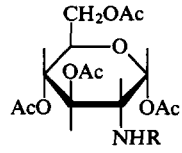
In order to diminish the hematotoxic activity of sarcolysine caused by the introduction of the ferrocene fragment, the methyl ester of N^{α}-ferrocenoylsarcolysine **9** and the ferrocenylamide of *N*-acetylsarcolysine **10** were synthesised.[18]



9 **10**

Fc = ferrocenyl.

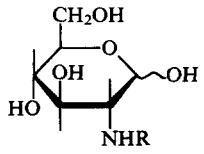
The combination of the biologically active carrier of the cytotoxic group and of the active principle of the latent activity was used in the synthesis of the 1,3,4,6-tetraacetyl-2-amino-2-deoxy-D-glucopyranose derivatives **11** and **12** of *N*-acetylsarcolysine.[19]



11, 12

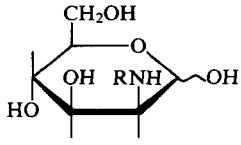
R = Ac-Sarc (**11**), Ac-Sarc – DL-Val (**12**).

Compounds **11** and **12** are readily soluble in water, are less toxic, and exhibit a somewhat higher antitumour activity than sarcolysine. A series of 2-amino-2-deoxy-D-glucopyranose derivatives **13**–**16** and the 2-amino-2-deoxy-D-mannose derivative **17**, in which the amino-group is acetylated by *N*-acetylsarcolysine or a peptide containing it, have been synthesised.[20] Compounds **13**–**17** possess a weak antitumour activity.



13–16

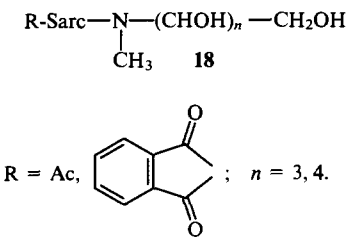
R = Ac-Sarc (**13**),
Ac-Sarc – Val (**14**),
Ac-Sarc – Leu (**15**),
Ac-Sarc – Gly – Gly (**16**).



17

R = Ac-Sarc (**17**).

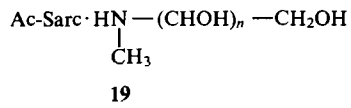
The sarcolysine derivatives of polyhydric 1-methylamino-1-deoxy-alcohols **18** (the 1-methylamino-1-deoxy-derivatives of D-glucitol, D-galactitol, D-mannitol, and L-arabitol) were obtained by the anhydride method or the mixed anhydride method.[20,21] A relation between the structures of the compounds and their biological activities was established. The highest activity was shown by the D-galactitol and D-mannitol derivatives. The spectrum of the antitumour activity of compound **18** resembles that of sarcolysine. In contrast to sarcolysine, all the substances exhibited a minimal effectiveness in the treatment of leukaemia and the highest in the treatment of the MORS-406 plasmacytoma.



18

R = Ac, ; $n = 3, 4$.

In order to make the compounds soluble in water, the salts of *N*-acetylsarcolysine with the amino-derivatives **19** of the polyhydric alcohols listed above were obtained.[22]

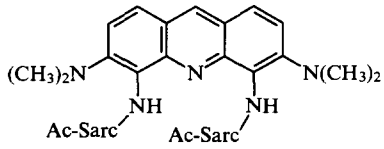


19

$n = 3, 4$.

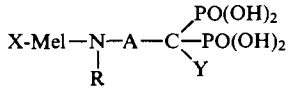
The acetyl derivatives showed a low toxicity and exhibited the highest antitumour activity towards MORS-406 plasmacytoma.

The varied biological activities of the disubstituted 3,6-acridines served as a basis for the synthesis of compound **20**.[23]

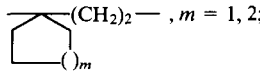


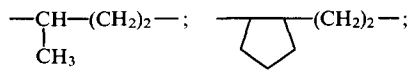
20

In view of the tropism of the 1,1-diphosphonic acid derivatives in relation to bone tissue, a series of melphalan amides **21**, containing two phosphonic acid residues, were synthesised. They exhibit an antitumour activity towards certain tumours.[24]



21

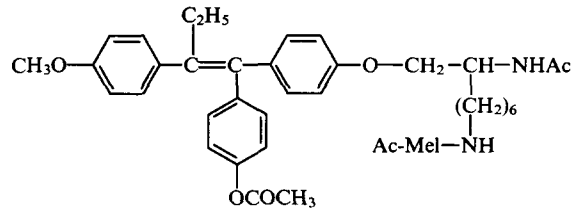
A = $-(CH_2)_n-$, $n = 2-5$;  , $m = 1, 2$;



R = CH_3, H; X = HCO, $(CH_3)_3COCO$, H; Y = OH, H.

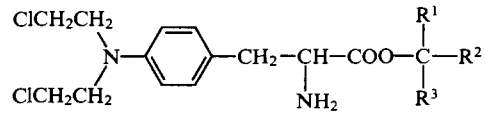
The above acids as well as their tetraethyl esters and sodium salts can be used in the treatment of dense tumours such as multiple myeloma, osteosarcoma, the mammary gland carcinoma, the carcinoma of the ovaries, leukaemia, and lymphomas. The substances are characterised by a high therapeutic index, a low toxicity, and a ready solubility in water, which permits their parenteral and oral administration.

Acetylmelphalan was used, among other cytostatic agents, for the synthesis of antitumour compounds (for example compound **22**) with an affinity for steroid hormone receptors.[25]



22

The antitumour activities and toxicities of the lower esters **23** differ little from those of sarcolysine.[5] The *tert*-butyl esters of sarcolysine **23** ($R^1 = R^2 = R^3 = CH_3$) have been used as therapeutic agents to prevent the occurrence of metastases in the brain.[26]



23

R^1-R^3 = H, Cl, Br, F, I, Alk(C_1-C_3).

One of the groups $R^1 = R^3$ may be a haloalkyl group.

III. The di- and tripeptides derived from the stereoisomers of 4-[bis(2-chloroethyl)amino]-phenylalanine

The procedure used in the synthesis of the 4-[bis(2-chloroethyl)-amino]phenylalanine peptides proved extremely fruitful in increasing the selectivity of the antitumour activity of this compound†. By virtue of the ready availability of sarcolysine, numerous studies have been carried out on the synthesis of peptides based on it with both optically active and racemic aminoacids (mixtures of stereoisomers were then obtained). In the early studies, the content of the stereoisomers in the mixtures was not determined, although interesting results were in fact obtained in the study of their biological activity. The development of methods of synthesis of sarcolysine-containing peptides has been justified objectively, because in the synthesis of potential biologically active compounds a mixture of stereoisomers was frequently isolated initially and then, when a high physiological activity had been discovered, the mixture was separated into the individual stereoisomers. The methods for the formation of the peptide bond, the selective removal of the protecting group, etc. developed for racemic mixtures, have not lost their importance to this day.

A large number of peptides derived from sarcolysine, in which the latter is the N- or C-terminal aminoacid or is present in the middle of the chain, have been synthesised and investigated.[5] Peptides with melphalan have also been described in the review of Rasteikene et al.[5]

A large series of studies on the synthesis of dipeptides, the preparation of individual diastereoisomers, the analysis of their diastereoisomeric purity, and the study of the relation between the biological activity of the compounds and their structure have been carried out under the supervision of E N Shkodinskaya. Dipeptides with *N*-acetylsarcolysine at the N-end occupy a special place among the sarcolysine peptides. It was found that the *N*-acetylsarcolysine dipeptides exhibit a high antitumour activity and at the same time act more selectively than sarcolysine or its dipeptides with a free, formylated, or benzoylated amino-group. The first peptide synthesised and investigated — the ethyl ester of *N*-acetylsarcolysyl-DL-valine **24** (asalin),[27] which has

† With the exception of specially stipulated instances and compounds **1** and **3**, all the aminoacids belong to the L-series.

found an application in practical oncology, was obtained by the dicyclohexylcarbodiimide (DCHC) method.

Ac-Sarc–DL-Val-OC_2H_5 (**24**),
Ac-Sarc–Phe-OC_2H_5 (**25**),
Ac-Sarc–DL-Met-OC_2H_5 (**26**),
Ac-Sarc–Met-OC_2H_5 (**27**),
Ac-Sarc–DL-Trp-OC_2H_5 (**28**),
Ac-Sarc–DL-Ser-OC_2H_5 (**29**),
Ac-Sarc–DL-Asp$(OC_2H_5)_2$ (**30**),
Ac-Sarc–Asp-$(OC_2H_5)_2$ (**31**),
Ac-Sarc–DL-Asp$(OCH_2C_6H_5)_2$ (**32**),
Ac-Sarc–DL-Asp$(OH)_2$ (**33**).

The ethyl esters of *N*-acetylsarcolysine peptides with both racemic aminoacids (methionine, cysteine, phenylalanine, and alanine)[27] and with optically active aminoacids [L-phenylalanine (asaphan **25**), L-methionine (asamet **27**)] were synthesised similarly. The syntheses of a series of *N*-acetylsarcolysine peptides by the mixed anhydride method using the chloride of isovaleric acid have been described.[28] The dipeptides **24–33** with DL-valine, L-phenylalanine, DL- and L-methionine, DL-serine, and L- and DL-aspartic acids have been obtained by this method. Subsequently asalin, asaphan, asamet, asaley (the ethyl ester of *N*-acetylsarcolysyl-L-leucine) and astyron (the ethyl ester of *N*-acetylsarcolysyl-L-tyrosine) became the subject of a more far reaching study in order to introduce the best of them into oncological practice.

A comparative study was made of the toxicity of asalin, asaley, and astyron administered in different ways.[29] Their toxic effects on the organism proved to be similar. Asalin and asaley exhibit a weaker inhibiting effect on the haematopoietic system compared with sarcolysine.[30] The mechanism of the antitumour activities of asalin and asaley[31,32] and their influence on the immune system[33,34] have been investigated comprehensively. The effect of asalin on haematopoiesis,[35–38] the molecular mechanism of antitumour activity,[39–41] the molecular mechanism of its effect on the functional state of mitochondrial membranes in vivo,[42] and its mutagenic activity[42] have been investigated. A method of synthesis of ^{14}C-labelled asaley, containing a label either in the sarcolysine or in the leucine residue, has been developed for the study of its pharmacokinetics.[44]

Asalin has undergone clinical tests and has been recommended for the treatment of myeloma, lymphosarcoma, reticulosarcoma, and ovarian seminoma. Asalin may find the most effective practical application in the treatment of tumours in patients with symptoms of a moderate inhibition of haematopoiesis after radiation therapy and the use of alkylating agents.[11]

In order to obtain water-soluble *N*-acetylsarcolysine dipeptides, a method has been proposed for the deblocking of the carboxy-group by means of the alkaline hydrolysis under mild conditions of their methyl and ethyl esters.[45] The bis(2-chloroethyl)amino-group is unaffected under these conditions. The dipeptides with DL-valine, DL-tryptophan, L-phenylalanine, L-methionine, and L-leucine were synthesised by this method.

The mixed anhydride method employing methyl chlorocarbonate has been used to obtain the sarcolysine-modified carnosine, homocarnosine, and anserine (compounds **34–38**).[46]

Ac-Sarc–β-Ala-OH (**34**),
Ac-Sarc–γ-Abu-OH (**35**),
Ac-Sarc–β-Ala–His-OH (**36**),
Ac-Sarc–β-Ala–N^{im}-Me-His-OH (**37**),
Ac-Sarc–γ-Abu–His-OH (**38**).

The solid-phase synthesis of the peptides **39–41**, analogues of compound **36**, employing *N,N'*-carbonyldiimidazole as the condensing agent, has been described.[47]

HCO-Sarc–β-Ala–His-OCH_3 (**39**),
HCO-Sarc–β-Ala–His-$OCH_2C_6H_5$ (**40**),
HCO-Sarc–β-Ala–His-OH (**41**).

As mentioned above, *N*-acetylsarcolysine dipeptides with optically active aminoacids are mixtures of two diastereoisomers differing in their biological activities. The maximum antitumour activity of each dipeptide is associated with a definite combination of optically active aminoacids. Thus the L,L-isomer is the most active for asaphan, while the L,D- and D,D-forms are the most active for asalin.[13] The preparation of optically active dipeptides of *N*-acetyl-4-[bis(2-chloroethyl)amino]phenylalanine was hindered by the low availability of compounds **2** and **3** and the appreciable racemisation of their acetyl derivatives during the peptide synthesis. It was found that the optically active dipeptides can be obtained most simply by the interaction of *N*-acetylsarcolysine (the racemic form) with the esters of L- and D-aminoacids with subsequent fractional crystallisation of the optical isomers.[13]

For example, the methods for the isolation and the properties of the enantiomers and of the diastereoisomeric mixtures of asalin **24** have been described.[48] The diastereoisomeric racemates were separated chromatographically into the racemate I (compounds **42** and **43**) and the racemate II (compounds **44** and **45**).

Ac-L-Sarc–L-Val-OC_2H_5 (**42**),
Ac-D-Sarc–D-Val-OC_2H_5 (**43**),
Ac-D-Sarc–L-Val-OC_2H_5 (**44**),
Ac-L-Sarc–D-Val-OC_2H_5 (**45**).

The optically active dipeptides **42–45** were isolated by chromatographic separation of the diastereoisomeric peptides synthesised by the reaction of *N*-acetylsarcolysine and the ethyl esters of L- and D-valine. The asalin specified in the pharmacopoeia consists mainly of the racemate II with an admixture of 0.8% of the racemate I. The racemate II proved to have the highest antitumour activity and the highest toxicity of the two racemic diastereoisomeric mixtures.

In order to investigate the influence of the stereoconfiguration of the aminoacids and of the protection of the amino-group on the antitumour properties of the diastereoisomers, the sarcolysylleucine diastereoisomers **46–57** were synthesised (from the aminoacid enantiomers).[49] These peptides contain sarcolysine with a free or formylated amino-group, the C-end being protected by an ester or remaining free. The starting materials employed were the enantiomers of *N*-formylsarcolysine and the *p*-nitrobenzyl ester of leucine. These were condensed with the aid of *N*-ethoxycarbonyl-2-ethoxy-1,2-dihydroquinoline, which prevents racemisation.

R^1-L-Sarc—L-Leu—OR^2

46–48

46: R^1 = CHO, R^2 = $CH_2C_6H_4NO_2$.
47: R^1 = CHO, R^2 = H.
48: R^1 = H, R^2 = H.

R^1-L-Sarc—D-Leu—OR^2

49–51

49: R^1 = CHO, R^2 = $CH_2C_6H_4NO_2$.
50: R^1 = CHO, R^2 = H.
51: R^1 = H, R^2 = H.

R^1-D-Sarc—D-Leu—OR^2

52–54

52: R^1 = CHO, R^2 = $CH_2C_6H_4NO_2$.
53: R^1 = CHO, R^2 = H.
54: R^1 = H, R^2 = H.

R^1-D-Sarc—L-Leu—OR^2

55–57

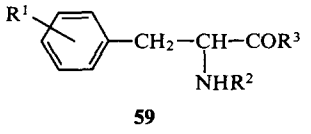
55: R^1 = CHO, R^2 = $CH_2C_6H_4NO_2$.
56: R^1 = CHO, R^2 = H.
57: R^1 = H, R^2 = H.

Dependent on the method of synthesis, isolation, and purification of the *N*-acetylsarcolysine dipeptides with optically active aminoacids, the products are dipeptides with different contents of the diastereoisomers, which is not always reflected in properties such as the melting point and the specific rotation but exerts an appreciable influence on the biological activity. A method has been developed for the quantitative determination of the diastereoisomers of *N*-acetylsarcolysine dipeptides,[50] which involves the chromatographic separation of the diastereoisomers on Silufol UV-254 plate or their preparative separation on silica gel plates with subsequent extraction of the diastereoisomer bands with alcohol and spectrophotometric measurements on the resulting solutions.

The study of the biological activity of the melphalan dipeptide with L-glutamic acid Ac-Mel-Glu(ONa)$_2$ (compound **58**) established that this compound possesses radiation protective properties.[51]

In the further consideration of the studies devoted to the synthesis of peptides modified by 4-[bis(2-chloroethyl)amino]-phenylalanine stereoisomers, special attention will not be given to the methods of formation of the peptide bond because all the peptides were obtained by methods widely known in peptide chemistry with protecting groups constantly employed in amino-acid chemistry and in accordance with schemes which the authors regarded as optimal. In most cases, sarcolysine or its enantiomers were attached to the peptide chain in the last step, because of the presence in the molecule of the labile nitrogen-containing nitrogen mustard group.

The studies of Italian workers headed by Barbieri,[52-54] who synthesised cytotoxic peptides with a postulated dual mechanism of action — alkylation and metabolic inhibition — merit attention. Peptides of melphalan and of its *meta*- and *ortho*-[bis-(2-chloroethyl)amino]-analogues with natural aminoacids (glycine, glutamic acid, lysine, histidine, arginine, phenylalanine, methionine, etc.) or their antagonists (norvaline, norleuceine, ethionine, methylmethionine, methylphenylalanine, *p*-fluorophenylalanine, β-2-thienylalanine, etc.) having the general formula **59** were obtained.

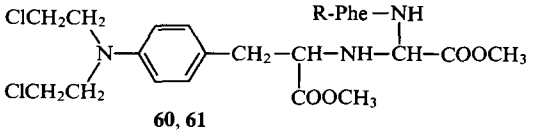


59

R^1 = $N(CH_2CH_2Cl)_2$; R^2 = H, $COOCH_2C_6H_5$, aminoacid residue; R^3 = OH, OAlk, aminoacid residue.

The chemotherapeutic activities of compounds **59** as well as the dipeptides listed above depend significantly on their stereo-configuration and may vary within wide limits. The effect of certain cytotoxic dipeptides on oxidative phosphorylation, etc. processes was studied in the same investigations using experimental strains. Data were obtained confirming the different effects of certain peptides on the enzyme systems of tumours and on the analogous systems in normal tissues.

In order to achieve the selective inhibition of pyruvate kinase in tumour cells, compounds **60** and **61** were synthesised. In these substances, the melphalan residue is attached via an amino-group to the α-carbon atom of the glycine in the phenylalanylglycine molecule.[55]



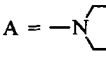
60, 61

R = $C_6H_5CH_2OCO$ (**60**), H·3HCl (**61**).

The antitumour activity of the conjugate **61** proved to be higher in experiments on animals and its acute toxicity was found to be lower than the corresponding properties of melphalan.

Melphalan-containing peptides **62-81**, which are 1,1-diphosphonic acid derivatives, were obtained.[56] These are analogues of the corresponding amides **21** incorporating two phosphonic acid residues.

Mel-Ala-$NH(CH_2)_3C(OH)[PO(OH)_2]_2$ (**62**),
Mel-D-Ala-$NH(CH_2)_3C(OH)[PO(OH)_2]_2$ (**63**),
Mel-Ala-$NH(CH_2)_4C(OH)[PO(OH)_2]_2$ (**64**),
Mel-D-Ala-$NH(CH_2)_4C(OH)[PO(OH)_2]_2$ (**65**),
Mel-Gly-$NH(CH_2)_3C(OH)[PO(OH)_2]_2$ (**66**),
Mel-Gly-$NH(CH_2)_4C(OH)[PO(OH)_2]_2$ (**67**),
Mel-Gly-$N(CH_3)(CH_2)_3C(OH)[PO(OH)_2]_2$ (**68**),
Mel-Pro-$NH(CH_2)_2C(OH)[PO(OH)_2]_2$ (**69**),
Mel-Pro-$NH(CH_2)_4C(OH)[PO(OH)_2]_2$ (**70**),
Mel-γ-Glu-$NH(CH_2)_4C(OH)[PO(OH)_2]_2$ (**71**),
Mel-γ-Glu-$NH(CH_2)_3C(OH)[PO(OH)_2]_2$ (**72**),
Mel-Ala-A-$(CH_2)_2C(OH)[PO(OH)_2]_2$ (**73**),
Mel-Ala-A-$(CH_2)_3C(OH)[PO(OH_2]_2$ (**74**),
Mel-Leu-$NH(CH_2)_2C(OH)[PO(OH)_2]_2$ (**75**),
Mel-Sarc-$NH(CH_2)_3C(OH)[PO(OH)_2]_2$ (**76**),
Mel-Val-$NH(CH_2)_3C(OH)[PO(OH)_2]_2$ (**77**),
Mel-Gly-Gly-$NH(CH_2)_4C(OH)[PO(OH)_2]_2$ (**78**),
Mel-Ala-Gly-$NH(CH_2)_3C(OH)[PO(OH)_2]_2$ (**79**),
Mel-Gly-Gly-Gly-$NH(CH_2)_3C(OH)[PO(OH)_2]_2$ (**80**),
Mel-Ala-Ala-$NH(CH_2)_4C(OH)[PO(OH)_2]_2$ (**81**)

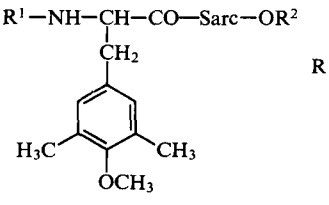
A =  .

It was established that compounds **62-81** have antitumour and antimetastatic properties and also exhibit a high inhibiting activity on the growth of nucleic acids in experiments in vitro and an appreciable antitumour activity in vivo. It is believed that these compounds can be used in the treatment of dense tumours: multiple myeloma, osteosarcoma, the metastases of the bone and mammary gland carcinomas, ovarian and testicular carcinomas, as well as various types of lymphomas and leukaemias.

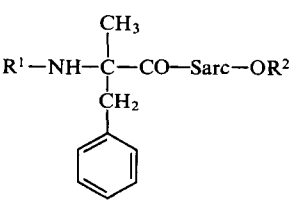
IV. 4-[Bis(2-chloroethyl)amino]phenylalanine peptides with nonprotein aminoacids

The synthetic sarcolysine peptides with protein aminoacids possess a high antitumour activity, but the latter is attained when they are administered in maximum tolerable or toxic doses. The inadequately selective activity of these preparations leads to serious damage to mucous membranes and to the breakdown of haematopoietic and metabolic processes. The hypothesis was put forward that the use of nonprotein aminoacids and the presence of anomalous peptide bonds would make it possible to alter the physiological properties of such peptides.

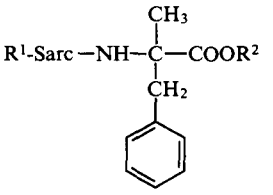
For this purpose, sarcolysine dipeptides with structural analogues of natural aminoacids — 4-methoxy-3,5-dimethylphenylalanine and α-methylphenylalanine (compounds **82-89**) — were synthesised.[57] Dicyclohexylcarbodiimide was used in the condensation stage and the protecting groups were removed by hydrogenolysis.



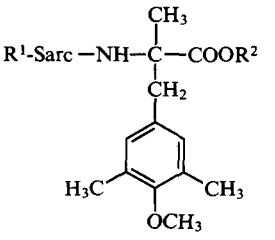
82, 83



84, 85



86, 87



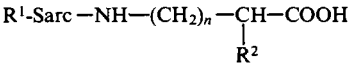
88, 89

R^1 = HCO, R^2 = $CH_2C_6H_5$ (**82, 84, 86, 88**);
R^1 = R^2 = H (**83, 85, 87, 89**).

The antitumour activities and toxicities of compounds **82–89** were investigated. As in the case of dipeptides with protein aminoacids, the antitumour activities of the diastereoisomers proved to be various.

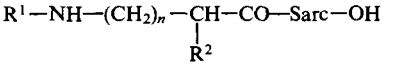
A series of experiments were carried out on the synthesis of peptides containing DL-α-aminobutyric acid (compounds **90, 93, 96,** and **99**), DL-β-aminobutyric acid (compounds **91, 94, 97,** and **100**), and DL-γ-aminobutyric acid (compounds **92, 95, 98,** and **101**).[58–60]

In relation to these compounds, an attempt was made to establish the rules governing the variation of toxicity and antitumour activity, depending on the position of the sarcolysine residue in the peptide, the structure of the second aminoacid, and the presence of the formyl protecting group at the N-terminal aminoacid group.[61–64]



90–95

90: R^1 = H, R^2 = C_2H_5, n = 0; **91**: R^1 = H, R^2 = CH_3, n = 1;
92: R^1 = H, R^2 = H, n = 2; **93**: R^1 = HCO, R^2 = C_2H_5, n = 0;
94: R^1 = HCO, R^2 = CH_3, n = 1; **95**: R^1 = HCO, R^2 = H, n = 2.



96–101

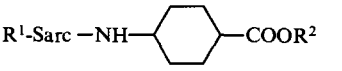
96: R^1 = H, R^2 = C_2H_5, n = 0; **97**: R^1 = H, R^2 = CH_3, n = 1;
98: R^1 = H, R^2 = H, n = 2; **99**: R^1 = HCO, R^2 = C_2H_5, n = 0;
100: R^1 = HCO, R^2 = CH_3, n = 1; **101**: R^1 = HCO, R^2 = H, n = 2.

It was found that the toxicity of the peptides with N-terminal sarcolysine is independent of the position of the amino-group in the C-terminal aminoacid. The toxicity of the peptides with C-terminal sarcolysine is reduced as the methylene bridge becomes longer. In the *N*-formylpeptides, the toxicity diminishes already in the presence of one additional CH_2 group. The peptides containing α-aminobutyric acid have the strongest antitumour activity. In terms of the spectrum of antitumour activity, compounds **90–101** differ little.

The mutagenic and inactivating activities of the peptides **90, 92–95, 96,** and **98–101** in the form of their sodium salts on bacteriophage systems in experiments in vitro have been investigated.[65] The compounds containing sarcolysine at the C-end proved to be more toxic, while those with sarcolysine at the N-end were less toxic. The presence of the formyl group in the peptide does not alter the toxicity of the compound in relation to the bacteriophage.

The study of the mutagenic activities of compounds **90, 92–95, 96,** and **98–101** showed that a change in the structure of the second aminoacid in the sarcolysine peptide molecule alters only slightly the effectiveness of the mutagenic activity. A correlation between the structural changes in the second aminoacid and the mutagenic and inactivating activities of the peptide was not found in the given series of compounds.

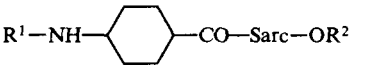
In the course of the continuation of studies designed to establish the possible relations between the toxicological and antitumour characteristics, on the one hand, and the characteristic features of the structure of the sarcolysine peptides, on the other, a series of compounds **102–113**, containing *cis*- and *trans*-4-aminocyclohexanecarboxylic acids (4-ACHCA), were obtained.[66]



102–109

cis	*trans*
102: R^1 = CHO, R^2 = C_2H_5;	**103**: R^1 = CHO, R^2 = C_2H_5;
104: R^1 = H·HCl, R^2 = C_2H_5;	**105**: R^1 = H·HCl, R^2 = C_2H_5;
106: R^1 = $C_6H_5CH_2OCO$, R^2 = $C_6H_5CH_2$;	**107**: R^1 = $C_6H_5CH_2OCO$, R^2 = $C_6H_5CH_2$;
108: R^1 = H, R^2 = H;	**109**: R^1 = H, R^2 = H.

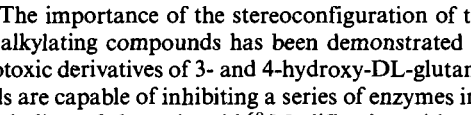
The 4-ACHCA derivatives containing N- and C-terminal sarcolysine residues with both formylated and unsubstituted amino-groups are less toxic compared with the initial sarcolysine. The compounds with a free carboxy-group in 4-ACHCA are less toxic compared with the corresponding esters. All the compounds exhibit a high antitumour activity. The derivatives containing amino- and carboxy-groups in the *trans*-positions are less toxic and have a more pronounced antitumour activity compared with the analogous *cis*-4-ACHCA derivatives.[67]



110–113

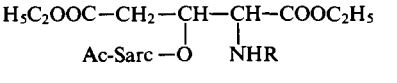
cis	*trans*
110: R^1 = $C_6H_5CH_2OCO$, R^2 = $C_6H_5CH_2$;	**112**: R^1 = $C_6H_5CH_2OCO$, R^2 = $C_6H_5CH_2$;
111: R^1 = H, R^2 = H;	**113**: R^1 = H, R^2 = H.

The importance of the stereoconfiguration of the 'carrier' of the alkylating compounds has been demonstrated in relation to cytotoxic derivatives of 3- and 4-hydroxy-DL-glutamic acids. The acids are capable of inhibiting a series of enzymes involved in the metabolism of glutamic acid.[68] Modification with sarcolysine can make the inhibition irreversible. By varying the method by which *N*-acetylsarcolysine is attached to the above compounds, i.e. by the formation of ester or peptide bonds with the *threo*- or *erythro*-diastereoisomers of 3- and 4-hydroxyglutamic acids, the derivatives **114–122** were obtained.[69–71]

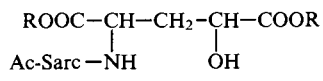


114–116

cis: R = $COOCH_2C_6H_5$ (**114**); H·HCl (**115**)
trans: R = H·HCl (**116**).



threo-**117**, *erythro*-**118**.



119–122

threo: R = $CH_2C_6H_5$ (**119**); H (**120**).

erythro: R = $CH_2C_6H_5$ (**121**); H (**122**).

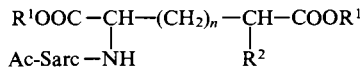
The stereoisomers of the esters **114–118** and the peptides **120–122** exhibited low antitumour activities and an appreciable toxicity, but differed both as regards the magnitude of the antitumour activity and the spectrum of the latter.[69, 71] This shows that, as in the case of the sarcolysine peptides with protein aminoacids, the configuration of the nonprotein aminoacids entering into the composition of the cytotoxic esters and peptides exerts an appreciable influence on the antitumour activity.

An attempt has been made[72] to investigate the influence of the stereoconfigurations of the individual aminoacids forming part of the peptide on the antitumour activity of the latter. The stereoisomers of the tripeptides **123–126** were synthesised.

Lys–Med–Glu (**123**), Lys–Mel–Glu (**124**),
Lys–Sarc–*threo*-4-OH-Glu (**125**),
Lys–Sarc–*erythro*-4-OH-Glu (**126**).

Compounds **123–126** are modified fragments of the ribonuclease S-peptides. Furthermore, the tripeptides **124** incorporate, as it were, two dipeptides: Lys–Mel and Mel–Glu, which exhibit a very high antitumour activity on various strains of tumours. However, the results of tests of compounds **123–126** on animals revealed their low antitumour activities, which precluded a conclusion about the influence of aminoacids on the latter.

In order to increase the proteolytic stability and biological activity of the sarcolysine dipeptides, peptides based on homoglutamic and diaminoadipic acids and the diastereoisomers of diaminoglutaric acid (compounds **127–133**) were synthesised.[73]

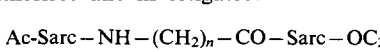


127–133

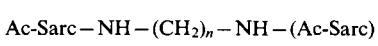
127: R^1 = C_2H_5, R^2 = H, n = 2;
128: R^1 = C_2H_5, R^2 = Ac-Sarc–NH, n = 2;
129: R^1 = C_2H_5, R^2 = Ac-Sarc–NH, *meso*-, n = 1;
130: R^1 = C_2H_5, R^2 = Ac-Sarc–NH, *threo*-, n = 1;
131: R^1 = Na, R^2 = H, n = 2;
132: R^1 = Na, R^2 = Ac-Sarc–NH, n = 2;
133: R^1 = Na, R^2 = Ac-Sarc–NH, *meso*-, n = 1.

Despite the increase in the susceptibility to alkylation in experiments in vitro, the introduction of a second sarcolysine residue into the molecules of compounds **128–130**, **132**, and **133** did not lead to an increase in the antitumour activity. This can probably be accounted for by the difficulty of transporting the disarcolysine compound through the membranes of the tumour cell.

The tripeptides of the β-, γ-, and ε-aminoacids **134** containing N- and C-terminal *N*-acetylsarcolysine residues with different numbers of CH_2 groups between them as well as their analogues — *N*-acetylsarcolysine alkylenediamides **135** — were synthesised and investigated.[74]



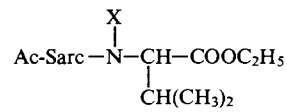
134, n = 2, 3, 5.



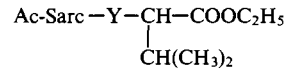
135, n = 2, 3.

Compounds **134** proved to be inactive, while compounds **135** exhibited a moderate activity.

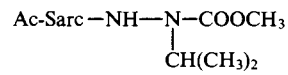
The antitumour preparations asalin[75] and asaphan[76] have been modified. The peptide bond was altered in asalin **24**. The hydrogen in the peptide amide group was replaced by various residues (compounds **136**): the amide group was replaced by ester, hydrazide, or amidoxy-groups (compounds **137**) and DL-valine was replaced by 2-azavaline (compound **138**).



136: X = C_2H_5, OC_2H_5, OH, $NH_2 \cdot HBr$.

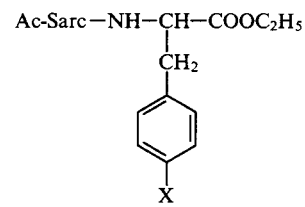


137: Y = O, NHNH, NHO.

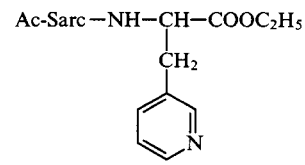


138

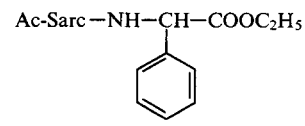
In asaphan, the benzene ring of phenylalanine was modified and its position in the aminoacid was also altered (compounds **139–142**).



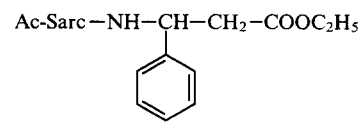
139: X = Cl, NO_2, n-C_3H_7, iso-C_3H_7, n-$C_7H_{15}O$.



140



141

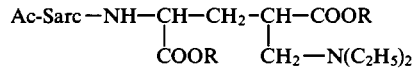


142

The asalin and asaphan analogues **136–142** obtained exhibited towards a series of tumours antiblastic activities similar to and in some cases lower than those of asalin and the ethyl ester of *N*-acetylsarcolysyl-DL-phenylalanine used as controls.

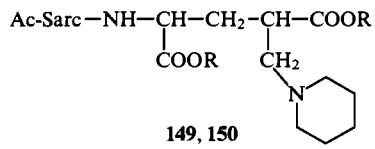
The *N*-acetylsarcolysine dipeptides with the ethyl esters of *N*-methyl-*N*-phenylglycine (compounds **143** and **144**) and of aminohydroxyacids (compounds **145** and **146**)[16] and also with glutamic acid derivatives (compounds **147–150**)[71] have been synthesised.

Ac-Sarc-N(CH_3)$CH_2COOC_2H_5$ (**143**),
Ac-Sarc-N(C_6H_5)$CH_2COOC_2H_5$ (**144**),
Ac-Sarc-NHOCH(C_2H_5)$COOCH_3$ (**145**),
Ac-Sarc-NHOC$H_2COOC_2H_5$ (**146**)



147, 148

R = $CH_2C_6H_5$ (**147**), H (**148**).



149, 150

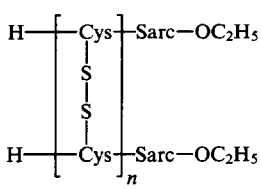
R = $CH_2C_6H_5$ (**149**), H (**150**).

Thus compounds of interest for practical oncology have not so far been discovered among the sarcolysine peptides with nonprotein aminoacids.

V. Polypeptides containing 4-[bis(2-chloroethyl)-amino]phenylalanine

One of the ways of increasing the selectivity of the action of cytostatic substances involves the use of biopolymers, and in the first place polypeptides, for their transport into the tumour cell. Polypeptides have a series of advantages: rapid passage of some of them through the membranes of cancer cells (compared with normal cells) and extensive possibilities for the variation of their composition. The antitumour activities of polypeptide derivatives have been investigated as a function of the nature and configuration of the aminoacid and the length of the peptide chain. A series of homopolypeptidyl derivatives of sarcolysine (compounds **151**–**154**,[77] **155**,[77,78] **156**, and **157**[79]) have been obtained by the polycondensation of the *N*-carboxyanhydrides of various α-aminoacids in the presence of the ethyl ester of sarcolysine. In the case of L-cystine, the derivative **158**, containing disulfide bonds, was synthesised.[80]

$(Val)_n$–Sarc-OC_2H_5 (**151**),
$(D\text{-}Val)_n$–Sarc-OC_2H_5 (**152**),
$(DL\text{-}Nle)_n$–Sarc-OC_2H_5 (**153**),
$(Sar)_n$–Sarc-OC_2H_5 (**154**),
$(Phe)_n$–Sarc-OC_2H_5 (**155**),
$(Lys)_n$–Sarc-OC_2H_5 (**156**),
$(Asp)_n$–Sarc-OC_2H_5 (**157**)



158

The toxicity of compounds **151**–**158** depends on the length of the peptide chain and on the nature of the α-aminoacid constituting the chain. An increase in chain length lowers the toxicity. The polysarcosyl derivatives **154** showed the highest antitumour activity.

The inclusion of an additional aminoacid between the polypeptide chain and sarcolysine alters the activity of the compound (compounds **159**–**165**).[81]

$(DL\text{-}Ala)_n$–Gly–Sarc-OC_2H_5 (**159**),
$(DL\text{-}Ala)_n$–DL-Val–Sarc-OC_2H_5 (**160**),
$(DL\text{-}Ala)_n$–DL-Nle–Sarc-OC_2H_5 (**161**),
$(DL\text{-}Val)_n$–DL-Ala–Sarc-OC_2H_5 (**162**),
$(DL\text{-}Ala)_n$–DL-Nle–Sarc-OC_2H_5 (**163**),
$(Gly)_n$–DL-Ala–Sarc-OC_2H_5 (**164**),
$(DL\text{-}Nle)_n$–Gly–Sarc-OC_2H_5 (**165**).

After the inclusion of an additional aminoacid, the polypeptidyl derivative of which is active, the antitumour activities of the initial homopolypeptides are retained.

Copolypeptides of two types but with the same composition, where one of the two aminoacids entering into the composition of the copolypeptide was introduced between the sarcolysine ethyl ester residue and the polypeptide chain, have been synthesised (compounds **166**–**169**).[81]

$[(DL\text{-}Ala)_{n-1}$–$(DL\text{-}Val)_n]$–DL-Ala–Sarc-OC_2H_5 (**166**),
$[(DL\text{-}Ala)_n$–$(DL\text{-}Val)_{n-1}]$–DL-Val–Sarc-OC_2H_5 (**167**),
$[(Gly)_{n-1}$–$(DL\text{-}Nle)_n]$–Gly–Sarc-OC_2H_5 (**168**),
$[(Gly)_n$–$(DL\text{-}Nle)_{n-1}]$–DL-Nle–Sarc-OC_2H_5 (**169**).

It was established that the antitumour activity of the polypeptide depends on which aminoacid is linked directly to sarcolysine.

A series of copolypeptidyl derivatives of sarcolysine with an irregular structure have been obtained (compounds **170**–**177**[78] and **178**–**184**[79]).

Poly(DL-Ala, DL-Val)–Sarc-OC_2H_5 (**170**),
Poly(Sar, DL-Val)–Sarc-OC_2H_5 (**171**),
Poly(Sar, DL-Nle)–Sarc-OC_2H_5 (**172**),
Poly(Gly, DL-Nle)–Sarc-OC_2H_5 (**173**),
Poly(Gly, DL-Leu)–Sarc-OC_2H_5 (**174**),
Poly(DL-Leu, DL-Nle)–Sarc-OC_2H_5 (**175**),
Poly(DL-Nle, Phe)–Sarc-OC_2H_5 (**176**),
Poly(DL-Nle, DL-Val)–Sarc-OC_2H_5 (**177**),
Poly(Lys, Gly)–Sarc-OC_2H_5 (**178**),
Poly(Lys, DL-Ala)–Sarc-OC_2H_5 (**179**),
Poly(Lys, DL-Val)–Sarc-OC_2H_5 (**180**),
Poly(Lys, DL-Nle)–Sarc-OC_2H_5 (**181**),
Poly(Lys, Phe)–Sarc-OC_2H_5 (**182**),
Poly(Asp, DL-Ala)–Sarc-OC_2H_5 (**183**),
Poly(Asp, DL-Nle)–Sarc-OC_2H_5 (**184**).

Among the copolypeptidyl derivatives, compounds containing glycine or DL-alanine are the most active. It has been shown that both the homopolypeptides and the copolypeptides exhibit a distinct antiblastic activity in relation to tumour strains, but they are largely inferior in their activity to sarcolysine. A number of substances have antitumour activities in relation to certain experimental tumour strains which are superior to that of sarcolysine and at the same time do not exert a general toxic effect on the organism such as that of sarcolysine.[82,83]

The use of conjugates of melphalan with poly-L-aminoacids, in particular with poly-L-lysine (compounds **185** and **186**) and poly-L-glutamic acid (compounds **187** and **188**) as agents transferring the alkylating substances into tumours has been described (Table 1).[84] Poly-L-lysine or poly-L-glutamic acid was condensed with melphalan or its derivative by the DCHC method, after which the protecting groups were removed if necessary.

The conjugates **185**–**188** exhibited in experiments in vitro an alkylating activity amounting to 42%–70% of that of melphalan. Studies of compounds **187** and **188** in experiments on animals established that they are transferred into tumours with the aid of the lymphatic system; this can be used to prevent the occurrence of metastases in lymph nodes.

Table 1. The composition of the conjugates of polyaminoacids with melphalan.

Positions of conjugates	Mel–poly(L-Lys)		Mel–poly(L-Glu)	
	185	**186**	**187**	**188**
Number of aminoacid residues per melphalan molecule	6.7	6.9	23.0	23.1
Number of melphalan molecules per polyaminoacid molecule	83.0	2.3	20.2	4.7

VI. Analogues of natural proteins containing 4-[bis(2-chloroethyl)amino]phenylalanine

In most of the studies quoted above, the combination of aminoacids in the cytotoxic peptides was empirical in character and did not correspond to a definite aminoacid sequence in natural peptides. Studies on the synthesis of analogues of natural proteins containing sarcolysine or its enantiomers are presented below.

Thus, in the search for compounds with a high selectivity in their antitumour activities, the short peptides **189**[85,86] and **190–193**[86] have been synthesised. These are fragments of biologically important proteins such as ribonuclease and histones, because it is known that certain fractions of histones have the ability to inhibit the DNA-dependent synthesis of RNA in experiments in vitro.[87–89] Sarcolysine was introduced into the peptide instead of phenylalanine or alanine or as an additional aminoacid.

Lys–Val–Sarc-OH (**189**),
Lys–Arg–Nle–Sarc-OCH_3 (**190**),
Lys–Sarc-OCH_3 (**191**),
Ala–Lys–Sarc-OCH_3 (**192**),
Ala–Ala–Lys–Sarc-OCH_3 (**193**).

Despite the presence of the labile bis(2-chloroethyl)amino-group, the peptides containing a sarcolysine residue can be obtained by solid-phase synthesis. Thus the sarcolysine-modified glutathione fragment **194** has been obtained on a partially chloromethylated styrene–divinylbenzene copolymer.[90] DCHC was used as the condensing agent. The sarcolysine residue was attached in the last stage.

HCO-Sarc–Cys–Gly-OH · $NH(C_6H_{11})_2$ (**194**)

In the mechanism of the antitumour activity of sarcolysine, two main components have been differentiated: the nuclear component, associated with the breakdown of the structure and functions of DNA and nuclear proteins, and the membrane component, associated with the damage to the internal membranes of mitochondria and the membranes of the endoplasmic reticulum. The second component actually became the basis of the search for substances interacting irreversibly with various membrane receptors. The peptide hormones, acting at extremely low concentrations and exhibiting a high biological activity and selectivity in their action, have become particularly attractive for the creation of new medicinal preparations from this standpoint. Compounds containing sarcolysine or its enantiomers have been synthesised from fragments of hypophyseal hormones such as the luteinising hormone (LH), the adrenocorticotropic hormone (ACTH), and the somatotropic and α-melanocyte-stimulating hormone (α-MSH). Investigations[91] showed that α-MSH is able to bind to plasma membranes of specific types of tumour cells, particularly to the membrane receptors of human melanoma.

A series of studies[92–102] have been devoted to the synthesis of α-MSH fragments (compounds **195–232**) containing sarcolysine or its enantiomers (Table 2, see over) in order to obtain substances with a high selectivity in their antitumour activity.

The stereoisomers of the tetrapeptides **195**, **196**, **198**, and **199** were synthesised from sarcolysine and separated by column chromatography. The protected pentapeptides **216–219** were obtained from them.[92]

Compounds **220–227** were synthesised from the corresponding peptides with N-terminal formylsarcolysine and were then separated chromatographically on silica gel columns and *N*-formylmelphalan and *N*-formylmedphalan were isolated. After the removal of the formyl group, the compounds were condensed with the N-terminal fragment.

In the study of the antitumour activity, it was established that some of the compounds exhibit an antiblastic activity towards a series of transplantable tumours. However, appreciable advantages compared with sarcolysine were not discovered.[101] The compounds with melphalan are more active. The conjugate **232** of α-MSH with melphalan exhibited a greater affinity for receptors than a simple mixture of these compounds.[102] It was established that the replacement of methionine, arginine, or phenylalanine in the initial sequence of α-MSH by melphalan leads to the irreversible binding of the conjugate to the receptor and the prolongation of activity and that on replacement of glycine no inhibition was observed.[96]

It was found that the peptides **214**, **215**, **228**, and **230** exhibit a lower mutagenic activity than melphalan. Presumably, when these compounds are used as antitumour agents, the probability of the appearance of secondary tumours is lower than in the case where melphalan is employed.[99] The peptides **214**, **215**, **228**, and **230** differ also in their toxicity to particular types of cells. They are all less cytotoxic than melphalan.[101]

Attempts have been made recently to increase the selectivity of the action of sarcolysine by attaching it to hypothalamic hormones, the so called releasing factors of releasing-inhibiting factors (according to another nomenclature—liberins and statins), which respectively stimulate or inhibit the liberation of hypohyseal hormones. By regulating the activity of the hypophyseal-adrenal system and steroid genesis, hypothalamic hormones act on hormone-dependent tumours. For example, analogues of the LH-releasing factor and the gonadotropin-releasing factor exhibit an antitumour activity towards experimental tumours.[103] One of the gonadotropin-releasing factor analogues has been used successfully in medical practice in the treatment of hormone-dependent tumours.[104] Melanostatin exhibits an inhibiting activity towards melanoma.[105–107] Hypothalamic hormones are peptides with a relatively small number of aminoacids, which makes their synthesis comparatively simple and easy to carry out.

This stimulated the synthesis and study of analogues of the α-MSH releasing-inhibiting factor (melanostatin)—compounds **233**,[108], **234**,[108–110] **235**,[108, 109] **236–238**,[108] **239**,[108, 110, 111] and **240**.[109, 111]

Pro–Leu–Gly-NH_2 (melanostatin),
Pro–Sarc–Gly-NH_2 (**233**),
Pro–Mel–Gly-NH_2 (**234**),
Pro–Med–Gly-NH_2 (**235**),
HCO-Sarc–Pro–Leu–Gly-NH_2 (**236**),
HCO-Mel–Pro–Leu–Gly-NH_2 (**237**),
HCO-Med–Pro–Leu–Gly-NH_2 (**238**),
Mel–Pro–Leu–Gly-NH_2 (**239**),
Med–Pro–Leu–Gly-NH_2 (**240**).

Table 2. Alkylating analogues of the α-melanocyte-stimulating hormone.

Compound	Formula	Ref.
α-MSH	$\overset{1}{\text{Ac-Ser}}\overset{2}{\text{—Tyr}}\overset{3}{\text{—Ser}}\overset{4}{\text{—Met}}\overset{5}{\text{—Glu}}\overset{6}{\text{—His}}\overset{7}{\text{—Phe}}\overset{8}{\text{—Arg}}\overset{9}{\text{—Trp}}\overset{10}{\text{—Gly}}\overset{11}{\text{—Lys}}\overset{12}{\text{—Pro}}\overset{13}{\text{—Val-NH}_2}$	
195	$\text{Ac—Sarc—Arg}(\text{NO}_2)\text{—OCH}_3$	92
196	$\text{Form}^{a}\text{-Sarc—Arg}(\text{NO}_2)\text{—OCH}_3$	92
197	$\text{Sarc—Sarc—Arg}(\text{NO}_2)\text{—OCH}_3$	92
198	$\text{Ac-Sarc—Lys}(\text{CHO})\text{—OCH}_3$	92
199	$\text{Form}^{a}\text{-Sarc—Lys}(\text{CHO})\text{—OCH}_3$	92
200	$\text{Sarc—Sarc-Lys}(\text{CHO})\text{—OCH}_3$	92
201	Ac-Sarc—OCH_3	93
202	$\text{Form}^{a}\text{-Sarc—OCH}_3$	93
203	Ac-Sarc—Lys—OCH_3	93
204	$\text{Form}^{a}\text{-Sarc—Lys—OCH}_3$	93
205	$\text{Mel—Arg}(\text{NO}_2)\text{—OCH}_3$	94
206	$\text{Med—Arg}(\text{NO}_2)\text{—OCH}_3$	94
207	$\text{Mel—Lys}(\text{Z}^{b})\text{—OCH}_3$	94
208	$\text{Med—Lys}(\text{Z}^{b})\text{—OCH}_3$	94
209	Mel—Lys—OCH_3	94
210	Med—Lys—OCH_3	94
211	Mel—OCH_3	95, 96
212	Med—OCH_3	95, 96
213	Mel—NH_2	96
214	Mel—NH_2	96 – 100
215	Mel—NH_2	96 – 100
216	$\text{Z—Mel—Arg}(\text{NO}_2)\text{—OCH}_3$	92
217	$\text{Z—Med—Arg}(\text{NO}_2)\text{—OCH}_3$	92
218	$\text{Z—Mel—Lys}(\text{CHO})\text{—OCH}_3$	92
219	$\text{Z—Med—Lys}(\text{CHO})\text{—OCH}_3$	92
220	H—Mel—OH	94, 101

Table 2 (continued).

Compound	Formula	Ref.
α-MSH	Ac-Ser(1)—Tyr(2)—Ser(3)—Met(4)—Glu(5)—His(6)—Phe(7)—Arg(8)—Trp(9)—Gly(10)—Lys(11)—Pro(12)—Val(13)-NH_2	
221	H———Med————OH	94, 101
222	H———Mel—Lys————OH	94, 101
223	H———Med—Lys————OH	94, 101
224	H————Mel————OH	94, 101
225	H————Med————OH	94, 101
226	H————Mel—Lys————OH	94, 101
227	H————Med—Lys————OH	94, 101
228	Nle————Mel————OCH_3	96, 98–100
229	Nle————Med————OCH_3	96
230	Mel————————OCH_3	96, 98–100
231	Mel————phe[c]————OCH_3	96
232	Ac————————Lys————NH_2 (Mel)	102

Note. Aminoacid residues identical to those in the initial natural peptide are designated by a continuous line.

[a] Form = HCO. [b] Z = $C_6H_5CH_2OCO$. [c] Here and henceforth the aminoacid designation starting with a lower case letter indicates the D-configuration.

Higher antitumour activity of the melphalan-containing melanostatin derivatives compared with the medphalan analogues was discovered.[109] It was noted that the melanostatin fragment in compound **237** protects the organism against the toxic effect of melphalan.[110]

Hypothalamic hormones and their analogues inhibit the secretion of the protein hormones from the hypophysis and the latter inhibit in their turn the secretion of the steroid hormones from the adrenal glands, the levels of which in the hormone-dependent tumours are unduly high. The analogues of hypothalamic hormones can therefore be used to synthesise agents with a high selectivity in their antitumour activity. The synthesis of derivatives of the LH-releasing factor (luliberin) led to the discovery of substances with agonistic and antagonistic properties. These compounds have been used as powerful contraceptives. Luliberin controls the liberation of LH and the follicle-stimulating hormone (FSH), which stimulate in their turn the synthesis of sex hormones. A series of medphalan-containing peptides (compounds **241–259**) have been synthesised from luliberin analogues with agonistic and antagonistic properties (Table 3).[112–116]

The introduction of hydrophobic D-aminoacids in the 1-, 2-, 3-, and 6- positions and partly in the 5-, and 10-positions in the initial luliberin sequence led to the creation of powerful antagonists. On the other hand, the introduction into the hormone molecules of fragments comprising antitumour preparations known in oncology, such as melphalan or its D-enantiomer, may help to solve the problem of the attainment of a higher selectivity in the antitumour activity. The peptide component of the luliberin analogue makes it possible to increase the selectivity of the action of the alkylating agent as a result of the increased affinity of the peptide fragment for particular receptors on the cell membranes of the hormone-dependent tumours. It has been established that the binding is reversible and no alkylation of the receptors takes place. It is then possible to observe under these conditions a chain of biochemical reactions occurring in the cell.[112]

The peptides have been synthesised mainly by the solid-phase method and only the side chains were attached by the 'classical' method. The compounds obtained were purified with the aid of HPLC. Medphalan was used as an extremely suitable hydrophobic D-aminoacid residue, which can ensure an increase in the biological activity of luliberin analogues.[113]

The medphalan residue was either introduced directly into the peptide chain in the 6-position instead of the glycine residue or it was attached to the ω-amino-groups of lysine and ornithine located in the 6-positions in the luliberin fragments. In a number of cases, a diaminopropionic acid residue was used as the connecting unit for the attachment of two medphalan molecules to lysine or ornithine. The increase in enzyme stability and the formation of active compounds were achieved by the additional incorporation of D-aminoacid residues in the peptide molecules. By estimating the results of the modification of the initial aminoacid sequence in luliberin (the 3- and 6-positions) in compounds **254–259**, one can demonstrate that there is a fine balance between the agonistic and antagonistic activities determined by the substituents in these positions. The replacement of D-lysine by D-ornithine in compounds **254** and **255** increased the affinity for the receptors of the mammary gland tumour. Among the luliberin analogues, compounds **241** and **244** exhibited the highest agonistic and antagonistic activities respectively. They exhibited a high affinity for the membrane receptors of the cells of a series of tumours.

Compounds **245–253** inhibit the incorporation of [^{3}H]thymidine in DNA in cultures of the mammary gland and prostatic gland tumours and also inhibit the growth of the prostatic gland tumour (in experiments on animals). The peptides **254–259** are characterised by a broad spectrum of their affinity for the receptors of the hypophysis and the cell membranes of the mammary gland and prostatic gland tumours.

Table 3. Alkylating analogues of luliberin.

Compound	Formula	Ref.
Luliberin	pGlu—His—Trp—Ser—Tyr—Gly—Leu—Arg—Pro—Gly-NH_2	
241	H—Med—NH_2	113, 114
242	Ac-Pro—Phe(pCl)[a]-trp—Med—NH_2	113
243	Ac-Nal(2)[b]—Phe(pCl)—trp—Arg—Med—ala-NH_2[c]	113
244	Ac-Nal(2)—Phe(pCl)—Pal(3)[d]—Arg—Med—ala-NH_2	113, 114
245	H—lys(Med)—NH_2	112, 115
246	H—lys($A_2pr^d(Med)_2$)—NH_2	112, 115
247	H—orn(Med)—NH_2	112, 115
248	H—orn($A_2pr(Med)_2$)—NH_2	112, 115
249	Ac-Nal(2)—Phe(pCl)—trp—lys(Med)—ala-NH_2	112
250	Ac-Nal(2)—Phe(pCl)—trp—Arg—lys(Med)—ala-NH_2	112
251	Ac-Nal(2)—Phe(pCl)—trp—Arg—lys($A_2pr(Med)_2$)—ala-NH_2	112, 115
252	Ac-Nal(2)—Phe(pCl)—Pal(3)—Arg—lys(Med)—ala-NH_2	112, 115
253	Ac-Nal(2)—Phe(pCl)—Pal(3)—Arg—lys($A_2pr(Med)_2$)—ala-NH_2	112, 115
254	IA[e]—lys(Med)—NH_2	116
255	IA—orn(Med)—NHC_2H_5	116
256	Ac—lys(Med)—NHC_2H_5	116
257	Ac—orn(Med)—NHC_2H_5	116
258	Ac—lys(Med)—NHC_2H_5	116
259	Ac—lys(Ac-Med)—NHC_2H_5	116

[a] Phe(pCl) = *p*-chloro-D-phenylalanine. [b] Nal(2) = 3-(2-naphthyl)-D-alanine. [c] Pal(3) = 3-(3-pyridyl)-D-alanine.
[d] A_2pr = diaminopropionic acid residue $[-NH-CH_2-CH(NH-)]CO-$. [e] IA = indole-3-acetic acid residue.

A series of analogues of the gonadotropin-releasing hormone (compound **260**), in which melphalan is attached to the transferring molecule via the additional functional group of the aminoacid in the 6-position, have been synthesised.[117] These compounds can be used in veterinary practice to sterilise animals and in medicine in the chemotherapy of hormone-dependent tumours.

pGlu—His—Trp—Ser—Tyr—X(Y(Mel))—Leu—Arg—Pro—Z

260

X = L- and D-Tyr, L- and D-Orn, L- and D-Glu, L- and D-Asp.
Y = binding element.
Z = $GlyNH_2$, NHC_2H_5, azaglycine amide.

Another series of structurally similar derivatives of the gonadotropin-releasing hormone **261** have been obtained for the same purposes.[118]

pGlu—His—Trp—Ser—Tyr—D-Lys—Leu—Arg—Y—Z
|
A_1
|
A_2
|
Mel

261

A_1 = —CO—X—N (succinimide ring) ;

A_2 = —CO—CH(NHCOR)—$(CH_2)_n$—S—, n = 1, 2;

R = H, CH_3, C_2H_5;

X = $-(CH_2)_n-$, n = 1–5; $-C_6H_4-$, ,

Y = Pro, 4-HO-Pro; Z = Gly-NH_2, NHC_2H_5, azaglycine amide.

The analogues of the hypothalamic hormone somatostatin are of special interest for oncology. The concept of the effect of somatostatin derivatives on tumours is analogous to that for luliberin. Somatostatin **262** — a tetradecapeptide — inhibits the liberation of the growth hormone and exhibits a broad spectrum of inhibiting properties.

1 2 3 4 5 6 7 8 9 10 11 12 13 14
Ala-Gly-Cys-Lys-Asn-Phe-Phe-Trp-Lys-Thr-Phe-Thr-Ser-Cys
(1–14 disulfide bridge)

262

Some of its derivatives have been introduced into medical practice.[119] Conformational analysis and studies of the relation between the structure and function of somatostatin analogues have shown that the sequence necessary for the manifestation of biological activity consists of the β-twisting fragment Phe-Trp-Lys-Thr corresponding to the 7–10 residues of somatostatin.

A group of compounds related to somatostatin (compounds **263–273**) have been synthesised.[120] They differ from one another in the aminoacid residues in the 1-, 3-, 6-, and 8-positions in the peptide chain (Table 4).

Somatostatin retards the growth of tumours in patients with endocrine pancreatic tumours such as insulinoma, glucanoma, and others. However, the hormone is relatively unsuitable for tumour therapy owing to its multiple activity and its brief antisecretary effect. Somatostatin analogues are effective in the treatment of certain types of tumours, including treatment in combination with luliberin analogues.[120] Somatostatin analogues with alkylating fragments can exert both direct and mediated effects on the hormone-dependent tumours, functioning as substances transferring chemotherapeutic agents.

Compounds **263–273** have been synthesised by the solid-phase method and purified by gel filtration on Sephadex or by inverse phase HPLC (all the operations were performed at 4 °C and in the shortest possible time in view of the decomposition of the peptide). They exhibit an inhibiting effect on the liberation of the hypophyseal growth hormone, bind to the membranes of tumour cells, inhibit the incorporation of [^{3}H]thymidine in DNA in cell cultures, and inhibit the growth of particular tumour cells. For use in medical practice, the compounds are obtained in the form of salts: chlorides, phosphates, acetates, etc. or in the form of salts of alkali and alkaline earth metals.[120]

Table 4. Alkylating analogues of somatostatin.[120]

Compound	Formula (1 2 3 4 5 6 7 8)
263	Mel—Cys—Tyr—trp—Lys—Val—Cys—Thr-NH_2
264	Med—Cys—Phe—trp—Lys—Thr—Cys—Thr-NH_2
265	phe—Cys—Mel—trp—Lys—Val—Cys—Thr-NH_2
266	phe—Cys—Tyr—trp—Lys—Val—Cys—Mel-NH_2
267	Mel—phe—Cys—Tyr—trp—Lys—Val—Cys—Thr-NH_2
268	Mel—phe—Cys—Phe—trp—Lys—Thr—Cys—Thr-NH_2
269	Mel—Phe—Cys—Phe—trp—Lys—Thr—Cys—Thr-NH_2
270	Mel—trp—Cys—Phe—trp—Lys—Thr—Cys—Thr-NH_2
271	Mel—phe—Cys—Tyr—trp—Lys—Val—Cys—Trp-NH_2
272	[A_2pr(Mel)$_2$]—phe—Cys—Tyr—trp—Lys—Val—Cys—Thr-NH_2
273	Mel—Mel—phe—Cys—Tyr—trp—Lys—Val—Cys—Thr-NH_2

A series of modified derivatives of bombesin have been synthesised as substances interacting irreversibly with the bombesin membrane receptors. Bombesin **274** has been isolated from frog skin and is a tetradecapeptide (Table 5).

The gastrin-releasing peptide, consisting of 27 aminoacid residues and constituting one of the growth factors of the small cell lung carcinoma, is a twin of bombesin in the human organism. By competing with the natural ligand for the receptors, the bombesin antagonists inhibit a series of events leading to abnormal cell proliferation. A large number of melphalan-containing peptides — the bombesin antagonists **275–314** have now been synthesised and patented (Table 5).[121–123] All the compounds have been obtained by the classical methods of peptide chemistry in solutions.

Melphalan has been introduced into both bombesin antagonists and into bombesin analogues with a high affinity for receptors and with agonistic properties. The modified analogues are peptides of the C-terminal component of bombesin obtained by the removal, inversion, or substitution of aminoacids. The analogues in which melphalan is in the 6-position in the bombesin chain exhibit a higher affinity for receptors than the compounds containing melphalan in the 3-position.

Compounds **282**, **285–288**, **293**, **307**, **308**, and **311–314** are less cytotoxic and do not bind to other receptors, for example the epidermal growth factor receptors, which is due to the aminoacid sequence of these compounds.

Gastrin **315** — the gastrointestinal tract hormone — stimulates almost all the functions of the tract: secretion, motor response, and absorption. The amide **316** of the C-terminal tetrapeptide exhibits the full spectrum of physiological activity albeit more weakly than that of the complete molecule.

Table 5. Alkylating analogues of bombesin **274**.

Compound	Formula	Ref.
274	pGlu – Gln – Arg – Leu – Gly – Asn – Gln – Trp – Ala – Val – Gly – His – Leu – Met-NH_2	
275	Mel – Leu-ψ^{a} – NH_2	121
276	Mel – Leu-ψ – Nle-NH_2	121
277	Ac-Mel – Leu-ψ – Nle-NH_2	121
278	Boc[b]-Mel – Leu-ψ – Nle-NH_2	121
279	Ac-Mel – phe – Leu-ψ – Nle-NH_2	121
280	Boc-Mel – phe – Leu-ψ – Nle-NH_2	121
281	Mel – phe – Leu-ψ – Nle-NH_2	122, 123
282	Boc-Mel – OH	
283	Boc-Mel – val – His(Dnp[c]) – NH_2	122, 123
284	Mel – val – His(Dnp) – NH_2	122, 123
285	Mel – His(Dnp) – NH_2	122, 123
286	Boc-Mel – His(Dnp) – NH_2	122, 123
287	Boc-Mel – NH_2	122, 123
288	Mel – NH_2	122, 123
289	Boc-Mel – val – NH_2	122, 123
290	Mel – val – NH_2	122, 123
291	Boc-Mel – val – phe – NH_2	122, 123
292	Mel – val – phe – NH_2	122, 123
293	Boc-Mel – phe – NH_2	122, 123
294	Mel – Thr – [d] – NH_2	122, 123
295	Mel – ala – NH_2	122, 123
296	Mel – Nle-NH_2	122, 123
297	Mel – NH($(C_2H)_4CH_3$)	122, 123
298	Mel – NH_2	122, 123
299	Mel – NH_2	122, 123
300	Mel – ala – Nle-NH_2	122, 123
301	Mel – ala – NH($C_2H_4C_6H_5$)	122, 123
302	H – [ ] – <Mel[e]> – Nle-NH_2	122, 123
303	H – Mel – phe – Nle-NH_2	122, 123
304	H – Mel – ala – Nle-NH_2	122, 123
305	Mel – Leu – $NHNH_2$	122, 123
306	Mel – NH_2	122, 123
307	$(Boc)_2$Lys – Mel – NH_2	122, 123
308	Lys – Mel – NH_2	122, 123
309	Mel – Thr – His(Dnp) – NH($(CH_2)_4CH_3$)	122, 123
310	Boc-Mel – Thr – His(Dnp) – NH($(CH_2)_4CH_3$)	122, 123
311	Boc-Mel – NH_2	122, 123
312	Mel – NH_2	122, 123
313	Ac-Lys(Boc) – Mel – NH_2	122, 123
314	Ac-Lys – Mel – NH_2	122, 123

[a] The symbol ψ indicates the reduced CH_2NH peptide bond. [b] Boc = $(CH_3)_3COCO$. [c] Dnp = 2,4-dinitrophenyl.
[d] The symbol [ ] denotes the absence of the corresponding aminoacid residue in the peptide chain.
[e] The Mel residue is incorporated in the peptide chain between the 5- and 6- positions.

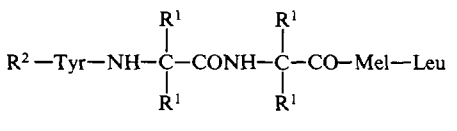
Glu – Gly – Pro – Trp – Leu – $(Glu)_5$ – Ala – Tyr – Gly – – Trp – Met – Asp – Phe-NH_2 (**315**),
Trp – Met – Asp – Phe-NH_2 (**316**),
Boc-Trp – Met – Asp – Sarc-NH_2 (**317**),
Boc-Trp – Met – Asp – Mel-NH_2 (**318**),
Trp – Met – Asp – Sarc-NH_2 (**319**),
Trp – Met – Asp – Med-NH_2 (**320**),
Trp – Met – Asp – Mel-NH_2 (**321**),
Asp – Sarc-NH_2 (**322**),
Asp – Med-NH_2 (**323**),
Asp – Mel-NH_2 (**324**).

In order to create gastrin analogues based on the modification of the C-terminal tetrapeptide **316**, which might act selectively on the tumours of the gastrointestinal tract, a series of derivatives **317**,[124] **318**,[125] and **319–324**[126] have been synthesised. Sarcolysine was used as the starting compound. The mixture of stereoisomers was separated by preparative chromatography. Compounds **319–324** proved to be active in relation to L-1210 lympholeukaemia, the mammary gland adenocarcinoma, the large intestine adenocarcinoma, and sarcoma 37. The peptide **318** has been used in the study of gastrin analogues as inhibitors in a radioimmunoassay system employing antisera, but it exhibited a weak affinity for antibodies and proved physiologically inactive under experimental conditions.

The introduction of various alkylating agents into the peptide chain makes it possible to investigate the characteristics of the interaction of hormones with the receptors and to obtain antagonists to peptide hormones. Melphalan has been used as a label in the study of the affinity of hormones for polypeptide receptors. Derivatives of bradykinin (compound **325**[127]), angiotensin II (compounds **326–328**[128]), and leucine-enkephalin (compounds **329**,[129,130] **330–332**,[130] and **333–336**[131]) have been obtained for this purpose.

Each of the compounds **325–336** synthesised was tested towards the type of receptors to which the corresponding hormone is bound. In particular, enkephalin analogues were studied as irreversible antagonists of the δ-opiate receptor.

Arg – Pro – Pro – Gly – Phe – Ser – Pro – Phe – Arg (bradykinin),
HCO-Sarc – Arg – Pro – Pro – Gly – Phe – – Ser – Pro – Phe – Arg (**325**),
Asn – Arg – Val – Tyr – Ile – His – Pro – Phe (angiotensin II),
Ac-Asn – Arg – Val – Tyr – Ile – His – Pro – Mel (**326**),
Ac-Asn – Arg – Val – Tyr – Ile – His – Pro – Mel-OCH_3 (**327**),
Ac-Asn – Arg – Val – Tyr – Ile – His – Pro – – Mel-$OCH_2C_6H_5$ **328**),
Tyr – Gly – Gly – Phe – Leu (leucine-enkephalin),
Mel – D-Ala – Gly – Phe – Leu-OCH_3 (**329**),
Tyr – D-Ala – Gly – Phe – Leu – Mel-OCH_3 (**330**),
Tyr – D-Ala – Gly – Mel – Leu-OCH_3 (**331**),
Mel – D-Ala – Gly – Mel – Leu-OCH_3 (**332**).



333–336

333: R^1 = H, R^2 = $CH_2CH{=}CH_2$.
334: R^1 = H, R^2 = $CH_2C_6H_5$.
335: R^1 = CH_3, R^2 = $CH_2CH{=}CH_2$.
336: R^1 = CH_3, R^2 = $CH_2C_6H_5$.

Studies on the synthesis and mechanisms of action of polypeptide hormones containing sarcolysine stereoisomers yielded extremely interesting results, the final interpretation of which requires further research.

Thus a large number of peptides, incorporating 4-[bis-(2-chloroethyl)amino]-DL-, L-, and D-phenylalanine and their derivatives have now been synthesised. Sarcolysine dipeptides with protein aminoacids were obtained initially. In many cases, these compounds were of considerable interest for practical oncology. Further search for effective antitumour compounds led to the incorporation of nonprotein aminoacids and aminoacids which are antimetabolites of natural aminoacids in the peptides. Particular attention was then paid to the dependence of the antitumour activity on the stereoconfiguration of the 'carrier' of the alkylating compound.

A series of studies have been devoted to the synthesis of biologically active polymers which are homo- and co-polypeptides modified by sarcolysine and melphalan. The dependence of the antitumour activity on the nature and configuration of the aminoacid and the length of the polypeptide chain in these compounds has been investigated.

Fragments of biologically important proteins, such as histones, enzymes, and hormones, modified by sarcolysine and its enantiomers, were obtained later. The introduction of melphalan or medphalan into fragments of peptide hormones makes it possible to study the mechanism of the interaction of these compounds with the corresponding receptors, which is exceptionally important for the creation of substances with prespecified properties. The presence of an alkylating fragment in the molecule has a mediating effect on the chain of reactions occurring in the cell and makes it possible to obtain compounds with a highly specific activity. These may be not only substances with antitumour activities but also compounds with other types of biological activity.

* * *

The data presented in the review demonstrate the usefulness of the development of methods for the synthesis and study of the peptides of 4-bis(2-chloroethyl)amino]-DL-, -L-, and -D-phenylalanine with natural aminoacids, their synthetic analogues, and fragments of biologically important proteins, because compounds with both high antitumour activity and other types of physiological activity may be discovered among these substances.

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Current advances in the X-ray crystallography of proteins

E M Popov

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Abstract. The present state and prospects for the development of the X-ray crystallography of globular proteins are analysed. The mechanisms of the functioning of membrane receptors, the immune proteins of T-lymphocytes, the histone octameric core of nucleosomes, DNA topoisomerase, the aspartate proteases of retroviruses, and the proteins of the actomyosin complex of skeletal muscles are examined on the basis of the three-dimensional structures of the protein molecules which have become known in recent years. It is shown that the results of the X-ray diffraction analysis of proteins has played a decisive role in the creation of an experimental basis and the development of the approaches necessary for the establishment of theoretical biology. A large proportion of the review is devoted to the advances in X-ray crystallography as regards the sources of radiation, the phase problem, and the experimental conditions. The use of synchrotron radiation and the abandonment of multiplet isomorphous substitution in the determination of phases not only significantly simplify the study of the molecular structures of proteins but permit an approach to securing information about the structures of protein intermediates which had previously been inaccessible. The bibliography includes 324 references.

I. Introduction

One of the most outstanding scientific investigations not only in biology but throughout natural sciences in the course of the passing century was completed at the end of the 1950s and the beginning of the 1960s. Perutz and Kendrew determined the three-dimensional structures of haemoglobin and myoglobin, having first solved the problem, posed more than a quarter of a century earlier by Bernal, of the determination of the three-dimensional structures of protein molecules with the aid of X-ray diffraction. This event implied the establishment of a new direction in the development of biology — the morphology of elementary biosystems, revealing previously invisible possibilities for discovering the structure of living matter. Without knowing the atomic-molecular structures of proteins, it is impossible to understand the nature and specific features of their interactions, and the mechanisms of the functioning of enzymes, the immune system, the genetic apparatus, the membrane proteins, and many others. The advances achieved in the first investigations were of universal importance, which was reflected in the state of virtually all aspects of the research into the organic world. After more than three decades have elapsed since the publications by Perutz and Kendrew, X-ray diffraction still remains the only direct method for the determination of the three-dimensional structures of protein molecules and their complexes at the atomic level. The data obtained with its aid still remain the irreplaceable experimental basis of any search for solutions to fundamental problems such as those of the structural and structural-functional organisation of protein molecules. Taking into account the active role of proteins in vital processes and their universal biochemical and biophysical properties, one may claim that the creation of theories of the structural and structural-functional organisation of proteins will entail the establishment of quantitative theoretical biology.

After the classical studies by Perutz and Kendrew and also Phillips, who established in 1965 the three-dimensional structure of the first enzyme (lysozyme), X-ray diffraction analysis began to develop rapidly in many scientific centres. After only two years, the structures of ribonuclease A,[1,2] α-chymotrypsin,[3] and carboxypeptidase A,[4] were elucidated. By 1975 some 70 proteins had had their crystal structure determined with a resolution of better than 3.5 Å (Blundell and Johnson[5]) and at the present time the number approaches 3000.[6] The rate of advance was determined mainly by the difficulties in obtaining single crystal specimens of sufficient size and with a high degree of order. Proteins do not form regular macroscopic structures in the cells and organisms and the growing of protein crystals under laboratory conditions requires much skill and patience. The difficulties in obtaining high quality specimens are mentioned in almost all investigations. The following is, for example, a typical remark made by investigators[7] who studied the three-dimensional structure of lipoxygenase-1, an enzyme made up of 839 aminoacid residues: 'the protein crystals were obtained after trying more than 1000 different crystallisation conditions'.

E M Popov Laboratory for Enzyme Chemistry,
Shemyakin and Ovchinnikov Institute of Bioorganic Chemistry,
Russian Academy of Sciences, ul. Miklukho-Maklaya 16/10,
117871 Moscow, Russian Federation. Fax (7-095) 310 70 07

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This review is devoted to the analysis of the current state of the X-ray crystallography of proteins and the prospects for the development of the method in the immediate future. For this purpose, the studies which in some way constitute the most major advances at the present time were selected from the multiplicity of publications.

Sections II – VI present the results of X-ray diffraction studies on proteins, the scientific importance of which is determined by the importance of the objects analysed themselves. The three-dimensional structures of the molecules of membrane receptors, the immune proteins of T-lymphocytes, the histone octameric core of nucleosomes, DNA topoisomerase, the aspartate proteases of retroviruses, and the proteins of the actomyosin complex of skeletal muscles, all of which have become known only in recent years, are discussed in these sections. Studies of this kind have given rise to an extensive development of the study of the morphology of biosystems at the atomic-molecular level and will continue with increasing intensity.

In Sections VII and VIII, the use of the first methodological improvements in the X-ray diffraction analysis of proteins, concerning the sources of radiation, the exposure time, the phase problem, and the experimental conditions, is emphasised. Novelties of this kind are of special interest because they yield previously inaccessible information and hence lead to a vigorous development of the study of the morphology of proteins.

II. Membrane proteins

One of the greatest advances in the X-ray diffraction analysis of proteins in recent years is the start made on the elucidation of the three-dimensional structures of the first membrane proteins. It is useful to report briefly what had been known about these proteins before their investigation by X-ray diffraction. In the usual plasma membrane, the protein content is about 50% of its mass. However, in certain membranes, for example in the internal membranes of mitochrondria and chloroplasts, the protein content increases to 75%, whilst in others, for example in the myelin membrane, it falls to 25%. The lipid bilayer is threaded by many membrane proteins right through and the proteins are in contact with the aqueous medium on either side of the membrane. The molecules of these proteins, referred to as the transmembrane proteins, as well as the lipid molecules surrounding them possess amphipathic properties because they contain hydrophobic sections, interacting within the bilayer with the hydrophobic tails of lipids, and hydrophilic sections turned towards water on either side of the membrane. Another group of membrane proteins is in contact with water only on one side of the bilayer. Some of them are immersed in the outer or inner layer of the membrane, others are associated via nonvalence interactions with transmembrane proteins, whereas a third set of proteins of this kind are attached to the membrane via the chains of aliphatic acids bound covalently to them and inserted in the lipid layer.

By virtue of the dynamic properties of the membranes, the proteins associated with them can be separated from the lipids. Sometimes this operation is fairly simple and can be performed under mild conditions, for example by extraction with a salt solution. The liberated membrane proteins are referred to as peripheral. In other cases, usually involving transmembrane proteins, the isolation is more complex and is not always successful. Many proteins, called 'integral' on the basis of the method for their purification, can be isolated only after the complete disruption of the bilayer with the aid of detergents and organic solvents. On mixing with the membrane, the nonpolar, hydrophobic ends of the detergent molecules interact with the lipids and, by disrupting their association with the proteins, bind to the hydrophobic sections of the latter. As a result of this, the polar, hydrophilic ends of the proteins become oriented in the direction of the aqueous medium. The solubilised membrane proteins, which acquire the ability to dissolve in water, pass into solution in the form of complexes with the detergent. After the removal of the latter, the proteins lose their solubility and precipitate, forming a mixture of different proteins. As a rule, the membranes are heated to 100 °C in a 1% solution of a strong detergent as a preliminary step, which leads to the disruption of all the noncovalent protein–protein and protein–lipid interactions. Helenius and Simons[8] developed a method for the separation of proteins by electrophoresis in a polyacrylamide gel in the presence of a detergent (sodium dodecyl sulfate).

Further studies on membrane proteins — the investigation of their functions, the mechanisms of their action, and their three-dimensional structures — encountered major difficulties. It was found that the liberation of the protein molecules from the membrane is frequently accompanied by the irreversible denaturation of their native structures and hence by the loss of activity. In the rare favourable cases when the proteins are solubilised under mild conditions and when their concentrations are low, their functional properties are not lost, which indicates at least partial retention of the native conformations. The most detailed information about the proteins in the lipid bilayer has been obtained in the study of the plasma membrane of human erythrocytes, which contain haemoglobin — a nonmembrane protein which is the most abundant constituent of these cells. The convenience of this object is due to the fact that the erythrocyte membranes, called 'shadows', are the only ones in the cell and they can be easily isolated in a pure form with and without rupture and can even be obtained turned inside out. In the study of erythrocyte shadows, it was possible to establish for the first time that the membrane bilayer is threaded right through by certain membrane proteins and that the outer and inner sides of the membrane are asymmetric. Studies on the proteins of the human erythrocyte plasma membrane by one-dimensional electrophoresis in a polyacrylamide gel in the presence of sodium dodecyl sulfate led to the identification of about 15 principal proteins with molecular masses ranging from 15 to 250 kDa. Three of them — spectrin, glycophorin, and the so called band III protein — constitute altogether 60% of the mass of all the membrane proteins in the cell. They are bound in different ways to the membrane and can serve as examples of three typical ways in which proteins are associated with membranes.

Spectrin (240 kDa) can be equally regarded as a membrane protein and as a component of the cytoskeleton of erythrocytes. Two of its polypeptide chains, which are twisted relative to each other, form mobile dimers, which are combined into tetramers, as a result of interactions with the short actin filaments and other proteins, covering the cytoplasmic surface of the membrane in a dense network. The structural organisation enables spectrin to regulate the mobility of proteins and their distribution in the plasma membrane.

Glycophorin is the first membrane protein for which the aminoacid sequence has been determined. This transmembrane glycoprotein contains 131 aminoacid residues and about 100 sugar residues; its molecular mass is 30 kDa. Fig. 1 shows that a large proportion of the polypeptide chain of glycophorin is on the outer surface of the membrane, where the hydrophilic N-terminal fragment is located. The C-terminal section of the chain, also made up predominantly of hydrophilic residues, is immersed in cytoplasm, while the hydrophobic fragment, in the form of a single α-helix comprising 20 aminoacid residues, passes through the nonpolar lipid bilayer.

The band III protein from the human erythrocyte membrane is a transmembrane protein with a molecular mass of about 100 kDa (approximately 800 aminoacid residues). This is a transport protein, two molecules of which form an anionic channel for Cl^- and HCO_3^- ions moving passively through the membrane in accordance with their concentration gradients. The bilayer is threaded several times by the polypeptide chain of the protein in the α-helical conformation; approximately one third of the chain from the N-terminus is immersed in cytoplasm, whilst the short C-terminal section is located in the extracellular space (Fig. 1).

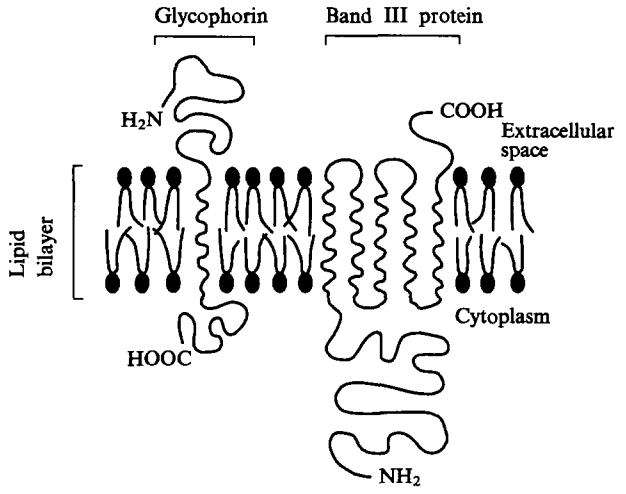


Figure 1. Schematic illustration of the disposition of glycophorin and the band III protein in the human erythrocyte membrane.

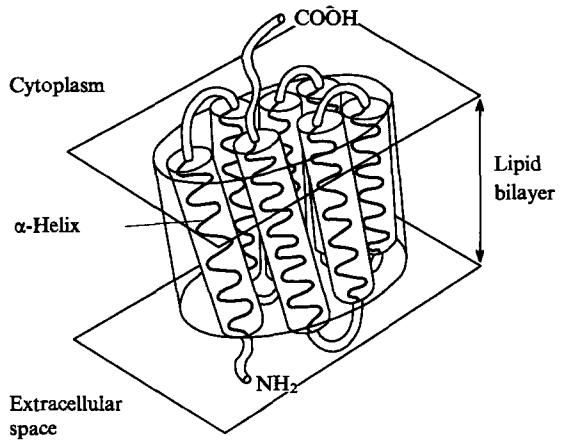


Figure 2. The structure of the bacteriorhodopsin molecule in the lipid bilayer.

In order to understand the mechanism of the functioning of the band III transport protein as well as the mechanisms of the action of other membrane proteins, it is necessary to know at least the three-dimensional structure of the molecule under the conditions of the lipid bilayer. Here it is necessary, first, to separate the transmembrane protein from the lipids and other membrane proteins without simultaneously damaging its three-dimensional molecular structure, which is very difficult; second, a highly ordered single crystal of the required size must be obtained from the isolated protein molecules. An alternative approach to the preparation of protein objects for X-ray diffraction analysis, which also concerned crystallographic studies on membrane proteins, arose in the 1980s. The approach involves genetic engineering based on the site-specific recombination of DNA. As a result, it became possible to devise specific, including artificial, genetic programs and to obtain the required proteins and their fragments in amounts sufficient not only for theoretical but also for applied purposes. However, genetic engineering methods have not radically facilitated the preparation of crystalline specimens made up of the native conformations of protein molecules and giving rise to distinct diffraction patterns. Nevertheless, the prospect of obtaining chemically pure membrane proteins, their mutants, and components of any length and with any variation of the aminoacid sequences greatly expanded the field where solutions to this problem may be sought.

Until recently, the only membrane transport protein for which certain details of its three-dimensional structure, obtained with a resolution of ~7.0 Å, were known was baceteriorhodopsin discovered in the plasma membrane of the purple bacterium *Halobacterium halobium*. Its polypeptide chain consists of 248 residues. Bacteriorhodopsin functions as a photoactive proton pump. After activation by a single light quantum, the excited chromophore induces conformational changes in the protein, as a result of which two protons are transferred from the inner surface of the cell to the outer surface. A proton concentration gradient and an electric potential gradient are created in the membrane and give rise to the synthesis of ATP. The bacteriorhodopsin molecules in the membrane form a planar crystal lattice resembling a two-dimensional crystal. Henderson and Unwin[9] used a combination of low intensity electron microscopy and small angle X-ray scattering to determine the three-dimensional structure of the protein and its orientation in the membrane. As a result of attaining record accuracy for both methods in the above investigation, it was shown that the polypeptide chain of bacteriorhodopsin forms seven α-helices in the membrane, each of which contains about 30 aminoacid residues (Fig. 2). All the helices intersect the lipid bilayer approximately at right angles to the plane of the membrane. They are close-packed and do not form a water-filled channel. The protons therefore apparently pass through the membrane via a series of protein chains of the α-helical residues, interacting with one another, the functioning of which is initiated by the excited chromophore.

A considerable proportion of the membrane proteins are receptors, i.e. are allosteric proteins capable of rearranging in a definite manner the three-dimensional structure of the molecule on interaction with hormones — specific signal mediators. The allosteric change in conformation is transmitted via the transmembrane chain of coupled proteins or domains of a single large protein within the cell and stimulates the corresponding physiological process in the latter. The available information about the three-dimensional structures of receptors and other components of transmembrane proteins is extremely scanty. Until recently, it has been possible to obtain the crystals and to determine the structures of only two specific membrane receptors — the photoreceptor centre[10,11] and porin.[12] In the 1990s, the studies on receptor proteins began to acquire a more systematic character. The information obtained hitherto about their three-dimensional structure refers, as will be shown below, not to the structures of whole membrane receptors but so far only to the outer portions of the molecules — extracellular domains.

1. The structure of the complex between the human growth hormone (hGH) and the outer part of the receptor (hGHbp)

De Vas et al.[13] established by X-ray diffraction with a resolution of 2.8 Å the three-dimensional structure of the protein complex between the hGH ligand and the extracellular domain of the hGHbp receptor, the interaction of which activates the growth and metabolism of the cells in the muscle, cartillage, and bone tissues. The molecule of the hGHbp membrane receptor consists of components separated in space: the extracellular fragment binding the hormone and located on the outer side of the membrane, the transmembrane fragment threaded through the lipid bilayer, and the intracellular component the function of which is as yet not entirely clear. There is also no clear idea about the mechanism of the interaction of all the components with one another and about the transfer into the interior of the cell of the signal which follows the association of the hormone with the outer part of the receptor.

The X-ray diffraction analysis of the hormone-receptor complex showed that the extracellular protein chain of the hGHbp molecule forms two easily distinguishable domains consisting of fragments incorporating the 1-123 and 128-238 aminoacid residues and linked by the 124-127 labile section. Each domain contains seven tiers of β-sheets, which give rise to a sandwich structure. De Vas et al.,[13] attribute a major importance

to the C-terminal octapeptide 239–246 section in the performance of the hormonal function. On sorption of the substrate, it ensures the conformational mobility of two domains of the receptor, which is necessary for the achievement of effective nonvalence contacts. In addition, it assists in the approach of the extracellular component of one receptor to the corresponding component of another and hence involves the two analogous outer domains of the latter in the binding of the hormone. This results in the formation of the complex hGH(hGHbp)$_2$, in which both receptors interact with the hormone virtually to the same extent despite the fact that there is no full structural similarity between the two centres for the binding of the hGH molecule to the pairs of domains of the two receptors. The three-dimensional structure of the complex hGH(hGHbp)$_2$ outwardly resembles the complex of an antigen with two pairs of domains (Fab) of immunoglobulin.

2. The structure of the extracellular domain of the aspartate receptor of the bacterium *Salmonella typhimurium* and its complex with the ligand

The three-dimensional structure of the domain in the free state of the receptor and in the receptor associated with aspartate has been determined by Milburn et al.[14] with resolutions of 2.4 and 2.0 Å. Being a typical transmembrane protein, the whole molecule of the aspartate receptor consists of three components: the outer ligand-binding domain, the cytoplasmic signal domain, and an intermediate domain located in the lipid bilayer. The periplasmic section of the 31–188 protein sequence, containing the Asp binding centre, is linked by two peptide fragments (7–30 and 189–212), threaded through the membrane, to the inner, largest domain, which is made up of the 1–6 and 213–552 residues.[15,16]

The aminoacid sequence of the extracellular 31–188 domain has been synthesised by a genetic engineering method.[17] The purified polypeptide crystallised exclusively in the form of a dimer having the same affinity for the aspartate ligand as the entire protein of the natural type. The diffraction pattern, which was initially diffuse, acquired a sharper outline on cross-linking of the two chains of the dimer by the disulfide bond formed by the Cys residues in positions 36. The preparation thus obtained did not differ from the domain of the native receptor as regards its functional properties.

The three-dimensional structures of the subunits of the dimer not associated with the ligand are identical and have the form illustrated schematically in Fig. 3. Each of them consists of four α-helices forming a cylinder ~20 Å in diameter and > 70 Å long.

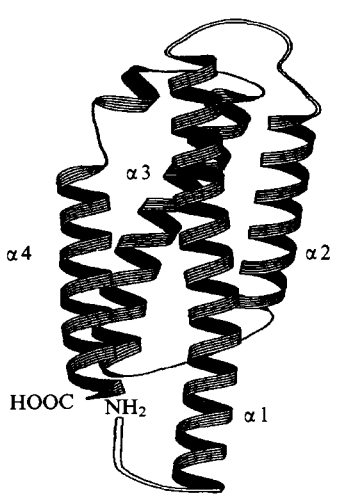


Figure 3. Schematic ribbon representation of the three-dimensional structure of the extracellular domain of the aspartate-binding receptor.[14]

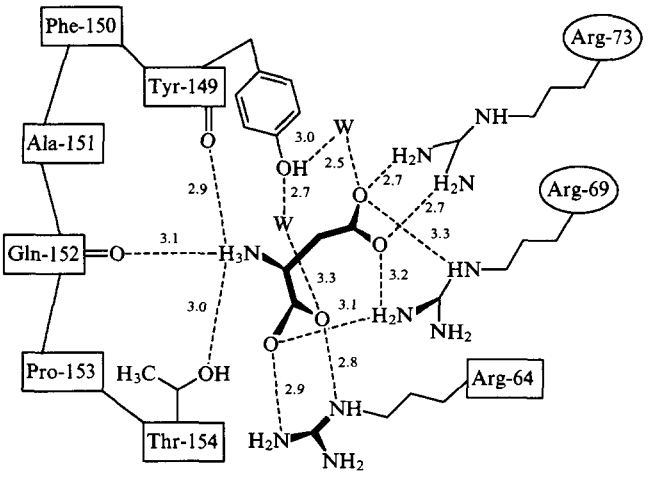


Figure 4. Schematic illustration of the hydrogen bonds between aspartate and the ligand-binding centre formed by the extracellular domains of two aspartate receptors. The aminoacid residues of one of the receptors are indicated in rectangles and those of the other in ovals; [14] W is a molecule of the water of crystallisation.

The dimer cross-linked by the disulfide bridge exhibits C_{2v} symmetry. On interaction with the ligand and formation of a complex, the symmetry breaks down. The centre for the binding of aspartate to the receptor is located near the apex of the dimer between the contact surfaces of the subunits at a height exceeding 60 Å above the postulated surface of the outer phospholipid layer of the membrane. In conformity with its symmetry, the dimer made up of the extracellular domains of two receptors has two hydrophilic ligand-binding pockets. One of them, most clearly manifested on electron density charts, is illustrated in Fig. 4. It incorporates the Arg-64 residue and the 149–154 fragment of one subunit and the Arg-69 and Arg-73 residues of another subunit, together with molecules of water of crystallisation, which form with aspartate a complex network of hydrogen bonds in the ligand–receptor complex. The sorption of two aspartate molecules induces the mutual approach of the residues forming the hydrophilic pockets and an overall compaction of the dimeric complex. The mean square deviation of the C^{α} atoms of one subunit (without taking into account the 77–85 fragment) is 0.47 Å and that of the C^{α} atoms of the other subunit (without taking into account the 25–36 fragment) is 0.34 Å. The deviations of the C^{α} atoms in the 77–85 and 25–36 sections exceed appreciably the above values. The conformational changes in the dimer on binding of aspartate lead to the rotation of the subunit by 4° relative to the short axis perpendicular to the twofold axis and the contact surfaces of the ligand-binding domains. The extent to which the above conformational deviations reflect the specific allosteric effect of the receptor still remains unelucidated.

3. The structure of prostaglandin H_2 synthase (PGHS)

Prostaglandins — aliphatic acid derivatives with 20 carbon atoms in the chain — constitute an important family of local chemical mediators, the source of which is cells of many types. They bind to a large number of receptors on the cell surface and induce the contraction of smooth muscle, diminish the capacity of thrombocytes for aggregation, activate the central nervous system, act on inflammatory processes, and liberate renin.[18] It has been established recently that prostaglandins also play an important role in the pathophysiology of cancer and of cardiovascular diseases.[19–21]

The crystal structure of the first membrane enzyme, prostaglandin H_2 synthase (PGHS), was first established in 1994.[22] The protein catalyses two processes in the first stage of the

biosynthesis of prostaglandins. It initiates and activates, firstly, the cyclooxidase reaction, during which arachidonic acid is converted into prostaglandin PGG_2 and, secondly, the subsequent peroxidase reaction, in which PGG_2 is converted into PGH_2, the latter being rapidly transformed into one of the prostanoids. The integral membrane protein PGHS is located predominantly in the endoplasmic reticulum. Its liberation from the membrane is achieved by extraction with a salt solution and by solubilisation with a nonionic detergent, in the presence of which crystallisation is also carried out. In the resulting specimen, the protein molecules are associated with flurbiprofen, a nonsteroid antiinflammatory preparation, and form dimeric complexes with a twofold symmetry axis. Two isomers of prostaglandin H_2 synthase have been detected in the cells: PGHS-1 and PGHS-2. These are distinguished by their activity and their distribution in the tissues. The three-dimensional structure of the sheep PGHS-1 has been determined[22] with a resolution of 3.5 Å. It is a glycosylated protein with a molecular mass of 70 kDa and 587 aminoacid residues, which participates in the maintenance of tissue homeostasis. As regards the function of PGHS-2, it has been suggested that the enzyme is responsible for the biosynthesis of prostaglandins during cell division and in inflammatory processes.

The three-dimensional structure of the PGHS-1 molecule consists of three largely autonomic and apparently independently coiling subunits: a small N-terminal domain, a membrane-bound section of the chain, and an enzyme domain. The first N-terminal domain comprises the 33–72 section of the polypeptide chain (the 1–24 residues constitute a signal sequence, which can be split off, and do not enter into the mature enzyme; the 25–32 residues could not be interpreted on the basis of the electron density maps obtained). Its conformation, stabilised by three intradomain disulfide bonds, is very similar to the structure of the epidermal growth factor (EGF). Polypeptide modules, similar to EGF, have been found in many extracellular proteins — factors stimulating the growth of neurons and the clotting of blood, and also in the proteins of surface cells necessary for their survival and proliferation. The function of the EGF-like domain of the PGHS-1 molecule is unknown. The second domain, incorporating the 73–116 residues, consists of four α-helices, oriented along one side of the monomer. Its conformation, highly amphipathic properties, and the hydrophobic surface profile quite definitely indicate the possible integration of the enzyme in only one lipid layer, so that the given membrane protein is monotopic according to Blobel's classification.[23] The third, largest catalytic domain of the PGHS-1 molecule (the 117–587 residues) has a globular structure consisting of two lobes twisted relative to one another but nevertheless fairly distinguishable. One of them, the larger, has a V-shape made up of two α-helices held together by an intermediate third helix acting in a manner resembling a pair of forceps. This construction serves as a framework around which a further four α-helices and the loops connecting them are packed. The small 'lobe' of the catalytic domain consists of a packet of six parallel helices.

As a bifunctional enzyme, the PGHS-1 protein has two active centres: the peroxidase and cyclooxidase centres. The former is on the surface of a narrow groove between the large and small 'lobes' of the catalytic domain and contains the prosthetic group — the high-spin Fe(III)-protoporphyrin IX — the proximal surface of which is turned towards the small 'lobe'. The peroxidase activity involves only the reduction of the PGG_2 synthesised in the cyclooxidase centre and the activation of the cyclooxidase reaction. This mechanism is typical for the haem-dependent peroxidases, which reduce hydroperoxidase substrates via a two-electron transfer reaction, leading to the formation of the oxoferrylporphin radical-cation. The oxidised haem returns to the initial stage after two successive one-electron transfers to the substrates being reduced or as a result of the transfer of oxygen to aryl sulfide compounds. The PGHS-1 molecules reduce preferentially PGG_2 and other long-chain aliphatic acids as well as aliphatic hydroperoxidases. The cyclooxidase active centre consists of a long narrow channel (8 × 25 Å) extending from the outer surface of the domain, linked to the membrane via its helix, to the centre of the monomeric PGHS-1 molecule. The diffuse diffraction pattern arising from the crystals, which have so far been grown for onlyone enzyme–inhibitor complex, did not allow the authors[22] to put forward on the basis of the data obtained a mechanism of the catalytic reaction occurring in the cyclooxidase centre.

In conclusion of the brief consideration of the results of the X-ray diffraction analysis of prostaglandin H_2 synthase, one should mention that the importance of this study, as the first investigation of the three-dimensional structure of a membrane enzyme, does not lie solely in the experimental facts themselves, the value of which is quite evident. A no less important feature of the study is associated with the influence of the data obtained on the very formulation of the relevant questions on a qualitatively different, higher level. The search for solutions to important problems such as the incorporation of enzymes in membranes, the function of the EGF-like module, the conformational and chemical aspects of the catalytic steps performed in the cyclooxidase and peroxidase active centres, and a number of others, which are of general interest, can now be based on concrete structural data.

III. Proteins of the immune system

Although the proteins of the immune system are membrane proteins, nevertheless, bearing in mind their functional characteristics, it is useful to consider the latest advances in X-ray diffraction analysis in the study of their three-dimensional structure in a separate section.

It was established in the 1960s that the two main types of immune responses are affected by different types of lymphocytes — T and B. The T-lymphocytes, which are responsible for cellular immunity, multiply in the thymus — the central lymphoid tissue. The antibodies produced and the B-lymphocytes responsible for the humoral response are formed from the stem cells of the haemopoietic tissue in mammals and in the Fabricius sac in birds. They subsequently migrate with the bloodstream to peripheral lymphoid tissues. The immune response of the cellular type implies the proliferation of specialised cells responding to foreign antigens, which are disrupted either directly on the surfaces of the cells produced or with the aid of other cells, such as macrophages. The humoral response consists in the activation of the synthesis of antibodies, circulating in the liquid media of the organism and interacting specifically with the foreign molecules. The binding of the antibody to the antigen facilitates the absorption of the latter by phagocytes and frequently activates the special system of the blood proteins — the complement system, which assists in the destruction of the antigen.[24,25] One of the functional problems in immunology is associated with the study at the atomic-molecular level of the mechanisms of the recognition and of the response reactions of the immune system to the appearance in the organism of infective antigens — foreign proteins, viruses, bacteria, and pathogenic substances.

According to Burnet's theory of clonal selection,[26,27] the specificity of the antigen response of lymphocytes is due to the presence on the surfaces of the T- and B-cells of receptor proteins, which interact selectively with particular antigens.

It is known that, on stimulation by the antigen, the T-lymphocytes begin to divide vigorously and are converted into active effector cells. Depending on the antibodies produced by them on the cell surface, they can be divided into at least three groups.[28] The first group comprises cytotoxic cells, which, by reacting with the foreign viral antigens, kill the infected cells before the onset of the replication of the virus. The molecular mechanism responsible for the destruction of the target cell has

so far not been elucidated. Nevertheless, it is known that this requires direct contact between the cytotoxic T-lymphocyte (the killer cell) and the infected cell (the target cell).[29] The second group of the activated T-lymphocytes includes the so called T-helpers, the helper cells required both by B- and T-cells to generate the humoral and cellular immune responses and also for the activation of macrophages. Finally, the third group is made up of T-suppressors, which suppress the response of the B-cells or other T-cells to antigens. It has been noted that, like the majority of T- and B-lymphocytes, the T-suppressors function only when they are continuously stimulated in this respect by the T-helpers, which, by activating the T-tissues of the suppressor, are themselves inhibited. Such feedback in the complex network of the interactions of lymphocytes ensures the self-regulation of the activities of cells of both types.

A large proportion of the T-lymphocytes recognise foreign agents, provided that they are not associated on the cell surfaces with membrane glycoproteins, which are coded by the genes of the major histocompatibility complex (MHC).[30] There are two classes of MHC molecules, I and II, each of which consists of a set of glycoproteins of the cell surface.[31-33]

The recognition by the T-lymphocytes of an antigen associated with the MHC glycoproteins on the surface of the target cell is effected by the T-cell antigen receptor (TCR) and one of the transmembrane proteins, CD4 or CD8, which are TCR coreceptors.[34-36] It has been suggested that a nonvalence complex is formed as a result of the stabilising contact between variable sections of the TCR molecule, the antigen, and the polymorphic sections of the MHC and also between the CD4 (or CD8) membrane proteins and the nonpolymorphic sections of the class II (or class I) MHC respectively. The coordinated interactions of TCR and CD4 (or CD8) with the MHC proteins of the target cells require a definite set of properties of the T-cells, which appear during the development of lymphocytes in the thymus, their differentiation, and maturation.[37-43]

The interaction of CD8 with MHC-I molecules triggers the intracellular signal system via the $p56^{lck}$ protein, an src-bound tyrosine kinase, associated directly in the lipoid cells with both CD4 and CD8.[44] In this case, the CD8–$p56^{lck}$ complex can function virtually like growth factor receptors, in which the linkage with the intracellular domain activates the intracellular tyrosine kinase.

The X-ray diffraction data on the three-dimensional structures of membrane proteins and their individual domains involved in the functioning of the T-cell immune system began to appear only in the 1990s. Since this concerns mainly the structures of the membrane proteins, the use of the X-ray diffraction method in cellular immunology has encountered major preparative difficulties which have not yet been fully overcome. Incidentally, the situation is also similar in all other aspects of molecular biology concerned with the study of phenomena occurring on the surfaces of cells. Therefore, in assessing the results of the X-ray diffraction analysis discussed below, one must bear in mind that they represent only the beginning of an extensive penetration of the method into the problems of T-cell immunology.

1. The structure of the extracellular fragment of the CD8 coreceptor of T-lymphocytes

The CD8 protein has been detected on the surfaces of T-cells in two forms: the disulfide-linked homodimer α_2 and the heterodimer $\alpha\beta$.[27] Both forms have N-terminal extracellular domains, the aminoacid sequences and structural features of which are similar to those of the variable domains of the immunoglobulin Ig-V.[45,46] The CD8 homodimer α_2 is illustrated schematically in Fig. 5. The extracellular region of CD8 includes 162 residues, 114 of which constitute the N-terminal immunoglobulin domain linked to the transmembrane section by a chain of 48 residues. The intracellular region consists of a highly polar aminoacid sequence interacting directly with tyrosine kinase $p56^{lck}$.

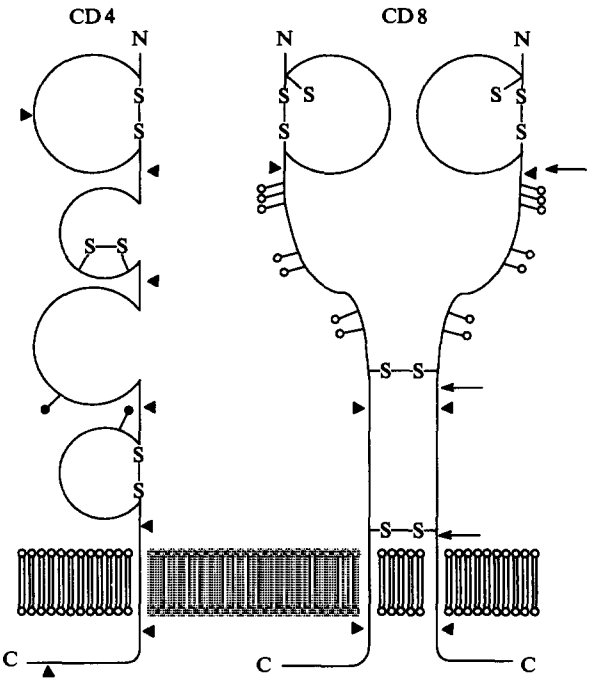


Figure 5. Schematic illustration of the CD4 receptor and the homodimer of the CD8 receptor. Each large circle corresponds to an immunoglobulin domain; the open circles denote the potential *O*-glycosylation sites, whilst the filled circles denote the corresponding *N*-glycosylation sites; the arrows indicate the ends of expression, whilst the dark triangles represent the limits of the intron sequences.[47]

The three-dimensional structure of a large part of the extracellular polypeptide chain of the human CD8 coreceptor, the length of which corresponds to 146 residues (CD8-146), has been established[47] with a resolution to within 2.6 Å. The crystals employed for the determination of the structure had the necessary size and gave rise to a satisfactory diffraction pattern only after the treatment of the protein preparation with neuraminidase, *O*-glycosidase, and V8-protease. In the CD8-146 structure thus determined, the overall character of the coiling of the polypeptide chain of the N-terminal domain proved to be identical to that of the variable domains of the immunoglobulin Ig-V. Its three-dimensional structure also contains, as can be seen from Fig. 6,

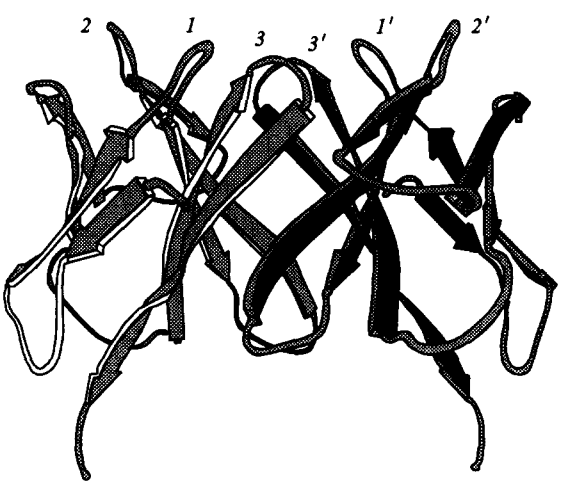


Figure 6. Schematic ribbon illustration of the three-dimensional structure of the CD8-146 homodimer. The numerals *1*, *2*, *3* and *1'*, *2'*, *3'* denote the CDR-1-, CDR-2-, and CDR-3-like loops of the two subunits.[47]

two antiparallel β-pleated sheets made up of five and four β-tiers linked by loops having the same topology. Two domains of the CD8-146 fragment make up a homodimer, similar to the immunoglobulin F_v, with a twofold symmetry axis. However, the electron density maps do not permit the identification of the geometry of the 115–141 fragment, which follows the N-terminal domain. The absence of the corresponding clear reflections from the diffraction pattern indicates a disordered state of this fragment in the crystal.

The joint consideration of the steric structure of the CD8 domain discovered and the crystal structure of the MHC-I (HLA-A2) protein established previously by Bjorkman et al.[48] revealed the existence of steric and electrostatic complementarity of the potential energy surface profiles of the two polypeptides and made it possible to reproduce their nonvalence complex and to construct the corresponding atomic model. The binary complex was supplemented by yet another participant — the T-cell receptor (TCR), the surface of which is apparently complementary to the residual unoccupied peptide-binding groove of the HLA-A2 molecule of the target cell. Thus Leahy et al.[47] concluded that the CD8 domain and TCR are linked simultaneously to the same MHC-I molecule in the antibody-antigen complex, while the second domain of the CD8 dimer is linked to a second MHC-I molecule. This scheme of the interactions of the receptors of the killer cell with the MHC-I molecules of the target cell agrees with experimental data.[49]

2. The structure of the extracellular fragment of the CD4 receptor containing domains 3 and 4

It was supposed previously that the three-dimensional structures of the molecules of the CD4 and CD8 receptors are very similar and that their interactions with the molecules of the class II and class I MHC should therefore have the same effect on the activation and development of the T-lymphocytes.[50] However, crystallographic studies on CD4 [51,52-54] and CD8 [47] showed that the three-dimensional structures of these proteins, at any rate in the extracellular region, differ significantly from one another. The principal differences concern two features. Firstly, the N-terminal Ig-V-like domain of CD4 functions in the monomeric state, while the N-terminal domain of CD8 forms the F_v-like homodimer. Secondly, the structure of CD4 in the extracellular region consists of four largely autonomous domains, while CD8 consists of only one domain, linked to the transmembrane component of the receptor by an apparently labile section comprising 48 aminoacid residues, which is virtually undetectable in the diffraction pattern. The only structural feature characteristic of both CD4 and CD8 and absent from the immunoglobulin variable domains is that the length of the CDR2 loop is greater by six aminoacid residues. The functional significance of such local alteration of the sequence remains obscure.

We shall deal in greater detail with the three-dimensional structure of the CD4 receptor. The CD4 molecule is that of a transmembrane glycosylated protein. It is present on the surfaces of T-lymphocytes belonging to the subpopulation which recognises the target cells containing antigens associated with the MHC-II proteins,[27] similarly to the way in which another subpopulation of the T-lymphocytes with CD8 molecules on the surface recognises foreign cells containing antigens linked to the MHC-I proteins.[55-57] The cytoplasmic region of CD4 is in close contact with the tyrosine kinase p56, which plays an important role in triggering the production of T-cells. The CD4 molecule is the principal receptor interacting with the human immunodeficiency virus (HIV-1),[58-61] which is discussed in detail in Section VI.

On the basis of results of the analysis of aminoacid sequences of CD4 and immunoglobulins, it was predicted that the extracellular part of the receptor would consist of four domains, which have been assigned to the IgSF superfamily.[58,62] This hypothesis was soon confirmed by the results of direct structural studies. Admittedly, all attempts to carry out the X-ray diffraction analysis of the entire extracellular component of the molecule comprising 371 residues were unsuccessful owing to its poor crystallisation. However, it was possible to obtain crystals giving an entirely satisfactory X-ray diffraction pattern, which were individually made up of the two halves [of one of the two halves? (Ed. of translation)] of this part of the CD4 sequence. Each crystalline specimen incorporated two domains — D1D2 [52,53] and D3D4.[51,54] The cryotechnique, which made it possible to determine the three-dimensional structure with a resolution to within 2.6 Å, was used in the crystallographic study of D3D4; at room temperature, the resolution was to within 2.8 Å. Cooling of the crystals to −150 °C was accompanied by a 1%–2% decrease in the size of the unit cell without disturbance of the symmetry group. The mean square deviation of the C^{α} atoms of the aminoacid residues following the change in temperature from room to −150 °C was 0.86 Å (0.93 Å for the D3 domain and 0.57 Å for the D4 domain). Comparison of the three-dimensional structures of the four domains showed that the three-dimensional structures of the sequences have a series of common features, the D1 and D2 domains resembling more closely the D3 and D4 domains respectively. The differences between the D3D4 and D1D2 geometries consist primarily of the greater distance in D3 between the β-pleated sheets, which is evidently associated with the absence of the disulfide bond in this domain and, secondly, of the change by ~25° in the mutual orientation of the D3 and D4 domains relative to the orientation of D1 and D2.

In the model of the entire extracellular part of the CD4 receptor, proposed by Lange et al.[51] on the basis of the known three-dimensional structures of D1D2 and D3D4 and consistent with a series of indirect data,[63,64] the four domains have a rod-shaped form with a length of ~120 Å, which is approximately equal to the sum of the lengths of the two D1D2 (65 Å) and D3D4 (60 Å) fragments. The conformation of the intervening section consisting of three residues (179–181) remained unestablished. In the D1D2 fragment, these residues are C-terminal and, since they are apparently appreciably mobile in the crystal, they are not manifested on the electron density maps. In the proposed CD4 model (D1D2D3D4), the N-terminal sections of the D1 and D2 domains are accessible to the establishment of contacts with the MHC-II proteins and some sections of the surfaces of the D3 and D4 domains are able to interact with the proteins of the T-cell receptor complex of their own lymphocyte; incidentally, the structures of the two components are so far unknown.

3. The structure of the class II HLA-DR1 antigen

The human MHC antigens HLA (human leukocyte antigens) were first discovered on leukocytes. Like MHC, the antigens of the HLA group can be divided into two classes, I and II, consisting of sets of cell surface glycoproteins. As already mentioned, in transplantation responses, the cytotoxic T-cells mainly respond to foreign class I glycoproteins, whereas the T-helpers respond to foreign class II glycoproteins. The HLA-II molecules are transmembrane αβ heterodimeric proteins with a molecular mass of 60 kDa. They are initially expressed by special antigen-producing cells such as macrophages, stem cells, and B-lymphocytes. The class II of the HLA antigens embraces proteins which are transformed from extracellular antigens into T-cell helpers in the course of the identification of foreign antigens and immune responses.[65,66] In man, the molecules of this class are polymorphous and can therefore interact specifically with sets of different proteins. The polymorphism of HLA is probably responsible for the different immune responses of different individuals exposed to the action of the same foreign agents; different susceptibilities to diseases, the breakdown of tolerance to own antigens, and the appearance of autoimmune responses are associated with such polymorphism.[67,68]

The crystals were grown in an aqueous solution of class II HLA-DR1 belonging to several variants of alleles. The protein

was first purified with the aid of immunoaffinity chromatography and detergents and then freed from the transmembrane region and the cytoplasmic domain by treatment with papain.[69,70] The three-dimensional structure of the extracellular part of HLA-DR1 was determined with a resolution to within 3.3 Å by means of a combination of X-ray diffraction data obtained from three different specimens.[70] In all cases, the protein crystallised as the dimer of the DR1 αβ heterodimer. The structure discovered was similar to the molecular structure of HLA-I [71] and was found to correspond to the hypothetical model of the peptide-binding centre of this protein constructed on the basis of crystallographic data for the three-dimensional structure of class I HLA-A2.[72] The three-dimensional structure of the monomeric unit of class II HLA-DR1 in the αβ heterodimer consists of two α-helical domains and two β-structural domains (β_1 and β_2). The molecule is intersected by a long peptide-binding groove, the bottom of which is lined with eight tiers of an antiparallel β-sheet and the walls are lined with two antiparallel helical sections. There are four contact regions between the DR1 molecules in the dimer (Fig. 7). Two of them are located near the two fold axis of rotation and include the interactions of the 49–55 (β_1) and 88–111 (α_2) residues. The other two contact regions, most remote from the membrane, are made up of five pairs of aminoacid residues of two close β_1 domains. The crystal structure of DR1 [70] permits the formation of a complex with CD4, postulated previously on the basis of the study of mutagenic derivatives.[73] If in the T-cell recognition of DR1, the latter is in a dimeric form, then, it follows from the X-ray diffraction analysis of the protein that the α_2 domain of the second molecule of the dimer can also be in contact with CD4, giving rise to an additional interaction of DR1 with CD4.

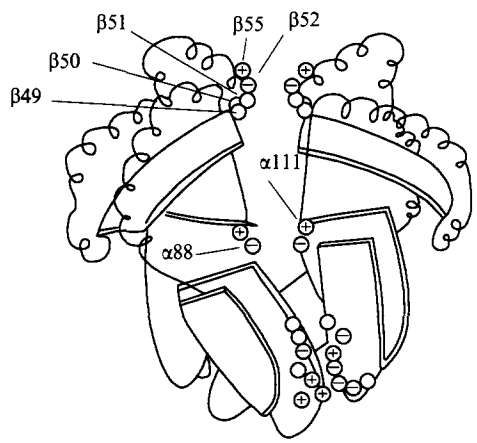


Figure 7. The contact regions of the subunits of the class II HLA-DR1 αβ heterodimer.[70]

Brown et al.[70] proposed a hypothetical mechanism of the assembly of the antigen-specific intercellular complex of HLA-II, TCR, and the CD4 coreceptor. It is suggested that in the first stage the αβ T-cell receptor and its associated CD3 and subunits form weak dimers, similar to the DR1 dimers, which are unstable before the appearance of the DR1–TCR complex. The complex becomes irreversible as soon as the DR1 molecules bind to specific peptides via TCR. The final stabilisation of the complex creates conditions for the appearance of effective interactions of the four-domain CD4 coreceptor simultaneously with both TCR monomers and the MHC-II proteins. The association of CD4 implies the inclusion of the signal system for the triggering of the immune response of the cellular type.

4. The structure of the HLA-DR1 – peptide complex

The antigens of the major histocompatibility complex (MHC or HLA in man) are transmembrane glycoproteins. They bind the peptides within the cell in the cytoplasmic space and supply them to the extracellular space, where they become accessible to the T-cells participating in the mechanism of the functioning of the immune system, in the identification of the foreign antigen, and in the response to its appearance.[74,75] The interaction of the T-cell antigen receptor with the peptide associated with the MHC(HLA) stimulates the expression of the proteins of the major histocompatibility centre in the T-cell. An individual organism has a small set of varieties of such proteins. Furthermore, there are facts indicating that each of them is able to bind an enormous number of pathogenic peptides and of signalling the need for response activities. The apparent contradiction is resolved by virtue of the broad polymorphism of the molecules of the MHC proteins, i.e. the lability of their three-dimensional structures or, in other words, the possibility that individual, predominantly surface sections of the protein globule can assume a large number of different conformational states. The polymorphism of the aminoacid residues of the class I and II HMC proteins forming the binding centres is responsible for their ready adaptability to peptides with different sequences. However, this does not rule out the specificity of the interactions. The MHC-I proteins are as a rule associated with short peptides, usually comprising ten residues, and are distinguished by a high selectivity in relation to aminoacids in fully defined sites of the oligopeptides sequence combined with tolerance in the nature of all other sections of the chain.[76–78] The MHC-I proteins function in the endoplasmic reticulum, where a vigorous peptide-generating proteolytic process takes place simultaneously. The MHC-II proteins act in the endosomal and liposomal compartments, where proteolysis also proceeds simultaneously. Representatives of this class usually bind longer peptides and also exhibit a high sensitivity to the locations of various aminoacids in the sequence.[79–82]

The results of the X-ray diffraction analysis of the extracellular parts of several human HLA-I [83–86] and mouse MHC-I [87,88] proteins indicate the operation of a common mechanism of the binding of peptides by class I proteins. In the structures of all the peptide–protein complexes investigated, the peptides had similar conformations stabilised at the binding centres by what is in principle the same system of hydrogen bonds and by the specific dispersion interactions of the side chains of several residues of the associated peptide with the hydrophobic pockets of the protein globule complementary to them.[86–92]

The binding of peptides to class II MHC (HLA) proteins can be inferred from the results of the X-ray diffraction study by Stern et al.[93] of the three-dimensional structure of the complex between the extracellular part of the HLA-DR1 protein and the peptide of the HA influenza virus — the tridecapeptide fragment (306–318) of haemagglutinin (the membrane glycoprotein of this virus). The diffraction pattern was obtained from a single crystal at −170 °C with the aid of synchronous radiation with λ = 0.910 Å. The three-dimensional structure of the HLA-DR1 – HA complex was determined with a resolution to within 2.75 Å.

The HA tridecapeptide was sorbed at the HLA-DR1 binding centre in the extended (twisted with a large pitch) form. It represents the best possibilities for interactions, on the one hand, with the aminoacid residues surrounding the peptide and, on the other, with the surface residues of the T-cell receptor. Thus the peptide is open to intercellular interactions. A schematic illustration of the twelve hydrogen bonds formed in the HLA-DR1–HA complex is presented in Fig. 8. The bonds are formed only between the atoms of the main chain of the HA peptide and the atoms of the conservative aminoacid residues of the α-helical and β-structural regions of HLA-DR1. Consequently the system of hydrogen bonds is independent of the particular sequence of the peptide, i.e. is universal for class II HLA-DR1 peptide complexes. This finding also indicates the similar orientations of the peptides in the complexes simultaneously in relation to the binding centres of the HLA-DR1 and TCR proteins belonging to other cells.

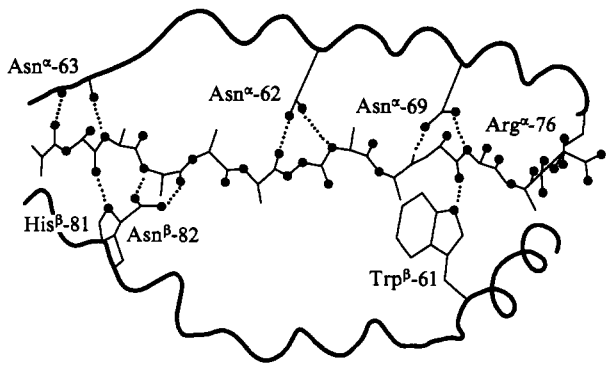


Figure 8. Schematic illustration of the hydrogen bonds between the peptide and the peptide-binding centre of the HLA-DR1 – HA complex.

IV. Aspartate proteases

The first attempt to solve with the aid of X-ray diffraction the problem of the structural organisation of membrane proteins, examined in Sections II and III, ended with relative success. The three-dimensional structures of the periplasmic domains, containing ligand-binding centres, were established for a series of transmembrane receptors and antigen-specific complexes of T-lymphocytes. Further development of studies on this aspect of the field should lead to the determination of the three-dimensional structures of whole receptor molecules, incorporating also transmembrane and cytoplasmic domains. The atomic-molecular foundations for the theoretical and experimental study of the structural-functional organisation of membrane proteins and the mechanisms of their functioning will be ultimately created. The difficulties on this path, which are mainly methodological in character, are still very large.

The latest advances in the X-ray diffraction analysis of proteins, the knowledge of the three-dimensional structures of which is of vital importance for man, are examined below. These are aspartate proteases, primarily the protease of the human immunodeficiency virus (HIV-1) and renin, one of the principal participants in the system for the regulation of the tonus of the blood vessel walls, skeletal muscles, and other tissues. It is becoming increasingly more evident that the search for radical therapeutic means of combating the acquired immunodeficiency syndrome (AIDS), other types of viral diseases, as well as hypertonicity, i.e. the solution of strictly applied medical-biological problems of extraordinary importance, requires a high level of development of theoretical molecular biology. A necessary, although not entirely sufficient, precondition for its attainment is information about the three-dimensional structures of the corresponding protein molecules. In contrast to structural studies on membrane receptors, the retarding factor in this instance is not the difficulties in the isolation, purification, and crystallisation of the proteins but difficulties of a more fundamental character.

Table 1. X-Ray diffraction analysis of native aspartate proteases and their inhibitors.

Enzyme	Inhibitor	Resolution/Å	Ref.
Pepsin	–	2.7, 2.3, 2.0, 1.8	94–98
	AcPhe–TyrOMe	3.0	99
Pepsinogen	–	1.8	100, 101
Chymosin	–	2.3	102–104
Renin	–	2.5, 2.8	105, 106
	His–Pro–Phe–His–Leu–Leu–Tyr–Tyr–Ser	2.5, 2.4, 2.6, 2.0	106–109
Penicillopepsin	–	2.8, 1.8	110–112
	Iva–Val–Val–Lysta–OEt	2.6, 1.8	113, 114
Endothiapepsin	–	3.0, 2.4, 2.1	115–117
	Pro–Thr–Clu–Phe(CH_2NH)Phe–Arg–Glu	2.0	118
	Boc–Thr–His[NHCH(CH_2Ph)CH(OH)N(CH_2CHMe_2)CO]Lys–Phe	1.8	119
	Boc–His–Pro–Phe–His–Sta–Leu–PheNH_2	2.2	120
Rhizopuspepsin	–	2.5, 1.8	115, 121
	AcVal–Sta–Ala–StaOH	2.5	122, 123
	D–His–Pro–Pro–Phe–His–Phe(CH_2NH)Phe–Val–Tyr	1.8	124
Proteinase of the bird myeloblastosis virus (BMV)	–	2.4	125
Proteinase of the Rous sarcoma virus (RSV)	–	2.0	126
Proteinase of the human immunodeficiency virus (HIV-1)	–	2.0, 2.8	127, 128
	Val–Ser–Gln–Asn–Leu ψ[CH(OH)CH_2]Val–Ile–Val (U-85548e)	2.5	129
	AcSer–Leu–Asn–Phe ψ[CH(OH)CH_2]Pro–Ile–Val–OMe (JG-365)	2.4	130
	AcThr–Ile–Nle–CH_2–Nle–Gln–Arg–NHMe (MVT-101)	2.3	131
	PR[a]–Gly–Gly–Ser–Ser–Gly–PR	1.8	132

[a] PR = HIV-1 proteinase.

Before considering the results of the X-ray diffraction analysis of the molecules of the HIV-1 protease, which belongs to the family of the RNA-containing viruses (*Retroviridae*) and of renin (a mammalian proteolytic enzyme), which have attracted exceptional attention in recent years as promising therapeutic targets, we shall deal briefly with the overall state of structural research into aspartate proteases.

The first crystalline structures of aspartate proteases became known in 1977, when the results of X-ray diffraction analysis of the molecular structures of four enzymes were published simultaneously: pepsin, penicillopepsin, endothiapepsin, and rhizopuspepsin (Table 1). The structures were determined with a resolution of 2.5–3.0 Å. About ten years elapsed before the resolution could be improved to 1.8–2.1 Å, which made it possible to infer with adequate reliability the details of the structures both of the enzymes themselves and of the inhibitor and water molecules interacting with them. The structures of a further two aspartate proteases were elucidated during this period — chymosin and renin, as well as the structures of a series of inhibitor complexes of the four enzymes mentioned above.

X-Ray diffraction analysis showed that, despite the significant differences between the aminoacid sequences, the three-dimensional molecular structures of the aspartate proteases of animals and microorganisms are similar. They are all made up of two symmetrically arranged domains which consist almost wholly of β-structures. Both domains reproduce the same structural motif and contain the Asp–Thr–Gly sections, which form part of the active centre of the enzyme. In the contact region, the domains form a groove intersecting a major part of the protein globule. The two catalytically important residues Asp-32 and Asp-215 (the numbering is that for pepsin), the carboxy-groups of which are close to one another and to several other residues as well as the molecules of water of crystallisation, are located at the centre of the groove. The system is stabilised by a network of hydrogen bonds and electrostatic and dispersion interactions (Fig. 9).

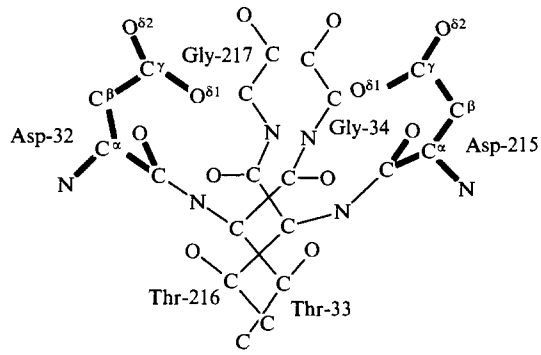


Figure 9. Catalytically important residues of the active centre in aspartate proteinases.

The studies on the three-dimensional structures of the complexes between aspartate proteases and substrate-like inhibitors (Table 1) made it possible to identify the sites of the active centre for each enzyme and to relate them to the sections of the substrate responsible for the primary and secondary specificity of the enzymic reaction. Comparison of the structures of native proteases with their inhibitor complexes showed that the binding of the oligopeptide ligands, differing only slightly from the substrates, is accompanied by the rotation of one domain relative to another by ~4° and its displacement by ~0.3 Å along the axis passing through the C^{α} atoms of the Asp-32 and Asp-215 residues. The change in the mutual orientation of the domains leads to the squeezing of the groove and an appreciable deformation of the active centre, an increase in the distance between certain residues by ~2.0 Å, and a displacement of the side chains by up to 3.5 Å. It was postulated that such changes are necessary for the occurrence of enzymic reactions and hence take place also on formation of enzyme–substrate complexes.[133]

The concept of the purely chemical aspects of the enzymic reactions of aspartate proteases was formulated even before the establishment of protein crystallography. Detailed studies on the nonenzymic hydrolysis of a wide variety of esters, amides, and model peptides, carried out mainly in the 1960s, showed that the catalysis is effective only in a medium incorporating the following three components: a nucleophile attacking the carbonyl carbon atom of the peptide bond to be cleaved, a basic catalyst promoting the elimination of a proton from the nucleophile, and an acid catalyst ensuring the protonation of the leaving group.[134] These investigations as well as the study of the kinetics and thermodynamics of the enzymic reactions of proteases permitted yet another important conclusion of a general character: the chemical mechanisms proper of the activity of all the proteolytic enzymes can be reduced to two types — covalent catalysis and general base catalysis. In the former case, the nucleophile of the protein molecule, interacting directly with the substrate and forming intermediate covalent compounds with the latter, is the component initiating the enzymic reaction. In the proteolytic hydrolytic reactions of the second type, the enzyme does not form covalent compounds with the substrate throughout the entire catalytic step. Its nucleophilic atom group behaves in this case as a basic catalyst, which, by interacting with a water molecule, deprotonates it and thereby converts it into an effective nucleophile, which attacks directly the carbonyl carbon atom of the peptide bond to be cleaved.

The employment by Antonov, Ginodman, and co-workers[134–137] of the method based on the incorporation of the heavy oxygen atom of the $H_2{}^{18}O$ molecule into the products of enzymic reactions has apparently played a decisive role in the determination of the type of catalytic reaction of aspartate proteases. The first comparative studies on the hydrolysis catalysed by various amide hydrolases[134] showed that the serine and cystein proteases function in accordance with the covalent mechanism, while the aspartate and metal-containing proteases function in accordance with the mechanism of the general base catalysis. This conclusion agrees with the most unambiguously interpreted results of chemical, kinetic, and thermodynamic studies on the catalytic reactions of endoproteases. It was subsequently confirmed by the results of the X-ray diffraction analysis of enzymes and is at present generally accepted.

1. The structure of the HIV-1 aspartate protease

Interest in the mechanism of the action of aspartate proteases has grown particularly in recent times in connection with the detection of enzymes of this group in the retroviruses inducing in human and animal organisms diseases such as AIDS, certain types of leukemia, sarcomas, and malignant mammary gland tumours. It is very significant that the aspartate proteases of these viruses play a key role in their life cycles.[138–141] In the host cell, they hydrolyse the proteins of the nuclear capsules surrounding the viral RNA and split the polyprotein chains into mature structural proteins and enzymes participating in the replication of the retroviruses. The viral proteases are also able to hydrolyse the proteins of the infiltrated cells, disturbing thereby the integrity of their structural-functional organisation. On the other hand, the cellular proteolytic enzymes are unable to cleave the viral proteases and to perform their functions. Thus, in the absence of proteases or when the latter are inhibited, the immunodeficiency viruses in man (HIV-1, HIV-2) and in monkeys (SIV), as well as the tumour-generating viruses would be unable to assume infective forms. This is why the proteases of retroviruses have become the object of such constant attention by enzymologists and medical scientists. The aspartate proteases of retroviruses have become some of the most thoroughly

Table 2. Distances (Å) between the atoms of the Asp-32 and Asp-215 side chains (numbering for pepsin) in the crystal structures of aspartate proteases.

Enzyme	$O^{\delta1}_{32}-O^{\delta1}_{215}$	$O^{\delta2}_{32}-O^{\delta2}_{215}$	$C^{\gamma}_{32}-C^{\gamma}_{215}$	$O^{\delta1}_{32}-O^{\delta2}_{215}$	$O^{\delta2}_{32}-O^{\delta1}_{215}$	$C^{\beta}_{32}-C^{\beta}_{215}$	$C^{\alpha}_{32}-C^{\alpha}_{215}$	Ref.
Pepsin	2.8	5.8	5.1	4.4	4.8	7.4	6.7	98
Renin	2.9	6.2	5.3	4.8	4.8	7.4	6.6	105
Penicillo-pepsin	2.9	5.8	5.2	4.4	4.8	7.5	6.6	112
Endothia-pepsin	2.9	5.7	5.2	4.4	4.8	7.6	6.6	117
Rhizopus-pepsin	3.1	6.1	5.4	4.4	5.0	7.7	6.8	121
HIV-1 protease	3.0	5.8	5.2	4.7	4.7	7.4	6.6	128
RSV protease	2.8	5.6	5.0	4.6	4.2	7.4	6.4	126

experimentally investigated enzymes after only 2–3 years since their discovery. Attention has been concentrated on the HIV-1 aspartate protease, about the structure and function of which more is perhaps known nowadays than about a classical object such as pepsin, which was discovered as early as 1836.

The aminoacid sequence of the HIV-1 protease consists of 99 aminoacid residues, whereas the aspartate proteases of vertebrates and microorganisms contain more than 300 aminoacids. The Asp–Thr–Gly fragment, present in each domain in all pepsin-like enzymes, is encountered in this sequence. According to Pearl and Taylor,[142] the physiologically active form of the HIV-1 protease includes two molecules associated via nonvalence interactions. This hypothesis has been confirmed experimentally.[143] A polypeptide chain of 203 aminoacid residues, constituting two molecules of the HIV-1 protease, the C- and N-ends of which are linked by the Gly–Gly–Ser–Ser–Gly pentapeptide section, has been synthesised by genetic engineering methods. This dimer, linked by valence bonds, assumed spontaneously the conformation of the native dimer under physiological conditions and exhibited an activity identical with that of the latter. This conclusion has been recently confirmed in a study[132] where the three-dimensional structure of a similarly linked dimer of the HIV-1 protease was determined with a resolution of 1.8 Å. When one of the two catalytically important Asp-25 residues is replaced by Gly, the activity is lost. Another investigation[144] of the valence-linked HIV-1 protease dimer with a Gly–Gly dipeptide bridge and with the replacement of Asp-25 by Asn and Glu led to the same results.

Tomasselli et al.[139] determined the dissociation constant of the native dimer of the HIV-1 protease, which proved to be 2 pM. According to the data of Cheng et al.,[143] its value is 50 pM. Despite the considerable discrepancy between the dissociation constants obtained, one can nevertheless postulate that the HIV-1 protease dimerises in the nanomolar region, i.e. at a concentration much lower than that in the viral particle. The study of Seelmeier et al.[145] showed that the catalytic activity of the HIV-1 protease is suppressed by pepstatin inhibitors, which is characteristic of all aspartate proteases. It was noted in the same study that the replacement of the Asp-25 residue in the aminoacid sequence of the viral protease by Thr leads to the complete loss of activity. The same effect has been observed following the replacement of the Asp-25 residue in the aminoacid sequence of the HIV-1 protease by Asn,[140,145] Ala,[146,147] Tyr, and His.[146] The activity also falls to zero in pepsin following a similar mutagenesis of one of its Asp catalytic residues.[148]

Thus one may claim that the dimeric form of the HIV-1 protease, in which both aspartic acid residues (Asp-25 and Asp-125) play a catalytically important role, is physiologically active. Only this form possesses all the distinctive features of aspartate proteases. Consequently, like pepsin, renin, rhizopus-pepsin, and other enzymes of the given group, the dimeric form of the HIV-1 protease should function in accordance with a general base catalysis mechanism. To some extent, the conclusion that there is a unique chemical mechanism of the catalytic reactions involving aspartate proteases has been confirmed by the results of the X-ray diffraction analysis of the retroviral proteolytic enzymes.

The three-dimensional structures of three retroviral aspartate proteases (HIV-1, RSV, and BMV) and of three complexes of the HIV-1 protease with substrate-like inhibitors (U-85548e, JG-365, and MVT-101) are known at the present time (Table 1). They are all dimers and are structurally related to one another and to the aspartate proteases from other sources. Furthermore, one can assume that all the known proteases have geometrically identical active centres (these are understood as the direct sites of the sorption of the peptide group to be cleaved). This is indicated by the similarity of the distances between the corresponding atoms of the two functional residues of aspartic acid in the enzyme molecules (Table 2). Thus one may conclude that the enzymic reactions involving aspartate proteases of the vertebrates, microorganisms, and retroviruses have the same initial conditions and hence should proceed by the same mechanism, namely the general base catalysis mechanism.

The crystal structures of the native HIV-1 protease and of its inhibitor complexes are compared in Fig. 10, and Fig. 11 presents a map of the distances between the C^{α} atoms (up to 10 Å) in two associated protease molecules. The numerous and varied, as regards their nature, nonvalence contacts (dispersion and electrostatic contacts and contacts via hydrogen bonds) between two pairs of N-terminal (1–8, 101–108) and C-terminal (87–99, 187–199) fragments make the greatest contribution to the stabilisation of the dimer. The arrangement achieved during

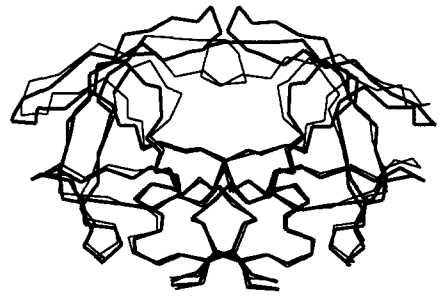


Figure 10. The principal chains of the native HIV-1 protease (thick line) and of its complex with the JG-365 inhibitor (thin line).

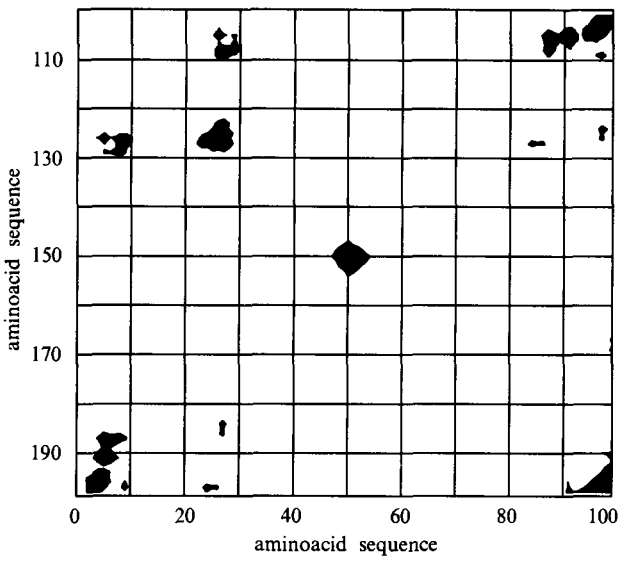


Figure 11. Map of the distances between the C^{α} atoms of the HLA-1 molecules of the protease in the homodimer (the shaded regions correspond to distances < 10 Å).

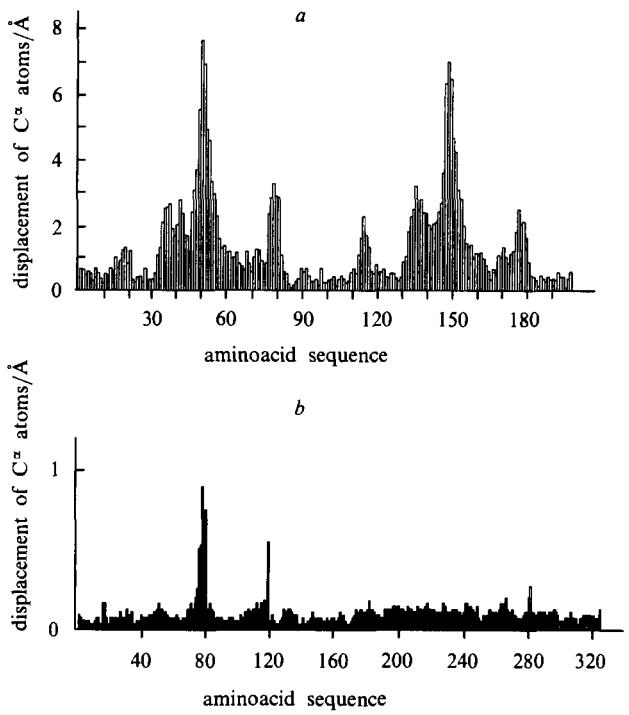


Figure 12. The displacements of the C^{α} atoms in the molecules of the dimeric HIV-1 protease on formation of a nonvalence complex with the JG-365 inhibitors (*a*) and in the rhizopuspepsin molecule on formation of a nonvalence complex with an inhibitor (*b*).

the dimerisation process in this close-packed and apparently most stable part of the HIV-1 protease exerts an appreciable and direct influence on the formation of the active centre in close proximity. The interactions of more than 40 aminoacid residues of the four terminal fragments are extremely selective. This is indicated, for example, by the absence of catalytic activity from the dimeric complex made up of mixed chains of the HIV-1 and HIV-2 viruses, which are closely homologous.[149] Three changes, in the 6, 92, and 95 positions, were found to be sufficient for activity to be lost, the sequences of the enzymes in the two viruses being identical in all other sections which are in contact within the dimer.

The 23–28 and 123–128 fragments also come close to one another in the dimeric complex of the HIV-1 protease. They include the effectively interacting tripeptide fragments Asp-25–Thr-26–Gly-27 and Asp-125–Thr-126–Gly-127—the permanent components of the active centres of all the aspartate proteases. This contact region of the two molecules is stabilised additionally by nonvalence interactions with the 7–9 and 107–109 residues of the N-terminal fragments and the 84–85 and 184–185 residues of the C-terminal fragments.

Finally, there is yet another region of intermolecular interactions in the dimeric HIV-1 protease. It is made up of two β-pleated sheets (45–57 and 145–157) overhanging, like open wings, the active centre (the term 'flaps' has been applied to them). In the native state of the enzymes, they do not participate in the stabilisation of the dimeric form and their position is maintained by the interactions of the 48–52 and 148–152 pentapeptide sections, which are in close proximity (Figs 10 and 11), and also apparently by the contacts with the neighbouring dimer in the crystal lattice.

The flaps play an important role in the stage involving the formation of the nonvalence complex. The enzyme–substrate (inhibitor) interactions entail an enormous, without precedent in the catalytic reactions of other enzymes (at any rate proteolytic enzymes), conformational rearrangement of a considerable proportion of the native structure. It involves not only the side chains of the residues in the active centre, which usually occurs, but also the main chains of both molecules of the HIV-1 protease. The sections 45–57 and 145–157 undergo the greatest changes on complex formation. Judging from the shifts of the C^{α} atoms, they reach ~8.0 Å in the central 50 and 51 and 150 and 151 residues, gradually diminishing to 1.0 Å in the terminal 45 and 57 and 145 and 157 β-structure residues (Fig. 12*a*). The ends of the flaps projecting towards one another, as in cantilevers, are displaced towards the substrate (inhibitor) molecule sorbed in the active centre. The 77–81 and 177–181 fragments undergo synchronously appreciable displacements (2.0–3.0 Å), which also diminish the size of the cavity in the active centre. The displacements of the C^{α} atoms in the two HIV-1 protease molecules in the dimeric complex are similar but not identical.

The changes in the positions of the flaps on formation of complexes were observed also in other aspartate proteases. However, as can be seen from Fig. 12*b*, which illustrates the displacements of the C^{α} atoms in the enzyme–inhibitor complex of rhizopuspepsin, here the differences are much less appreciable. As regards other sections of the main chain of the protein, the latter hardly respond to the association with the inhibitor.

The knowledge of the HIV-1 protease dimerisation process is of considerable interest, primarily in the search for antiviral medicinal preparations. The question whether the association of the molecules occurs without change in their three-dimensional structure or whether the process is accompanied by the conformational adaptation of the partners merits special attention in this instance. If the changes occur, then it becomes possible to prevent the formation of the active complex by a specific action on the enzyme molecules, which would preclude the conformational rearrangements necessary for their combination. It may be that this aspect of the development of an antiviral therapy will prove to be the most promising by virtue of the exceptional nature of the mechanism of the formation of the active forms of the retroviral proteases compared with the aspartate proteases from other sources.

However, it is not possible to observe directly the three-dimensional structure of an individual HIV-1 protease molecule in order to compare it with the structure of a subunit in the dimeric complex, because the enzyme crystallises only in the form of the dimer. Only a theoretical procedure remains for the solution of the problem: a priori calculation of the conformation of a free HIV-1 protease molecule from the known aminoacid sequence.

Fig. 13 presents projections of the three-dimensional structure of one of the subunits in the native dimeric associated species, from which it is seen that the first nine N-terminal and subsequent six C-terminal residues of the sequence do not interact either with one another or with the remainder of the molecule because of their remoteness. The uncoiled conformational states of these fragments are more favourable for the intermolecular interactions which they undergo in the structure of the catalytically active HIV-1 protease dimer (Figs 10 and 11). It was noted above that the intermolecular contacts of the four terminal groups of the two sequences actually make the main contribution to the stabilisation of the dimer. On the other hand, the uncoiled forms of the 1–9 and 94–99 sections are energetically unfavourable for the free enzyme molecules and their occurrence in a dilute solution is unlikely. Consequently, the dimerisation process should involve a conformational transition from the coiled forms, favourable for the free molecules, to the uncoiled forms preferred by the associated molecules. It is seen from Fig. 13 that the conformational state of the 45–57 flap should change simultaneously. In the complex, this state is determined by the interaction of a second molecule with the flap and possibly by the interactions with the dimer of an adjoining unit cell.

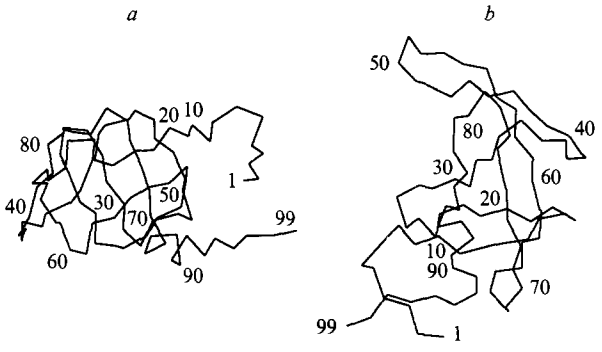


Figure 13. Projections (*a*, *b*) of the HIV-1 protease molecule in the dimer.

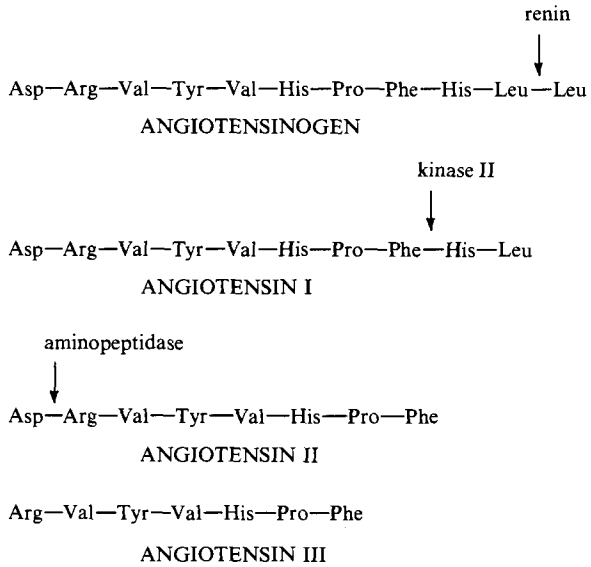
From the foregoing, one may conclude that there is the possibility of a search for therapeutic agents for protection against retroviruses, in particular the human immunodeficiency virus — of devising preparations which would prevent the dimerisation of the molecules of aspartate proteases. Without this, the functioning of the enzyme and hence the operation of the life cycle of the virus are impossible.

Another approach to the preparation of the necessary medicines involves the creation of special inhibitors of the retroviral aspartate proteases. This is an extremely complex task and at the present time has not yet been achieved. Among the requirements which must be met by the properties of the inhibitors, the main and most difficult one concerns the selectivity of their action. Inhibitors exhibiting a therapeutic effect should be primarily highly specific to such an extent that, while deactivating the retroviral protease, they do not disturb the normal functioning of both aspartate and other proteolytic enzymes of the host cell. The specific search for inhibitors satisfying this requirement requires the availability of quantitative data on all the stages of the catalytic step performed by the viral protease, similar to the data concerning the mechanisms of the functioning of the proteases of the infiltrated cell and the methods for the solution of the reverse structural problem, i.e. the development of the chemical structure of the inhibitor on the basis of the specified three-dimensional form. In connection with the problem of the specificity of the enzyme–substrate interactions, X-ray diffraction data on renin — the aspartate protease of blood plasma — are especially important.

In contrast to not only the other aspartase proteases but in general amidohydrolases, this enzyme exhibits a virtually absolute specificity. Renin is known to hydrolyse only its own natural substrate angiotensinogen, abstracting from its N-terminal part of a decapeptide, as well as a small number of synthetic analogues which are highly homologous with respect to the N-terminal aminoacid sequence of angiotensin.[134,150] Almost any aminoacid replacement in the pentapeptide fragment of the substrate before the bond to be cleaved ($P_5 - P_1$) and in the tetrapeptide section beyond it ($P_1' - P_4'$) leads to a nonproductive Michaelis complex and the absence of hydrolysis. The reason for such phenomenal specificity of renin still remains unelucidated.

2. The structure of renin and of its inhibitor complexes

Renin, a glycosylated protein, forms part of the enzyme system which effects the biogenesis and decomposition of the octapeptide tissue hormone angiotensin II, the most powerful of the known pressor agents in the blood circulation system. Angiotensin II stimulates the narrowing of the peripheral arterioles throughout the organism and hence increases the arteriole pressure. Apart from this, it activates the secretion of a series of hormones (mainly aldosterone) and influences the work of the heart, the liver, the central and peripheral components of the nervous system, etc. Its direct precursor, angiotensin I, is formed from the globular blood protein angiotensinogen, already mentioned, as a result of the abstraction from it of the N-terminal decapeptide by renin. According to the scheme presented below, the hydrolysis of the peptide bond between the Leu-10 and Leu-11 residues is the first and rate-determining stage in the cascade of enzymic reactions leading to the conversion of angiotensinogen into angiotensin II with its subsequent decomposition.



The three-dimensional structure of renin has been investigated in a number of studies.[105–109] The three-dimensional structure of the partially deglycosylated native human recombinant renin has been identified with a resolution of 2.5 Å. Some of the peptide sections on the periphery of the globule were disregarded on the electron density maps and for this reason they were assigned to the group of conformationally labile loops lacking defined structures. The X-ray diffraction analysis of the glycosylated native human renin and of its inhibitor complexes was subsequently carried out[106] with resolutions of 2.8 and 2.4 Å respectively. The structure of the enzyme–inhibitor complex of this protein was also determined in another study[109] with a resolution of 2.6 Å. The stabilising interactions of specific pockets of the active centre of the enzyme with the side chains of the $P_4 - P_4'$ residues on the octapeptide sections of the inhibitors were described in the above communications.

Table 3. Dihedral angles of rotation φ, ψ, and ω (deg) of the main chain of the CH-66 inhibitor in the active centre of renin and of the U-85548t, JG-365, and MVT-101 inhibitors in the active centre of the HIV-1 protease.[108,129-131]

Designation of residue	Renin				HIV-1 protease											
	residue	CH-66			residue	U-85548e			residue	JG-365			residue	MVT-101		
		φ	ψ	ω		φ	ψ	ω		φ	ψ	ω		φ	ψ	ω
P_5	His	−76	114	−170	Val	−	11	175	−	−	−	−	−	−	−	−
P_4	Pro	−81	147	−175	Ser	−106	126	178	Ser	−64	169	180	−	−	−	−
P_3	Phe	−103	123	180	Gln	−108	148	−177	Leu	−123	138	178	Thr	−	125	−176
P_2	His	−111	92	−178	Asn	−138	101	−178	Asn	−143	104	180	Ile	−121	92	−178
P_1	Leu(ψ)	−101	44[a]	167[a]	Leu(ψ)	−97	63[a]	133[a]	Phe(ψ)	−94	47[a]	151[a]	Nle(ψ)	−92	72[a]	142[a]
P_1'	Leu	−89[a]	130	177	Val	−56[a]	150	173	Pro	−57[a]	174	175	Nle	−92[a]	154	−179
P_2'	Tyr	−75	133	174	Ile	−139	124	177	Ile	−130	122	−177	Gln	−151	123	178
P_3'	Tyr	−130	145	−174	Val	−126	157	−	Val	−143	138	−	Arg	−81	129	−
P_4'	Ser	−85	−	−	−	−	−	−	−							

[a] The angles correspond to the nonstandard P_1-P_1' sections of the inhibitor chain.

The crystal structure of the submaxillary mouse renin, inhibited by the substrate-like CH-66 decapeptide, has been studied in greatest detail and with the best resolution (2.0 Å).[151]

Piv-His-Pro-Phe-His-[Leu(ψ)-CH(OH)CH_2]-Leu-Tyr-Tyr-Ser-NH_2

($P_6-P_5-P_4-P_3-P_2-P_1$——————$P_1'-P_2'-P_3'-P_4'$),

Here Piv is a pivaloyl blocking group and CH(OH)CH_2 is a hydroxyethylene group with the (*S*)-configuration of the second asymmetric carbon atom of Leu(ψ). The positions of 10038 and 325 aminoacid residues of the glycosylated enzyme, 364 atoms of the inhibitor, and 613 oxygen atoms of the water of crystallisation were determined. The mean square error in the coordination of the atoms was 0.21 Å and the standard deviations from the standard bond lengths and angular distances were 0.026 Å and 0.54 Å respectively.

The three-dimensional structures of the renins investigated have the same characteristic features as other aspartate proteases. They are also structural proteins consisting of two domains. Between them, there is a substrate-binding groove, in the centre of which the catalytically important Asp-32 and Asp-215 residues are accommodated and, as in other enzymes of this group, these residues are followed by Thr and Gly. The three-dimensional structures of the renin molecules from different sources are very similar. For example, the difference in the orientations of the domains in the structures of mouse and human renins does not exceed 1.7°. The positions of the domains in pepsin and endothiapepsin differ from that in mouse renin by 6.9° and 18.8° respectively.

The decapeptide ligand in the enzyme–inhibitor complex has the β-pleated sheet conformation extended along the substrate-binding groove (Table 3).[128-131,151] Its carboxyethylene group between two Leu residues occupies in the active centre of the enzyme a sensitive site of the substrate and forms hydrogen bonds with the carboxy-groups of the Asp-32 and Asp-215 catalytic sections. The conformational states of the main and side chains of all the inhibitor residues in the complex with renin correspond to the lowest-energy forms of the free aminoacids and, being uncoiled structures, provide at the same time the best conditions for effective interactions with the residues of the active centre of the enzyme. Table 3 lists the dihedral angles φ, ψ, and ω, which determine the geometry of the main chain of the renin inhibitor (CH-66)[151] and three inhibitors of the HIV-1 aspartate protease (U-85548e, JG-365, MVT-101).[129-131] It follows from the comparison of the data in Table 3 that, on association with the active centres of the mammalian and retroviral aspartase proteases, the completely different inhibitors assume similar conformational states. At any rate, the differences between the dihedral angles of the inhibitors of renin and the HIV-1 protease are not greater than the differences between the angles of the inhibitors of a single enzyme. This finding as well as the data in Table 2 indicate that the structural states of the substrate-binding centres of the aspartate proteases are similar regardless of their source.

X-Ray diffraction analysis of the inhibitor complex between mouse renin and the decapeptide[151] made it possible to identify the aminoacid residues of the enzyme which form specific pockets and to make certain quantitative assessments of their interactions with the side chains of the inhibitor residues. Bearing in mind the similarity of the latter to the N-terminal aminoacid sequence of angiotensinogen, the data presented in this instance are of undoubted interest for the subsequent theoretical study of the nonvalence interactions of renin with a true substrate and for the solution of the problem of the nature of its exceptional specificity.

Table 4 presents the 34 renin residues which form ten substrate-binding pockets (S_6-S_4'), the interatomic contact distances between which and the inhibitor in the complex do not exceed 4.2 Å. The residues presented in Table 4 are located on the surface of the globule of the water-soluble protein and yet they are all hydrophobic (with the natural exception of the catalytically important Asp-32 and Asp-215), like the substrate

Table 4. The aminoacid residues of renin, the atoms of which form close contacts with the P_6-P_4' residues of the CH-66 inhibitor (< 4.2 Å).[151]

Designation of pocket	Renin residues forming substrate-binding pockets
S_6	Leu-10, Ser-12, Phe-220, Leu-276, W7, W8, W138
S_5	Ser-12, Pro-111, Leu-114, Ser-219, W7, W8
S_4	Ser-219, Phe-220, His-287, W77, W138, W147
S_3	Gln-13, Ser-77, Pro-111, Leu-114, Ala-115, Phe-117, Gly-217, Ser-218, Ser-219, W7, W11, W77
S_2	Tyr-75, Gly-76, Ser-77, Ser-218, Ser-222, His-287, Met-289, Val-300, W77, W147
S_1	Asp-32, Gly-34, Tyr-75, Phe-117, Val-120, Asp-215, Gly-217
S_1'	Gly-34, Ile-73, His-74, Tyr-75, Gly-76, Glu-128, Val-130, Val-213, Asp-215, Ile-291, Val-298, Val-300, W76, W87
S_2'	Gly-34, Ser-35, Ile-73, His-74, Tyr-75, Glu-128, Val-130, Ile-291, Thr-295, W28, W73, W74, W76
S_3'	His-74, Tyr-75, Gly-76, Ile-291, Pro-292, Thr-295, W74, W75
S_4'	Pro-294, Thr-295, W75

Table 5. Changes in the contact area of the renin active centre residues accessible to the solvent during inhibition by CH-66.[151]

Residue	Area/Å²			Residue	Area/Å²		
	free renin	CH-66 complex	surface area accessible to solvent		free renin	CH-66 complex	surface area accessible to solvent
Leu-10	37.3	30.1	7.2	Gln-128	14.0	5.5	8.5
Ser-12	7.1	0.2	6.9	Val-130	14.2	9.9	4.3
Gln-13	7.3	1.0	6.3	Val-213	5.1	0.8	4.3
Ile-30	4.8	1.8	3.0	Asp-215	4.8	0.0	4.8
Asp-32	3.2	0.0	3.2	Ser-218	5.7	0.0	5.7
Ser-35	2.7	0.0	2.7	Ser-219	10.2	0.4	9.8
Ile-73	3.3	0.1	3.2	Phe-220	12.4	2.5	9.9
His-74	33.1	19.2	13.9	Leu-276	12.7	7.1	5.6
Tyr-75	11.7	0.0	11.7	Thr-283	9.3	5.7	3.6
Gly-76	4.2	0.3	3.9	His-287	16.0	4.8	10.2
Ser-77	15.2	4.2	11.0	Met-289	18.5	14.3	4.2
Ile-110	36.1	32.2	3.9	Ile-291	10.3	0.5	9.8
Pro-111	13.1	1.2	11.9	Pro-292	30.0	19.0	11.0
Phe-112	3.6	0.6	3.0	Pro-294	37.6	29.5	8.1
Leu-114	34.9	21.5	13.4	Thr-295	25.4	10.0	15.4
Phe-117	7.2	0.1	7.1	Val-300	5.6	0.2	5.4
Val-120	3.6	0.0	3.6				

residues interacting with them, so that the complexes are stabilised mainly via dispersion forces.

The highly complementary nature of the potential energy surfaces of the active centre of renin and of the decapeptide inhibitor (substrate) and hence their predisposition to undergo effective nonvalence interactions can be inferred from the numerous interatomic contacts between the enzyme and the ligand. This is confirmed quantitatively by the data presented in Table 5. They demonstrate a sharp contraction, on sorption of the inhibitor, of the surface (accessible to the solvent) of the aminoacid residues forming the $S_6 - S_4'$ loci. Approximately half of the residues, including Asp-32, and Asp-215, and certain residues of the flap, behave as ligands fully shielded from contact with the external medium. The overall area of the active centre accessible to the solvent, which is ~460 Å², diminishes to ~220 Å² in the complex.

The accessible surface areas of the side chains of the $P_5 - P_4'$ residues of the CH-66 inhibitor in two complexes — with renin and with endothiapepsin — are compared in Table 6. According to a calculation,[151] this area is ~64 Å² in the former case and ~130 Å² in the latter. The data in this table indicate an appreciably greater packing density of the same inhibitor in the active centre of renin compared with that of endothiapepsin. Exceptionally pronounced complementary conditions in the renin complex occur in the middle part of the decapeptide ligand, i.e. in the region of the peptide bond being cleaved.

Table 6. Comparison of the accessible surface areas of the side chains of the $P_5 - P_4'$ residues of the CH-66 inhibitor in complexes with renin and endothiapepsin.

Designation of residue	Residue	Surface area of complex accessible to solvent/Å²	
		renin	endothiapepsin
P_5	His	20.6	35.7
P_4	Pro	7.7	11.3
P_3	Phe	0.4	6.9
P_2	His	0.5	8.7
P_1	Leu(ψ)	0.0	0.5
P_1'	Leu	0.6	0.9
P_2'	Tyr	7.8	7.2
P_3'	Tyr	12.4	38.0
P_4'	Ser	13.9	20.2

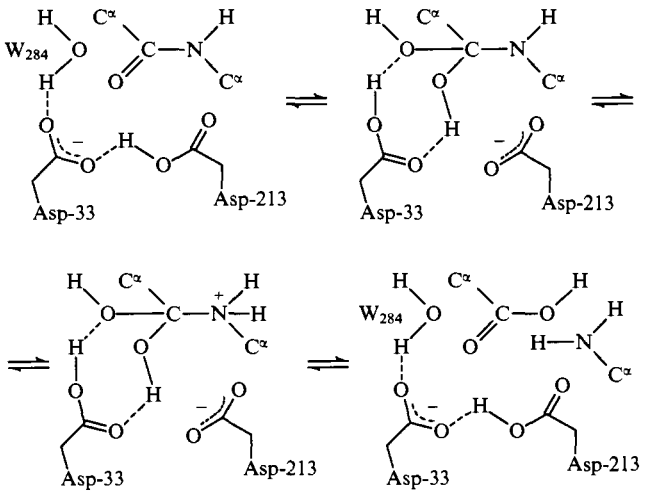
We shall attempt to answer the question of the advances contributed by X-ray diffraction analysis in the study of aspartate proteases and to what extent the knowledge of the three-dimensional structures of these enzymes and of their inhibitor complexes can deepen our understanding of the mechanisms of the catalytic reaction of aspartate proteases. The answer to this question is of general importance for enzymology, because, as already mentioned, proteases are objects in biocatalysis which have been most thoroughly investigated in all respects. We shall consider the hypothetical models of the mechanisms of the action of aspartate proteases, which have been developed on the basis of data on the three-dimensional structures of the enzymes and their complexes with substrate-like inhibitors.

3. The mechanism of the catalytic reaction of aspartate proteases

The first stereochemical model was proposed in 1985 by James and Sielecki,[112] who used for this purpose the crystal structure of penicillopepsin, solved with a resolution of 1.8 Å.[111,112] A series of considerations, based on the knowledge of the three-dimensional structures of the enzymes, had been put forward earlier concerning the mechanism of the action of aspartate proteases.[111,123,152-158] However, they were all to some extent incomplete and did not claim to provide a consistent description of the entire process involving the hydrolysis of the peptide bond catalysed by aspartate proteases. The W_{284} molecule of the water of crystallisation plays an important role in the stereochemical model of the productive covalent Michaelis complex devised by James and Sielecki. In the active centre of penicillopepsin, it occupies a site which is extremely convenient also for the formation of an effective hydrogen bond with the side chain of Asp-33, which increases its nucleophilicity, and for attack on the carbonyl carbon atom of the bond being hydrolysed, which weakens the latter. The protonated carboxy-group of the Asp-213 residue, polarising the carboxy-group of the substrate via a hydrogen bond and hence acting as an electrophilic component of the system, acts in the same direction (Scheme 1).

The three interactions noted above initiate the disruption of the delocalised $\pi - n$ electron system of the peptide bond being cleaved, the pyramidalisation of the nitrogen and carbonyl carbon atoms, and the appearance at the latter of *gem*-hydroxy-groups, which are involved in hydrogen bonding with the protonated carboxy-group of Asp-33. The return of the lone electron pair to the nitrogen atom enhances its tendency to be protonated and, according to James and Sielecki,[112] can be

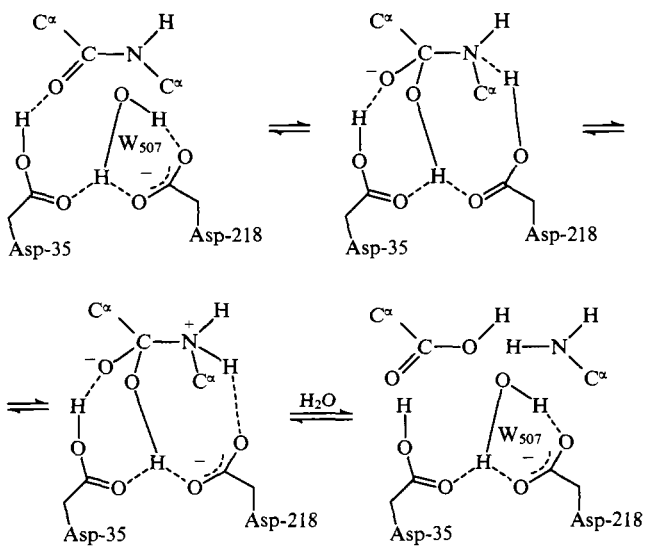
Scheme 1



achieved in two equally probable ways. In one of them, the inversion of the configuration of the bonds involving the nitrogen atom, occurring via the rotation of the amino-group of the substrate by ~60° around the C–N bond, is postulated. As a result, the lone pair is oriented towards the solvent and the nitrogen is readily protonated, particularly in aspartate proteases with a highly acid pH. The alternative procedure involves the transfer of a proton to the nitrogen atom from one of the hydroxy-groups of the tetrahedral adduct, which is in the *syn*-configuration relative to the lone pair of the nitrogen atom. The compound formed is unstable and decomposes into two parts, one of which includes the amino-group and the other the carboxy-group.

The initial hypothesis of James and Sielecki[112] that the nucleophile in the catalytic reaction of aspartate proteases is the W_{284} group has been rejected by Suguna et al.,[124] who hold a different view on the mechanism of the action of the enzymes. The stereochemical model which they constructed is based on crystallographic data for the three-dimensional structures of native rhizopuspepsin[122] and its complex with an octapeptide inhibitor having a reduced peptide bond, which is cleaved on interaction with substrates. Suguna et al.[124] chose as the nucleophile the W_{507} water molecule (W_{39} in terms of the numbering for penicillopepsin), which is located between the two carboxy-groups of the Asp-35 and Asp-218 residues and forms three hydrogen bonds with the latter (Scheme 2). It is suggested

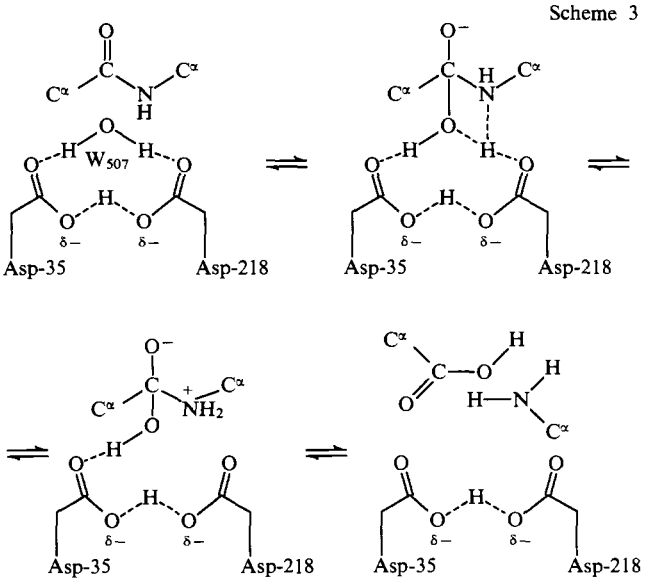
Scheme 2



that the W_{507} molecule is not displaced by the substrate because, following its sorption, the peptide bond to be hydrolysed is subjected to steric hindrance and assumes a nonplanar energetically unfavourable configuration. In this position of the substrate, the carbonyl carbon atom of the bond being cleaved is located opposite the attacking oxygen atom of the W_{507} molecule and the oxygen of the carbonyl group is placed at a distance from the hydroxyl of the Asp-35 side chain which is optimal for the formation of a hydrogen bond. As a result of the formation of the tetrahedral adduct, the OH group of the water molecule passes to the substrate, while the hydrogen atoms initially pass to the carboxy-group of the Asp-218 residue and then to the nitrogen atom. The reorganisation of the intermediate leads to the rupture of the peptide bond of the substrate, the desorption of the reaction products, and the regeneration of the active centre.

In the mechanism of the catalytic reaction of aspartate proteases proposed by Pearl,[159] the nucleophile is the W_{507} water molecule, as in Scheme 2 examined above (Scheme 3). The new feature in this model consists in the hypothesis of the equality of the acidity constants and hence of the electronic equivalence of the carboxy-groups of the Asp-35 and Asp-218 residues having a delocalised proton and, furthermore, in the introduction as an electrophilic component, giving rise to an additional polarisation of the carbonyl oxygen atom of the bond being cleaved, of the two NH groups of the Gly-78 and Asp-79 residues (according to the numbering for rhizopuspepsin), which enter into the aminoacid sequence of the flap overhanging the substrate. According to the previous models of the mechanism of the functioning of aspartate proteases, the effects of the nucleophile and the electrophile lead to the formation of an unstable intermediate compound, which decomposes from the N- and C-ends. In both this case and in those discussed above, the author follows the concept of stress and enforced deformation, i.e. he postulates the possibility of the transformation of the energy of enzyme–substrate nonvalence interactions into an energy of distortion of the peptide bond, which brings it closer to the transition state and hence facilitates the hydrolysis.

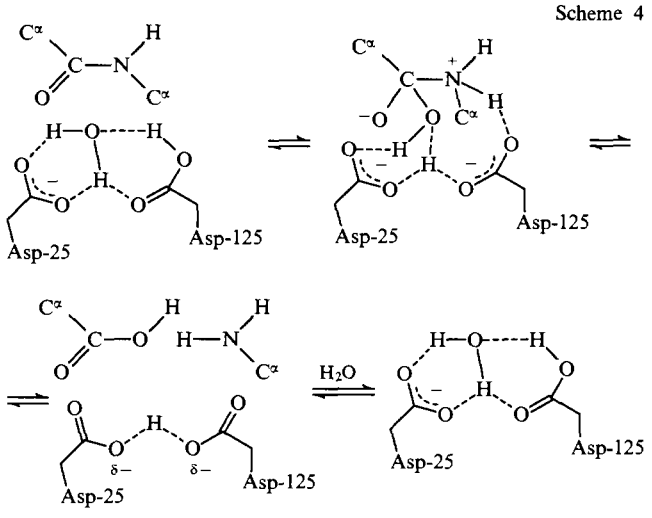
Scheme 3



The model of the mechanism of action of aspartate proteases proposed by Jaskolski et al.[129] is based on the three-dimensional structure of the HIV-1 retroviral protease. The W_{507} molecule (the numbering is that for penicillopepsin), located in an equidistant position between the side chains of the Asp-25 and Asp-125 residues (Scheme 4), was chosen as a nucleophile in this case also. Bearing in mind the symmetry of the enzyme, the authors placed one of the hydroxy-groups of H_2O along the twofold axis in such a way that it is able to form a

forked hydrogen bond with the inner carboxyl oxygen atoms of the aspartic acid residues. The second hydroxy-group of H_2O is directed towards the outer oxygen atom of the Asp-25 carboxylate. The acid proton of the unionised Asp-125 side chain forms a hydrogen bond with the oxygen atom of the W_{507} molecule of the water of crystallisation. Thus, according to the dynamic model,[129] the native HIV-1 protease in the equilibrium state contains a symmetrical system of five oxygen atoms, in the field of which the hydrogen atoms migrate in an appropriate manner. The symmetry of the active centre breaks down on interaction of the enzyme with the substrate. As a result of nucleophilic attack, there is a simultaneous disruption of the carbonyl group of the bond being cleaved, the hybridisation of the carbon and nitrogen atoms changes ($sp^2 \rightarrow sp^3$), a C–OH valence bond is formed, and the nitrogen is protonated. In other words, the enzyme–substrate complex passes in one stage through an unstable intermediate state, which is completed by the formation of the reaction products and the return of the enzyme to its initial state.

Scheme 4



Despite the significant differences between the models proposed, they are unified as regards their initial postulates.

Firstly, it is suggested that the aspartate proteases function through general catalysis and therefore do not form covalent intermediate complexes with the substrate during the reaction.

Secondly, it is claimed that the manifestation of the catalytic activity of proteases required the presence in the system of a nucleophile — basic and acid catalysts (the differences concern their selection).

Thirdly, it is postulated in all the hypotheses that the enzymic reaction involving the hydrolysis of the peptide bond proceeds via a stage of an unstable intermediate (a tetrahedral adduct).

Fourthly, a common feature of all the proposed stereochemical models is the treatment of the stimuli to the functioning of aspartate proteases based on the concept of deformation and stress.[160]

These postulates were formulated and confirmed experimentally in the study of enzymic and model nonenzymic reactions even before the X-ray diffraction analysis had been carried out on even one aspartate protease. The determination of the three-dimensional structures of the enzymes and their complexes with substrate-like inhibitors provided additional confirmation of some of the earlier conclusions and made it possible to visualise the ideas already established.

Thus the mechanism developed for enzyme catalysis are interesting in the sense that they arose, in essence, from the same experimental data, including X-ray diffraction data obtained in recent years, and are based on the same theoretical ideas concerning the nature of biocatalysis which arose before the establishment of protein crystallography and have long become traditional. The imperfection of the generalisations made is indicated by the fact that, whilst the initial experimental data and theoretical foundations were the same and also a single approach was followed, not one but four different models of the functioning of aspartate proteases have been proposed and their number may, incidentally, be even greater. They do not form a series indicating a quantitative development of knowledge about the mechanism of the action of enzymes, but are more likely to represent different points of view. The hypotheses examined correspond to a single level of understanding of the phenomenon investigated and are equivalent as regards the arguments adduced and their predictive power. The question arises what new advances have been contributed by the X-ray crystallography of proteins to the study of the catalytic reactions of aspartate proteases and other enzymes.

In the first place, one should note that X-ray diffraction data have made it possible to determine not only the region of the active centre of the enzyme but also its geometry at the level of atomic coordinates. It would at present be impossible to achieve this quite so fully and reliably by any other procedure. Furthermore, the use of this method to solve the three-dimensional structures of the native enzyme and its complexes with various inhibitors made it possible to discover the conformational rearrangements of the active centres which may occur at different stages of the catalytic step. These data are also unique and informative.

X-Ray diffraction played a major role in the study of the specificity of enzyme–substrate interactions and of the locations of the regions of the active centres which bind to the sensitive sites of the substrate and the residues adjoining it on either side. As regards the mutual orientations of the bond being cleaved and of the catalytically active residues of the enzyme corresponding to the productive binding of the true substrate, the problem remains unsolved. As can be seen in relation to the four different stereochemical models of the functioning of aspartate proteases which have been proposed, the views expressed can be divided into more or less probable, but, despite the knowledge of the conformations of the enzyme in the native state and in the complex with the inhibitor, both are hypothetical in character.

The data concerning aspartate proteases examined here as well as the similar data on chymotrypsin, trypsin, carboxypeptidase, and lysozyme described previously[161] provide grounds for the conclusion that the appearance of unique quantitative information about the three-dimensional structures of enzymes and their complexes did not entail a conceptual development of enzymology and revision of the existing ideas about the nature of biocatalysis.

With the advent of X-ray diffraction analysis of enzymes, there was no transition from speculative ideas about enzyme catalysis to a rigorous quantitative description of this phenomenon. Nor has there been any change in the direction of biocatalytic investigations, which, as before, follow from function to structure, which is not fortuitous because X-ray diffraction studies can only lead to the knowledge of the morphology of biosystems at the atomic-molecular level, which by itself is not the final aim of the study of enzymes. The morphology of the object is always a preliminary feature which is completely necessary for the subsequent investigation of the structural and structural-functional organisation of biosystems. For this reason, the three-dimensional structures of many hundreds of enzyme molecules discovered with the aid of X-ray diffraction did not solve the problem of biocatalysis, but led to a real development of an approach to the study of enzyme catalysis in the direction from structure to function and to an a priori quantitative description of the mechanism of the catalytic reaction. By virtue of the development of the crystallography of proteins, the problem of creating a general theory of biocatalysis and the corresponding computational methods acquired for the first time the form of a truly scientific problem soluble at the present level of scientific knowledge.

V. DNA-binding proteins

This section describes certain crystallographic studies on proteins carried out in recent years. The studies examined below demonstrate the latest advances in crystallography which have made it possible to solve at the atomic level the three-dimensional structures of proteins and complexes consisting of thousands and more of aminoacid residues. The technical development of the method was manifested in the transition noted at the beginning of the 1990s, from X-ray diffraction studies on individual protein molecules to the no less detailed investigation of the three-dimensional structures of macromolecular protein oligomers and their aggregates with other compounds and subcellular systems. In other words, structures of more complex biological systems began to be understood at the atomic level.

Objects which were of interest as regards their structural-functional organisation and at the same time illustrated clearly the current advances in protein crystallography were chosen for consideration. These undoubtedly include the DNA-binding proteins, which participate directly both in the establishment of the genetic apparatus and in all the stages of its functioning. In eukaryotic cells, such proteins are traditionally subdivided into two groups: the histone proteins participating in the establishment of a definite structure of DNA within the cell nucleus and the nonhistone proteins ensuring the biosynthesis of RNA. The results of X-ray diffraction analysis of histones and β-galactosidase, which are representatives of both groups of the DNA-binding proteins, are considered below.

1. The structure of the histone core of the nuclesome

Histones constitute five varieties (H1, H2A, H2B, H3, and H4) of small structural proteins, the aminoacid sequences of which contain respectively 220, 128, 124, 134, and 102 residues. They ensure the close packing of the DNA double helix, which is very long in the extended state. For example, in each human chromosome it is on average 5 cm long. Histones are necessary primarily for the ordered disposition of the long double-stranded polynucleic acid within the small volume of the cell nucleus. However, this is not their only purpose: the nature of the packing of DNA influences the activity of the corresponding sections of the genome. Consequently its histone structural organisation is one of the ways of regulating and controlling the transcription of RNA from DNA. The aminoacid sequences of histones contain about 40 positively charged Lys and Arg residues, which enables them to bind effectively to the DNA double helix regardless of its nucleotide composition.

Histones, especially H2A, H2B, H3, and H4, are some of the most conservative of the known proteins. The rates of change in the aminoacid sequences for a series of proteins and the histone H4 throughout the period of evolution are compared in Table 7. The figures presented suggest that approximately four out of each five random aminoacid replacements are harmful in haemoglobin and 17 out of each 18 replacements are harmful in cytochrome *c*, while in histone H4 there are virtually no harmless replacements.

Table 7. Changes in the aminoacid sequences of proteins throughout evolutionary time.[162]

Protein	Unit of evolutionary time/million years[a]
Fibrinopeptide	1.2
Haemoglobin	6.1
Cytochrome-*c*	21.0
Histone H4	600.0

[a] The unit of evolutionary time is the average time necessary for the appearance of one acceptable replacement in the given protein for each 100 aminoacid residues.

Since all the DNA base pairs are equally subject to random mutations, the evolutionary stability of histones suggests that they play an extremely responsible role in the organisation and functioning of the genetic apparatus.

Histones constitute about half of the mass of the chromosome, where they participate in the organisation of several levels of packing of the DNA double helix. Together with other proteins, histones form complexes with DNA, which are called chromatin. In 1974, Kornberg isolated the repeating structure of the chromatin unit for the first time[163] and later established[164] that it consists of an octameric protein core comprising two molecules of each of the histones H2A, H2B, H3, and H4 and a fragment of the DNA double helix. It was postulated[165] that the double-stranded DNA is twisted around the histone core and forms two turns of a superhelix made up of 165 base pairs. This figure was later corrected to 146.[166] The observed chromatin structural unit was called a nucleosome.[167] Studies on the histone core with the aid of different physicochemical methods showed that the octamer consists of a heterogeneous protein ensemble $(H2A-H2B-H3-H4)_2$ comprising three structural subunits: a tetramer $(H3-H4)_2$ and two dimers (H2A–H2B). The DNA double helix in chromatin extends as a continuous filament from one nucleosome to another. The linear DNA linker sections located between the nucleosomes have different lengths, which are usually small, amounting on average to 60 nucleotides. The nucleosomal filament is responsible for the higher levels of compaction of chromatin. Ultimately it appears under the electron microscope in the form of the so called 30-nanometer chromatin fibril.

The histone H1 is responsible for the packing of the nucleosomal filament within the chromatin fibril. The central part of its molecule consists of a globule, which interacts with a specific section of the nucleosome. The N- and C-terminal fragments of the protein have extended forms. The N-terminal fragment is associated with the preceding linker DNA in the region of its contact with the nucleosomal particle, while the C-terminal fragment is in contact with the histone core of the next nucleosome. Furthermore, it has been noted[168] that a free H1 molecule interacts more readily with DNA in the vicinity of another histone molecule, which has already been added, than in the region separate from it. This is the reason for the tendency of the H1 proteins to bind to DNA in groups of eight and more molecules. It has been suggested that the interaction of this type, called cooperative binding, constitutes the basis of the activation of genes. The condensation of the H1 molecules induced by such interaction converts certain chromatin sections into a kind of microcrystals, the 'fusion' of which under the influence of an external regulator signal leads to the disruption of the histone cluster and a local rearrangement of chromatin.[162,169]

The elucidation of the internal structural organisation of the histone core and of its interactions with the DNA double helix, began, as already mentioned, in 1974.[163] Soon the structure of the octamer was investigated in solution by a small angle neutron and X-ray scattering methods with a resolution of ~20 Å[170-172] and in the crystalline state by X-ray diffraction[166,173,174] (with resolutions of 22 Å,[175] 7.0 Å,[176,177] and 3.5 Å). According to crystallographic data,[177] the pure histone core of the chick erythrocyte is an octamer having the form of an ellipsoid with axes 110 and 65–70 Å long. The model proposed by the authors of the above study consisted of three parts: the central tetramer $(H3-H4)_2$ and two dimers (H2A–H2B) disposed on its opposite sides. However, both the form and the size of the octamer differed significantly from the parameters obtained in a series of other investigations.[166,173-175] Repeated diffraction analysis[178,179] established the external dimensions of the histone core, which agreed with the data obtained from other studies (height ~ 55 Å, diameter ~ 70 Å).

According to some workers, the three-dimensional structure of the histone core resembles a flat disc, others see it as a pin or a spool, while according to a third group it is a wedge. Therefore,

only one thing is clear: the structure of the octamer is fairly complex and has no direct analogies. A more detailed discussion of the geometry of the complex $(H2A-H2B-H3-H4)_2$ may be based only on the results of the later studies,[178,179] since they were obtained with a resolution of 3.1 Å, which already permits the identification of the conformational state of the aminoacid residues and even of individual side chains.

In an earlier X-ray diffraction analysis of a whole nucleosome,[166,170,173] it was shown that the right-handed DNA double helix is twisted around the histone core in the form of a left-handed superhelix ~55 Å long and with an internal diameter of ~70 Å. This was confirmed in a study of the structure of an isolated octamer,[178,179] on the surface of which the groove of a protein superhelix was observed. It had an external diameter of ~65 Å, a pitch of ~28 Å, and a left-handed twist, which is fully consistent with the parameters of the DNA superhelix in the nucleosome. Thus, the surfaces of the histone core and of the DNA double helix twisted round it bear the same relation to one another as the surfaces of a screw and a nut. Nevertheless, the formation of a nucleosome can hardly be regarded as the screwing of the protein octamer into a strictly defined nucleotide structure. This is prevented firstly, by the presence on the helical groove of the nucleosome core of alternating hillocks and hollows, and secondly, by the fact that the superhelix of the DNA molecule in a free state is not a stable form, although it is apparently a low-energy conformation. It is more likely that the nucleosome is formed by the screwing of the labile DNA double helix onto the histone core, in a manner resembling the winding of a thread on a spool. The mechanism of the opposite process involving the liberation of the double-stranded DNA from the protein complex is the same. This model is supported by the finding that the hillocks and hollows on the inner central part of the nucleosome are complementary in relation to the profile of the contact surface of the DNA superhelix formed by the B-form of its double helix.

In connection with the determination of the three-dimensional structure of the histone octamer $(H2A-H2B-H3-H4)_2$ and of its steric interrelations with DNA, a whole series of fundamental problems have arisen. For example, the question arises: what is the mechanism and the causes of the spontaneous appearance of the protein complex and the self-assembly of the nucleosome as a whole. No less interesting is the question how the nucleotide chain is liberated from the histone core. The point is that the accessibility of the DNA forming part of the composition of nucleosomes is significantly restricted on those sections where the double helix is in contact with the surface of the octamer. The attachment of specific regulator proteins to the functionally active nucleotide sequence becomes possible only when the corresponding DNA binding sections are liberated from the nucleosomes. The elucidation of the cause of the decomposition of the nucleoprotein complexes is therefore just as important as the study of the cause of their appearance. One may assume that, after the mechanisms of the creation and decomposition of nucleosomes has been subjected to a quantitative treatment, one of the most intriguing questions concerning histone proteins will also be solved, namely why the histones H2A, H2B, H3, and H4 are some of the most conservative proteins in nature as regards their aminoacid sequences (Table 7). One cannot rule out the possibility that the nucleosome is a unique cell subunit in terms of its structural organisation. On the grounds of general considerations, one may postulate that it should combine an ideal consistency between the intramolecular and intermolecular interactions of the proteins constituting the histone octamer, complementary surfaces of the nucleosomal core, and the contact surface of the DNA superhelix, together with a fine balance between forces acting from opposite directions, the disturbance of which, combined with the corresponding changes in external forces, leads to the rapid shift of the equilibrium towards the appearance or decomposition of the nucleoprotein complex. The conservative nature of the histones H2A, H2B, H3, and H4 shows that the normal functioning of such a system virtually rules out changes in aminoacids.

2. The structure of the N-terminal fragment of DNA topoisomerase I

In the replication of DNA, the rate of polymerisation in bacteria and mammals varies from 500 to 50 nucleotides per second. For each ten base pairs of the newly synthesised chain, the parent DNA double helix must execute one complete turn around its axis in order to avoid being tangled up (Fig. 14). Hence, in order to achieve an obstacle-free movement of the replication fork at the experimentally observed rate, the entire chromosome, ahead of the fork, must execute 50 ± 5 turns per second. Exactly the same 'twisting problem' evidently arises in the transcription and recombination of DNA. In all cases, it is solved with the aid of special enzymes, DNA topoisomerases, which form a kind of 'hinge' within the helices.

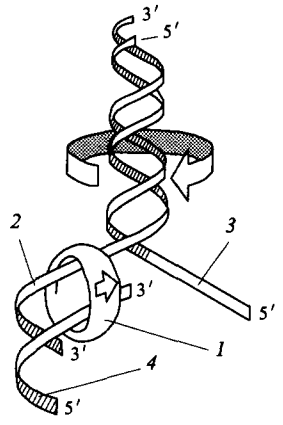


Figure 14. Rotation of the DNA double helix during its replication; (*1*) DNA polymerase on the leading chain; (*2*) matrix for the synthesis of the leading chain; (*3*) matrix for the synthesis of the lagging chain; (*4*) newly synthesised DNA chain.

DNA topoisomerase I cleaves the phosphodiester bond in one of the DNA chains and becomes covalently attached, as a rule via a tyrosine side chain, to the free 5'-end formed. Chain termination enables the two halves of the double helix to rotate freely around the phosphodiester bond located opposite the break and hence to release the accumulated stress. The protein–DNA covalent bond is of the high-energy type and the enzymic hydrolysis of the phosphorus diester bond is therefore a reversible reaction and does not require the involvement of ATP. After the removal of stress, the broken ends of the DNA chain are rejoined. Thus, in terms of its function, the DNA topoisomerase constitutes something in the nature of a 'reversible nuclease' or a 'reversible DNA polymerase'. DNA topoisomerase was first isolated from the cells of *E. coli* in 1971.[180] It still remains the most widely investigated enzyme of the subfamily of type I DNA topoisomerases, which includes the topoisomerases III of the bacteria *E. coli*[181] and *Saccharomyces cerevisiae*[182,183] as well as the reversible gyrase of the archebacterium *Sulfolobus acidocaldarius*,[184,185] which were discovered many years later. Apart from the reaction described, enzymes of this type catalyse the relaxation of an incorrectly twisted linear DNA superhelix, the disentanglement and ring closure of a single-stranded DNA chain, the pairing of complementary rings, and a series of other related operations. A common feature of the type I DNA topoisomerases is the mechanism of the catalytic step, which proceeds without the employment of the energy of ATP and invariably includes the stage in which only one chain of the DNA double helix is temporarily broken. Enzymes with similar

functions, which, however, cleave not one but two phosphodiester bonds and are bound covalently to both chains of the double helix, constitute the subfamily of the type II DNA topoisomerases.[186]

The results of the X-ray diffraction analysis of the three-dimensional structure of the N-terminal fragment of the DNA topoisomerase I of *E. coli* were published in 1994.[187] The three-dimensional structure of the fragment of the polypeptide chain comprising 553 aminoacid residues and having a molecular mass of 67 kDa (that of the whole protein is 97 kDa) was determined with a resolution of 2.2 Å following the interpretation of the diffraction patterns obtained at a temperature of −168 °C using synchroton radiation. This was the first crystallographic study of a topoisomerase.

DNA topoisomerase I is a metalloenzyme, the C-terminal fragment of which contains three zinc(II) atoms and three sections with two disulfide bonds.[188] The catalytic reaction involving the cleavage of the DNA nucleotide chain includes transesterification between the phosphodiester bond of the substrate and the Tyr-319 side chain of the enzyme.[189] The C-terminal fragment of the protein with disulfide bonds does not participate in this reaction. The zinc atoms also do not affect the phosphodiester bond cleavage stage, but are necessary for the reconnection of the broken chain after the relaxation of DNA.[190] The fragment of DNA topoisomerase I with a molecular mass of 67 kDa, investigated by Lima et al.,[187] can therefore catalyse the cleavage of a single nucleotide chain, but is unable to restore the integrity of the DNA superhelix. Its substrate specificity and kinetic characteristics are the same as those of the native protein or the zinc-free protein.[190,191]

The three-dimensional structure of the N-terminal fragment consists of an irregular extended torus with external dimensions of ~67 × 43 × 86 Å. It is made up of domains I–IV, which are separated from one another and are easily observable. Domain III includes the catalytically important Tyr-319 residue (Fig. 15, Scheme 5).

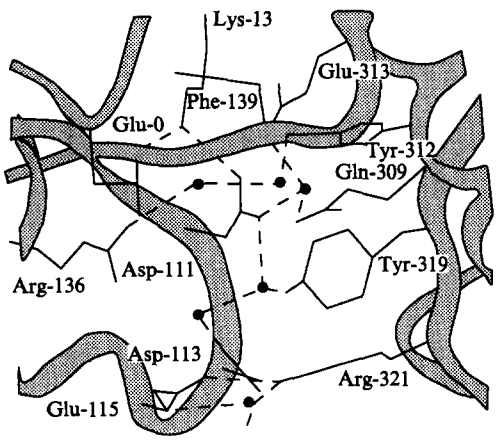
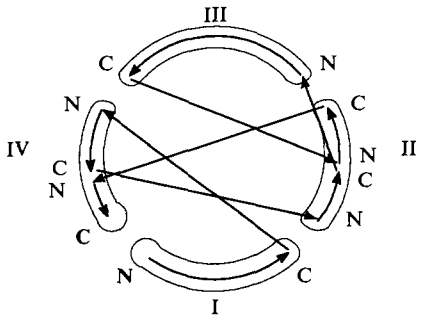


Figure 15. The active centre of DNA topoisomerase formed by domains I and II. The hydrogen bonds are designated by dashed lines.[187]

Scheme 5



The aperture in the torus, free from the side chains of the residues, has a diameter of ~28 Å, so that the insertion of the DNA double helix in the B-form into it should not be accompanied by steric hindrance. The arrangement of the effectively interacting domains I, III, and IV led to the formation of a large substrate-binding groove and of yet another aperture in the immediate vicinity of the principal aperture in the torus and the active centre with the Tyr-319 aminoacid residue. The second aperture has a small diameter but it is quite sufficient for the passage of a single DNA chain.

The view that the appearance of new complex proteins in the course of evolution takes place as a result of the merging of preexisting proteins has come to be generally accepted.[192,193] The three-dimensional structure of the multidomain protein is thus represented as an ensemble of largely independent globular domains which had previously existed as individual proteins, and the aminoacid sequence is represented by a set of polypeptide chains of the domains in which the C-terminus of the preceding domain is linked to the N-terminus of the next domain. The structural organisation of DNA topoisomerase is in no way consistent with this method of the formation of complex proteins, and its polypeptide chain cannot be represented by the sequential and independent formation of domains.

Assembly of the aminoacid sequence of the 67 kDa fragment apparently begins from the N-terminal domain I, which consists of a continuous polypeptide section (Scheme 5). Then, instead of proceeding immediately to domain II, the chain extends to domain IV and only then proceeds to domain II, having, however, completed the formation of domain IV only to the extent of one third. Next, having participated in this instance in the construction of only half of domain II, the chain passes to domain III. After completing its organisation, it returns again initially to domain II and then to IV, completing their construction. In the aminoacid sequence described, all the interactions of domain III with domains I and IV are restricted to nonvalence contacts. The covalently linked domains II and III, the polypeptide chain of which is not intertwined with the chains of other domains, can migrate as a solid body relative to the remainder of the protein. Such structural organisation of the enzyme molecule with two forms of the torus (open and closed) is, according to the authors,[187] of decisive importance for the functioning of the DNA topoisomerase I, since the migration of domains II and III makes the active centre accessible to both single-stranded and double-stranded DNA.

The hypothesis that appreciable conformational changes in the molecule of the DNA topoisomerase in the course of the formation of the nonvalence Michaelis complex are necessary is confirmed also by a number of other no less convincing structural features of the enzyme. One of them concerns the catalytically most important Tyr-319 residue. It belongs to domain III and is located next to the substrate-binding chain. In the native enzyme, Tyr-319 is accommodated in the narrow gap between domains I and III and is shielded from contact with the external medium by the Arg-321 protein chain, forming salt bridges simultaneously with the Asp-113 and Glu-115 side chains. The transition from the closed form of the molecule to the open form not only permits the penetration by DNA into the inner part of the torus but also moves the Tyr-319 residue onto the surface, providing conditions for the approach of the latter to the nucleotide chain of the substrate and attack on the phosphodiester bond. The migration of domains II and III as a single whole is stimulated by the nonvalence protein–DNA interactions, because a cofactor such as ATP is absent in the given instance. This feature distinguishes DNA topoisomerase I from DNA topoisomerase II, the catalytic action of which also involves conformational changes, but these require the participation of ATP.

In a study of the three-dimensional structure of the N-terminal fragment of DNA topoisomerase I,[187] the authors devoted much attention to the description of many details of the

mechanism of the catalytic step. However, these data, like the results of other similar investigations, are phenomenological in character.[194] The importance of X-ray diffraction data for enzymes clearly does not lie merely in making possible the adjustment of the existing theoretical mechanisms of catalytic action for consistency with them or in inventing new ones. These data are valuable by virtue of the potential possibility of their being used as a unique experimental basis for an a priori approach to a quantitative description of the catalytic step as a spontaneous process.[195]

3. The structure of β-galactosidase

The following two factors led me to include, in the section devoted to DNA-binding proteins, an enzyme which strictly speaking does not belong to this group: first, the structural organisation of the β-galactosidase molecule, which it had proved interesting to compare with the organisation of DNA topoisomerase just examined above; and second, the involvement of the enzyme in the regulation of the transcription activity of DNA, manifested by its influence on the effectiveness of the reading process in the course of the transcription of a whole cluster of genes (including its own gene) responsible for the metabolism of lactose. β-Galactosidase has played an historical role in the development of molecular biology, specifically in the concept of the general molecular principles of the regulation of the action of genes. It is in fact the study of the biosynthesis of this enzyme at the transcription level in bacteria which enabled L'vov, Jacobi, and Monod at the beginning of the 1960s to develop a theory of the transfer of genetic information and of the regulation of the protein synthesis (the operon concept). According to this concept, each operon incorporates a regulator gene, a promoter, an operator, and the structural genes of specific proteins (cystrones), in which the corresponding iRNA (polycystrone RNA) is transcribed and for the operation of which the three preceding regulator sections of the DNA double helix are responsible.

The first studies on the mechanism of genetic control were devoted to the synthesis of β-galactosidase, which hydrolyses lactose (a disaccharide) to glucose and galactose (monosaccharides) in the *E. coli* cell. The experiments led to the discovery of the repressor protein for the lactose operon initiating the transcription of structural genes (in the given instance the gene of β-galactosidase, as well as permease and galactoside transacetylase). This is achieved by binding the repressor to the operator section of DNA with a length equivalent to 21 nucleotides, which overlaps the aminoacid sequence of the promoter. This blocks the access by RNA polymerase to its binding section and the transcription of cystrones becomes impossible. The induction and repression of the synthesis of the protein, i.e. the changes in the rate of the process in opposite directions, require the presence in the model of the regulator mechanism of yet another inductor element, which should, on the one hand, control the action of the lactose operon repressor protein and, on the other, should be directly or indirectly related to the function of the enzyme being synthesised. Such as inductor has indeed been discovered and it proved to be the substrate of β-galactosidase, namely lactose or, more precisely, allolactose.

β-Galactosidase is an inducible enzyme, the rate of synthesis of which depends on the composition of the medium and the conditions in the latter, in particular on the lactose concentration. The amount of enzyme increases rapidly with increase in the substrate concentration, so that the relation between the inductor and β-galactosidase is evident. The effect of lactose, via allolactose, on the repressor is allosteric in character. When the intracellular lactose content begins to exceed the norm, the concentration of allolactose increases, which induces conformational changes in the repressor molecule. Its linkage with DNA is weakened and it liberates the promoter and hence enables RNA polymerase to transcribe the β-galactosidase genes. Depression of the gene takes place, iRNA is formed, and the enzyme, which is necessary only when the cell contains lactose, begins to be synthesised.

The three-dimensional structure of the *E. coli* β-galactosidase has been recently investigated with a resolution of 2.5 Å.[196] X-Ray diffraction analysis demonstrated that the aminoacid sequence of the protein comprising 1023 residues has an extended N-terminal 1–51 α-peptide section and five structurally autonomous domains: 51–217 (I), 220–334 (II), 334–627 (III), 627–736 (IV), and 736–1023 (V). In contrast to the type I DNA topoisomerase, where the polypeptide chain passes from one incomplete domain to another and, without completing its construction, is directed to the third, etc. (see Scheme 5), in galactosidase the chain passes from the N-terminus of the molecule to its C-terminus in strict succession through all the domains. The assembly of the long polypeptide chain of the protein is thereby facilitated, because in the modular structural organisation of the native enzyme each domain may act as an independent subunit capable of coiling up.

The quaternary structure of β-galactosidase in the form of a homotetrameric nonvalence complex with a molecular mass of 465 kDa exhibits an enzyme activity. Structural analysis showed that the complex belongs to the 222 symmetry point group. The four tetramers constitute an asymmetric unit cell belonging to the space group $P2_1$ with the parameters a = 107.9 Å, b = 207.5 Å, c = 509.9 Å, and β = 94.7°. At the present time, among all the three-dimensional structures of proteins identified at the atomic level, the molecular structure of β-galactosidase has the longest polypeptide chain. The study by Jacobson et al.[196] demonstrated for the first time the possibility of investigating protein crystals with a unit cell size exceeding 500 Å and a relative molecular mass of ~2000 kDa per asymmetric unit.

It had been shown earlier that the Glu-461, Met-502, Tyr-503, and Glu-537 residues should play an important role either directly in the catalytic reaction itself or in the construction of the active centre.[197,198] Indeed, in the observed three-dimensional structure of the enzyme they proved to be close to one another, being located around a deep well, which apparently represents a substrate binding pocket. The residues constituting it, like the four residues noted above, are highly conservative.

VI. Proteins of skeletal muscles

One of the most surprising properties of proteins, which are not manifested by other compounds, is undoubtedly their capacity for a macroscopic displacement i.e. greatly exceeding the dimensions of their molecules. This is due to the presence in a series of proteins, which have been called allosteric of several energetically preferable and comparatively readily interconvertible conformations which are sensitive to changes in the external medium and interact selectively with other molecules. When energy is consumed, the conformational transitions lose their reversibility and become ordered; the displacement becomes directional and the protein performs useful work.[199] For example, it can 'pass' through a thin filament, a microtube, or a DNA double helix. Such allosteric 'striding' proteins, employing the energy of the hydrolysis of ATP, are DNA helicase participating in the replication of DNA, kinesin, and dynein, which ensure intracellular mobility, and the muscle protein myosin, to the structure and functions of which this section is mainly devoted.

Myosin is a multifunctional protein. In the contraction of skeletal, hard, and smooth muscles, and in intracellular movement, it performs simultaneously at least three key functions: structural, allosteric, and enzymic. The most useful information about the functions of myosin may be obtained by investigating the tranversely striped skeletal muscle, which contracts spontaneously, as well as the analogous tissues of the invertebrates, primarily the flying muscles of insects. Electron microscope study of the longitudinal and transverse thin sections through skeletal muscles, carried out for the first time in 1953 by Huxley,[200]

revealed a high level of their structural organisation. By the following year, Huxley[201] had already proposed the so called sliding filament model, which was of fundamental importance for an understanding of the nature and the molecular mechanism of muscular contractions.

Skeletal muscles are bundles of muscle fibres, the largest repeating structural element of which is the myofibril, a cylindrical filament 1–2 μm (1000–2000 Å) in diameter, which extends from one end of the cell to the other. The myofibril contains in its turn protein filaments of two types—thick and thin. The principal proteins of the thick and thin filaments are myosin and actin filaments in the myofibril are strictly ordered. The functional contractile unit of the myofibril is the sarcomer, which is about 2.5 μm long and is subdivided into discs I and A (Fig. 16). The thick filaments (~1.6 μm long and 0.015 μm thick) extend from one edge of disc A to the other, while the thin filaments (~1.0 μm long and 0.008 μm thick) extend from the *Z* line and enter the gaps between the thick filaments of disc A. In muscle contraction, each sarcomer is shortened in proportion to the entire muscle, only disc I being compressed, while the dense disc A does not change its dimensions. The essential feature of the filament sliding model[201] is that the contraction of the myofibril and hence of the muscle fibre takes place as a result of the sliding of the thick filaments relative to the thin ones, whilst the lengths of both remain the same.

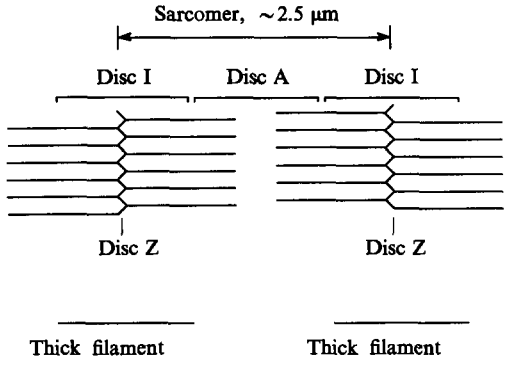


Figure 16. Schematic illustration of the structure of the sarcomer.

The filament sliding model has undergone prolonged experimental tests and has been confirmed most convincingly by data obtained by the direct electron microscope and X-ray diffraction methods. They demonstrated that the shortening of the muscle is indeed unaccompanied by changes in the intrinsic length of the filaments and in the nature of their packing in the sarcomer. The force developed by the muscle proved to be proportional to the degree of mutual overlap of the myosin and actin filaments and is therefore due to their interactions over the entire overlapping section. Following the introduction of high-resolution electron microscopy (second half of the 1960s; resolution 20–40 Å), it became possible to observe a multiplicity of lateral projections, forming ~0.013 μm (~130 Å) transverse bridges between the thick and thin filaments. It became evident that the relative displacement of the filaments is effected with the aid of these bridges. They belong to myosin and operate by employing the energy of the hydrolysis of ATP, like miniature oars. The presence of ATP in muscle fibres has been known since 1929, because it was in fact isolated for the first time from muscles. The fact that myosin catalyses the hydrolysis of ATP, i.e. is an ATPase, was established by Engelhardt and Ljubimova in 1939.[202] This discovery was the first indication of the source of energy for the contraction of muscles and of the role of myosin in the utilisation of the energy.

Towards the beginning of the 1970s, the phenomenological stage in the study of the functioning of muscles was largely complete; the overall mechanism of the process, its principal participants, and the source of energy were discovered.[203–206] Further study consisted in the search for answers to the following questions: what is the molecular mechanism of the contraction of muscles, how is the chemical energy of the hydrolysis of ATP transformed into mechanical work at the molecular level, and how does a nerve pulse trigger the movement of the muscle fibres?

The study of this problem began with experimental structural investigations by electron microscope methods, especially by cryoelectron microscopy, which can lead to a resolution at the atomic level under favourable conditions,[207,208] X-ray diffraction of oriented fibres, and X-ray crystallography. The combined approach, employing the results of both electron microscopy and X-ray diffraction analysis for the construction of models of the three-dimensional structures of the protein molecules consistent with the data obtained by these methods, has been recently (the 1990s) gradually introduced into practical use.[209] This approach has already found an application in studies on muscle proteins and spherical viruses.[210–212]

1. The structure of actin filaments

The thin filaments include as part of their composition actin, which, as already stated, constitutes the basic component of the filaments, tropomyosin, and troponin. The standard procedure for the isolation of actin involves the extraction of the dried and ground muscle tissue with a dilute salt solution. Such treatment cleaves the actin filaments into globular subunits, each of which is made up of a single polypeptide chain with a molecular mass of 41.8 kDa; this is globular actin or G-actin. One Ca^{2+} ion is bound to each molecule of G-actin, stabilising its globular conformation. In addition, one ATP molecule is associated with G-actin via a nonvalence interaction. In the nonvalence polymerisation of globular actin, the terminal phosphate of ATP is split off and fibrillar actin or F-actin is formed. The polymerisation may be induced by increasing the salt concentration to nearly the physiological level. The process does not require the consumption of energy, although it is in fact accompanied by the hydrolysis of ATP, which appreciably increases the rate of polymerisation and influences its dynamics. According to data obtained by electron microscopy, the actin filaments consist of two chains of globular molecules, the length of which is ~65 Å and the thickness in the widest part is ~40 Å. The F-actin chains form a double helix consisting of 13 molecules in six turns repeated at 360 Å intervals.[213]

After attempts in the course of many years, the G-actin molecules were crystallised but only together with the molecules of deoxyribonuclease I in proportions of 1:1. The three-dimensional structure of monomeric actin at the atomic level was therefore discovered from X-ray crystallographic data for the G-actin–deoxyribonuclease I complex.[214] The X-ray scattering pattern for the F-actin fibre was obtained simultaneously with a resolution of 6 Å and the orientation of the G-actin monomer and of the double helix of the polymer was found by comparing the calculated and observed X-ray diffraction patterns.[213] The remaining uneliminated differences reflect the fact that the polymerisation of actin is accompanied by slight conformational changes, but only to some extent, because the use of a refined structural model of G-actin in the construction of a model of the F-actin filament led recently to a better agreement between the calculated and experimental results.[215] Further refinement of the model is difficult owing to the lack of the X-ray diffraction pattern for F-actin with a resolution better than to within 6 Å. A solution may be found by resorting to a theoretical approach and to the employment of conformational analysis[216] and molecular dynamics[217] methods. The atomic model of F-actin, constructed by adjusting for consistency the results of X-ray

diffraction of G-actin crystals and thin F-actin filaments, agreed with the model reconstructed from cryoelectron photomicrographs of the actin filament.[218,219]

Two auxiliary proteins, tropomyosin and troponin, are closely associated with each actin filament. Their principal function is the regulation of muscle contractions as a function of the concentration of Ca^{2+} ions and hence nerve impulses. The rigid rod-shaped α-helical tropomyosin molecules ~400 Å long are located in longitudinal grooves extending along the actin filament, imparting thereby the necessary rigidity to the F-actin double helix (Fig. 17). The globular form of troponin is made up of three different subunits (troponins T, I, and C). Troponin T has a section for the binding of tropomyosin and is responsible for the attachment of the entire complex to the actin filament. When troponin I is added to troponin T and tropomyosin, a complex preventing the interaction of actin with myosin even in the presence of Ca^{2+} ions is formed. In the presence of troponin C, this complex continues to block the interaction of myosin with actin, but only in the absence of Ca^{2+}. When free calcium appears in the medium, troponin C binds four Ca^{2+} ions and removes the blockade in this state. Precisely this effect actually constitutes the basis of the excitation of the muscle contraction by calcium ions. We shall return to the problem of the way in which tropomyosin and troponin control the interaction of myosin with actin after considering the structural organisation of the thick filaments.

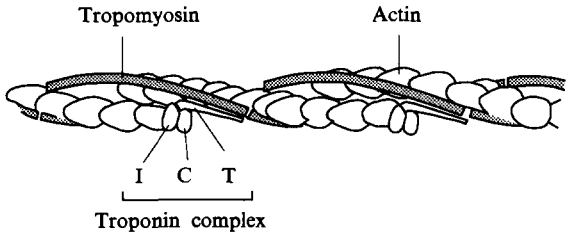


Figure 17. Schematic illustration of the thin filament.

2. The structure of myosin filaments

The contents of myosin, actin, tropomyosin, and troponin in the myofibrils are approximately 55%, 25%, 15%, and 5% respectively. A distinctive feature of the myosin in the skeletal muscles is its ability to form spontaneously, under in vitro conditions, giant polymeric complexes greatly exceeding in size the myosin aggregates from nonmuscle tissues. Myosin can be extracted from skeletal muscles with concentrated salt solutions, in which it is readily soluble. Muscle treated in this way loses only the thick filaments, which decompose into the component myosin molecules having a molecular mass of ~520 kDa. On treatment with a concentrated solution of urea or another detergent, the myosin molecule decomposes into six polypeptide chains: two identical heavy chains with a molecular mass of ~220 kDa and two pairs of light chains with molecular masses of ~22 and

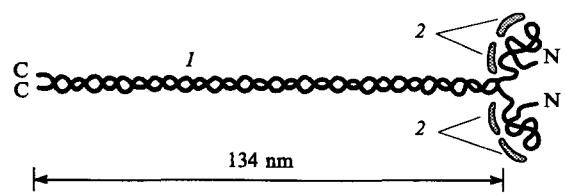


Figure 18. Schematic illustration of the structure of the myosin molecule: (*1*) twisted α-helices; (*2*) light chains.

~15 kDa.[220-224] It was established for the first time in 1963 with the aid of electron microscopy[223] that myosin consists of two globular 'heads', each of which is attached to a heavy chain, containing a long α-helical section. In the native myosin molecule, the α-helices of two heavy chains are twisted round one another into a super helix, forming a rod-shaped tail, from which two heads project. Each head is made up of the globular part of the heavy chain (~95 kDa) and includes one molecule of each of the two types of the light chain (Fig. 18).

The thick filaments are formed as a result of the association of the myosin molecules via their rod-shaped tails: several hundreds of molecules, arranged in parallel with lengthwise displacements, form a bundle from which laterally disposed heads project (Fig. 19). The entire structure is dipolar. The projecting heads are absent only along the small middle section of the filament, where two oppositely directed bundles of myosin tails are joined together. The globular heads of the myosin molecules interact with actin and form transverse bridges between the thick and thin filaments.

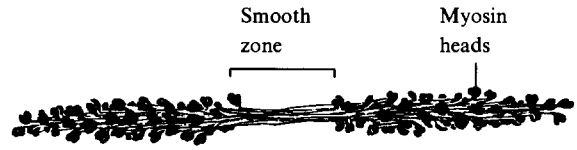


Figure 19. Schematic illustration of the thick filament of the skeletal muscle.

The proteolysis of the heavy filaments showed that the myosin head can be readily separated from the remainder of the protein, forming the so called subfragment-1 (S1) and a superhelical rod, responsible for the self-assembly of myosin and for the creation of the structural base of the thick filaments.[220,225] The subfragment-1 contains the nucleotide-binding active centre for ATP, an actin-binding surface, and two regions corresponding to contacts with the light chains. Thus the globular head retains all its function even outside the filament. The light chains incorporated in it differ from one another in structure and properties. In some forms of myosin, they do not exert an appreciable influence on the ATPase activity of the enzyme.[226] However, in certain types of myosin the light chains of its head may participate in the regulation of the hydrolysis of ATP, but only in the presence of actin.[227,228]

As early as the end of the past century, it was noted that myosin exhibits double refraction. However, until recently, the entire knowledge about the three-dimensional structure was limited to information about the external outline of the molecule and its size obtained with the aid of electron microscopy. In particular, it was known that the myosin head has a pear-shaped form approximately ~190 Å long and 50 Å wide, while the double helix of the tail section is ~1500 Å long and ~20 Å wide.[228-231] Rayment et al.[232] were able to obtain the crystals needed for analysis by employing the procedure, altogether unusual in protein crystallography, involving *N*-methylation under mild conditions, of the side chains of all the Lys residues of the myosin fragment-1. In order to make sure that the methylation did not lead to a drastic alteration of the conformational and enzyme properties of the protein, the authors subjected lysozyme to a similar chemical modification and did not observe after this procedure significant changes in the three-dimensional structure of the enzyme. In addition, the kinetic properties of the methylated myosin S1 were tested.[233] It retained its catalytic activity, although deviations of the kinetic parameters of the hydrolysis of ATP from the values for the native specimen were in fact observed.

The three-dimensional structure of the myosin subfragment-1 was determined[232,234,235] by X-ray diffraction with a resolution of 2.8 Å. This resulted in the refinement of not only the external dimensions of the myosin head, which confirmed that it lacks any kind of symmetry, is 165 Å long, and has a cross-section of 65 × 40 Å in the thickest part, but also led to the construction of an atomic model comprising 1072 aminoacid residues (out of the total number of 1157). The structure contains many α-helices (~48%), the longest of which extends over a distance of 85 Å from the thickest part in the direction of the C-end of the S1 heavy chain. Most of this helix is surrounded by light chains, ELC (essential light chain) and RLC (regulatory light chain), one of the principal purposes of which is conformational stabilisation of the heavy chain of the myosin head (for example, when RLC is removed, the S1 structure breaks down).[236] In addition, the light chains promote the conformational rearrangements which occur when the nucleotide is bound to and liberated from the thickened part of the head. In order to facilitate the description of the three-dimensional structure of subfragment-1, its heavy chain can be usefully divided into three parts: the N-terminal part incorporating the Asp-4–Glu-204 residues, the central part with Gly-216–Tyr-626, and the C-terminal part with Gln-647–Lys-843. Loops lacking secondary structures are located between them. These are subjected to tryptic cleavage, which gives rise to heavy chain fragments with molecular masses of 25, 50, and 20 kDa.

The thickened part of the myosin head contains nucleotide and active binding centres and thus has all the components necessary for the generation of motion. The essential moving, motor part of myosin is a complex of secondary structures disposed around the β-layer consisting of seven largely parallel β-tiers. It includes the components of all three trypsin-cleaved fragments of the heavy chain. The nucleotide-binding packet is located at the end of the central β-pleated sheet and adjoins the 25 kDa fragment on one side and the 50 kDa fragment on the other. The location of the aminoacid residues forming the nucleotide active centre of myosin has been determined by the tracer atom method[237] and by analogy with the sequences of the phosphate loops in the adenylate kinase and ribonuclease structures.[238,239] The binding pocket is ~13 Å deep and approximately just as wide. Since the crystals were grown in the absence of ATP, the active centre corresponds to an open conformation in the observed structure of the myosin subfragment-1.

The interrelation between the hydrolysis of ATP and muscle contraction, discovered, as already mentioned, as early as 1939, was considered in a large series of kinetic studies. The results, obtained for the first time in 1971[240] and in subsequent years,[234,241–243] have not undergone fundamental changes and lead to the same idea about the actin-myosin mechanism of muscle contraction. It is illustrated in Fig. 20 and corresponds to a four-stage process involving the conversion of the energy of the hydrolysis of ATP into mechanical work. In the first stage (*a*) of the proposed mechanism, the myosin head, carrying the ATP-hydrolysis products (ADP and phosphate), is attached to the actin filament. The second stage (*b*) (the 'working step') begins with a change in the conformation of the head induced by its interaction with actin, which liberates the hydrolysis products and results in the appearance of stress in the actomyosin complex, which is released during the longitudinal displacement of the thin filament. After the completion of the motion, conditions arise for the addition of a new ATP molecule to the myosin head, which is accompanied by the breakdown of the actin–myosin contacts (stage *c*). The cycle terminates with the hydrolysis of ATP and a change in the conformation of the head, which assumes the initial position (stage *d*). It has been suggested that each head of the myosin molecule executes its own cycle independently.

Thus the most significant features of the mechanism of the action of the actomyosin complex are that, firstly, the hydrolysis of ATP is completed at the time when myosin does not interact with actin, and, secondly, the driving force of the process arises on liberation of the ADP and γ-phosphate produced.

Not only the results of kinetic studies but also a multiplicity of experimental data obtained by other methods agree with the idea described above that the myosin heads 'stride' along the actin filaments. In particular, the generally accepted idea is confirmed by the three-dimensional structures of monomeric actin[213,214] and the myosin head,[232,234] which were discovered recently, as well as the structural model of the actomyosin complex constructed, with a resolution of 5–8 Å on the basis of these structures using cryoelectron microscope data.[235] One of the key features of this complex, which became evident after the construction of the model, is the existence of nonvalence contacts between actin and the C-terminal domain of the 50 kDa tryptic fragment. Interactions of this type may stimulate conformational changes in myosin at the instant of its mutual approach with actin in the second stage of the muscle contraction process (Fig. 20). In a study of skeletal muscles by the small angle X-ray scattering method, data were obtained recently, indicating convincingly a significant change in the form of the myosin head during the binding of nucleotides.[244]

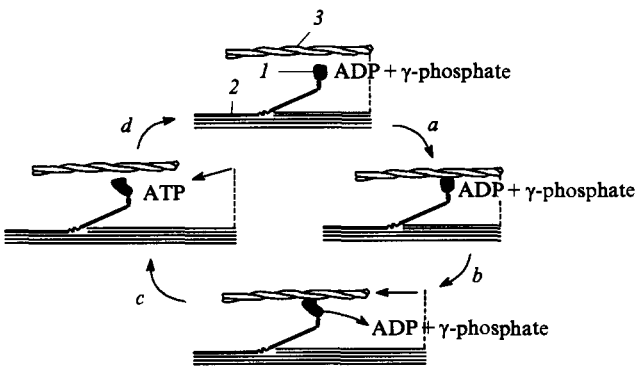


Figure 20. Schematic illustration of the mechanism of the utilisation of the energy of the hydrolysis of ATP for the movement of the actin filament relative to the myosin filament: (*1*) myosin head; (*2*) thick filament; (*3*) thin filament.

The conformational rearrangement of myosin is accompanied by an allosteric effect — the closure of the long narrow groove at the boundary between the thick and thin halves of the pear-shaped head. This results in the mutual approach of actin and the nucleotide centre of myosin and in the liberation of ADP and inorganic phosphate. This is the reason why myosin is an actin-dependent ADPase. It was noted long ago that the rate-limiting stage of the catalytic reaction is not the binding of the ATP molecule to the active centre and not the hydrolysis proper, but the liberation of the products of the enzymic reaction, remaining firmly bound to myosin, which in fact prevents the onset of the next catalytic step.[203,204] The ATPase activity of the purified myosin is low: the enzyme requires approximately 30 s for the hydrolysis of one ATP molecule. In the presence of actin, each myosin molecule is capable of hydrolysing from 5 to 10 ATP molecules per second.

The thick filament contains ~500 myosin heads and they all operate simultaneously but not synchronously, drawing in the actin filament. In the new cycle of the interaction with actin, the head is attached to another monomer of the thin filament located closer to the *Z*-plate. The limiting contraction of the muscle develops in hundredths of a second (~0.02 s). The muscle at rest is elastic and can be easily stretched. The contracted muscle, on the other hand, is inelastic and rigid; its extension is prevented by the bonds between the actin and myosin filaments, which persist when the ATP concentration is inadequate.

Skeletal muscle contracts when the action potential of the nerve fibre is switched on and when a signal is obtained from the corresponding motoneuron. The electrical excitation spreads rapidly over the so called T-tubes, which surround each myofibril in the region of the *Z*-plates. Here the electric signal is transmitted to the sarcoplasmic reticulum—a system of branched intercommunicating vesicles. At the instant of activation by the electric pulse which has passed through the T-tubes, the sarcoplasmic reticulum injects into the cytosol large amounts of Ca^{2+} ions stored in the vesicles, which initiates the contraction of the myofibrils. The signal from the muscle cell membrane reaches the sarcomers in several milliseconds via the T-tubes and the sarcoplasmic reticulum, so that all the myofibrils of the muscle cell contact almost simultaneously. The relation between the muscle contraction and the changes in the Ca^{2+} concentration is due to the functions of the auxiliary proteins tropomyosin and troponin, which are associated with the actin filaments (Fig. 17). They participate in the regulation of the muscle contraction of the Ca^{2+} ions and thereby render the ATPase activity of myosin sensitive to the concentration of these ions.

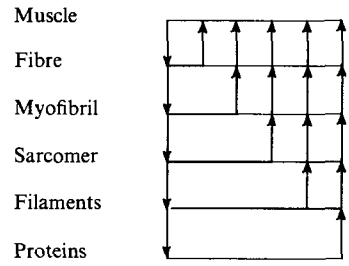
It has been suggested that tropomyosin and troponin effect the Ca^{2+}-dependent regulation of the muscle contraction via steric hindrance to the mutual contacts between actin and myosin. With increase in the concentration of Ca^{2+} ion, the positions of the tropomyosin molecules change, possibly as a result of the change in the shape of the troponin molecules bound to them, in the first place troponin C molecules. In the absence of Ca^{2+}, tropomyosin, troponin T, and troponin I form a complex, which prevents the interaction of actin with myosin. After the appearance of calcium ions, troponin C binds four Ca^{2+} ions and in this state removes the blockade and enables the myosin heads to interact with actin.[245]

The determination of the three-dimensional atomic structures of the proteins G-actin and the myosin subfragment-1, and the reproduction on this basis, resorting to electron microscopy and small angle X-ray scattering, of the three-dimensional structures of the thin and thick filaments, implies the virtually complete visualisation of the elementary constituent sarcomer, capable of demonstrating the principles of the contraction of skeletal muscles and a concrete conformational-electronic mechanism of the transformation of chemical energy into mechanical work. The development of the atomic-molecular model of the actomyosin complex has been one of the outstanding achievements in molecular biology during recent years both in methodological and in purely scientific respects. Without dwelling in detail on the possibilities for the experimental study of the muscle contraction process which have greatly expanded in recent years,[246] we shall only observe that the most notable event in this instance has been the application of the molecular genetics[247] and 'laser trap'[248] methods, which effectively supplement X-ray diffraction and electron microscopy. The 'laser trap' method makes it possible to follow the 100–200 Å displacements of single proteins and to measure the strength of their interactions up to 7 pN (7×10^{-7} dyn). We shall consider below the further improvement of the model itself—the problem of the transition from the phenomenological description of the mechanism of action of the molecular muscle motor to the creation of a rigorous theory of the contraction of muscles and of a quantitative method for the analysis of this process.

The model of Rayment and Holden does not merely constitute a general description of the authors' and coworkers' own work,[232,234,235] but constitutes a logical completion of a series of numerous investigations during the last four decades and in the first place the studies during the 1990s on G- and F-actins by X-ray diffraction and cryoelectron microscopy.[213,214,218,246]

The relation between the knowledge of the structure of the muscle system and the understanding of the mechanism of its action, i.e. between the morphology of the various levels of the structural organisation and the physiology of the muscle, is illustrated in Scheme 6. The thick arrows indicate the direction of the successive steps in the discovery of the structure and the oppositely oriented thin arrows denote the steps in learning about the function of the biosystem. It is seen from the scheme presented that the more complete and detailed the information about the form and composition of the simplest subsystems, the deeper the understanding of the mechanism of the functioning of the entire system. This nature of the dependence of the depth of understanding of the essential features of the physiological phenomenon and the knowledge of the morphology of its participants is a common feature of the processes involved in learning about biological systems. The treatment of the properties of a biological system is always relative and is based on information about the structures of the underlying subsystems.

Scheme 6



The existence of common characteristics and of a single fundamental plan in the development of research into biosystems leads, despite their perhaps self-evident nature, to nontrivial conclusions which are of special interest at the present time. The development of biology throughout history has been determined by two countercurrent streams of investigations: morphological, directed from objects and phenomena with a complex organisation to simpler ones, and physiological, with the opposite direction. The first and second streams were the driving and driven components respectively. However, at the beginning of the second half of the 20th century, in its progress from complex to simple constructions based on the advances in morphology, biology reached the most universal and simplest level in biosystems—a kind of molecular 'bottom'. Further development on the same lines (from morphology to physiology) and in the same direction (from complex to simple constructions) has become impossible. The usual source of qualitatively new information has fizzled out, because the morphological data about the possible underlying subsystems (individual aminoacids, atomic groups, and atoms) contain no specific biological features and hence are not directly linked to the function of any of the biosystems considered.

Thus the approach employed in biology is completed by the determination with the aid of X-ray diffraction, electron microscopy, or another experimental method of the three-dimensional structures of proteins. The preexisting or newly formulated more detailed and better founded ideas about the mechanism of the functioning of the biosystem are confirmed, an atomic-molecular model of the process is developed, and the corresponding hypothesis is formulated on the basis of experimental data on the structure of the biosystem at the molecular level. All that was done previously as regards biosystems with a complex organisation is in essence done in securing new information about the morphology of the underlying subsystems.

The importance of the role of X-ray diffraction analysis of proteins consists in the fact that the study of biosystems at the molecular level was initiated with its aid, and without which it is difficult to imagine the establishment of molecular biology.

The question arises: what is required for further progress in biology and for its transition to the next improved qualitative state. Since the paths leading to the development of studies on all biosystems are in principle the same, the answer to the question posed above does not lose its significance and generality if it is obtained by considering some kind of concrete object, for example, the actomyosin complex. Another question is what additional information (apart from morphological) about the structures of myosin, actin, and certain other proteins is needed in order to not only compare the hypothetical idea about the operation of the actomyosin complex, about the interactions with the ATP molecules supplying it with energy, and about the Ca^{2+} ions regulating its functioning but also to proceed further and attempt to understand why this occurs. This requires data (quantitative data) on the conformational and chemical changes which have taken place, on their sequence, and on the stimuli and their interdependence. With the three-dimensional structure of the actomyosin complex already known, the quantitative description of the mechanism of its action as a spontaneous periodic process may serve as a criterion of the reliability of our knowledge. Here the main problem is not so much the amount and even the quality of the experimental data as its physicochemical interpretation, i.e. the availability of the corresponding theories which provide a logical and quantitative link between the aminoacid sequence, the three-dimensional structure, and the function of the protein molecule.

VII. Synchrotron radiation

The application of synchrotron radiation, which is much more powerful than the radiation from the traditional X-ray tubes, in protein crystallography may be regarded as one of the most significant methodological advances in X-ray diffraction structural analysis during the last decade. In the 1960s–1970s, the majority of the three-dimensional structures of proteins were solved with the aid of sealed sharp-focus tubes with a copper anode giving rise to a characteristic wavelength $\lambda(K_\alpha)$ of approximately 1.54 Å. Their intensity, estimated from the stream of photons in a collimated X-ray beam (10^9–10^{10} photons s^{-1}), is several times higher than for the usual tubes and the focussing of the beam onto a much smaller area makes it possible to obtain diffraction patterns with a higher resolution and a shorter exposure.

In 1959, Parratt proposed that a synchrotron be used as a source of X-rays in crystallography.[249] Moving in a circle within the synchrotron at relativistic velocities in a homogeneous magnetic field, charged particles begin to emit, following retardation and curvature of their trajectories, a continuous spectrum of electromagnetic waves in the form of a very sharp conical beam with a divergence angle of $\sim 1'$ and an axis which coincides with the instantaneous (tangential) direction of motion. The short-wavelength part of the synchrotron (magnetic retardation) radiation spectrum has a broad maximum in the region of interest for X-ray diffraction analysis. In contrast to traditional sources, the polychromatic radiation of the synchrotron may be rendered monochromatic over a much wider range of wavelengths and hence can give rise to a powerful X-ray flux. Thus, in the synchrotron in Daresbury (Great Britain), the useful flux $N(\lambda)$ is at least 10^2–10^3 times more intense than in the best current X-ray tubes with a rotating anode. Parratt's idea became the subject of serious discussions, but remained unrealised for a long time. Both the possibility of the actual increase in the intensity of the diffraction beams and the ability of protein crystals to withstand an intense radiation gave rise to doubts.[250] It was not until 1971 that synchrotron radiation was applied in diffraction studies on biological objects. Studies on muscle fibres by the small angle scattering method showed that, after being rendered monochromatic and after focussing, the intensity of the synchrotron radiation employed is two orders of magnitude higher than the maximum intensity of the collimated filtered CuK_α radiation from an X-ray tube and does not cause the disruption of the irradiated object.[251–253]

The question of the possible application of synchrotron radiation in the X-ray diffraction analysis of protein single crystals was first examined theoretically by Wykoff[254] and Harrison[255] and experimentally by Phillips et al.[256] The last group of workers obtained X-ray diffraction patterns for protein single crystals comprising those of rubredoxin, azurin, the nerve cell growth factor, and L-glutamine-aspariginase, using an electron–positron synchrotron (Stanford, USA).

The authors showed that, when the radiation from an X-ray tube is replaced by synchrotron radiation (keeping all other experimental conditions the same), the intensity of the scattering by the same protein crystals increases by a factor greater than 60 and hence the exposure time diminishes by the same factor, but the risk of the rapid decomposition of the crystals was not eliminated. On the other hand, owing to the decrease in exposure time, the rate of decomposition of the test object proved to be significantly lower than in the case where the radiation from an X-ray tube is used. Together with the above advantages, the authors also noted the small angular divergence of the synchrotron beam and the ease of tuning the synchrotron to a chosen wavelength, which facilitates the selective optimisation of the anomalous contributions to the scattering factor. More than one third of the studies on X-ray crystallography of proteins are nowadays carried out with the aid of synchrotron radiation and multichannel recording systems.

A no less important factor in the X-ray diffraction of proteins (as is incidentally the case in the entire modern X-ray diffraction analysis) was the appearance of the so called coordinate (multichannel) X-ray detectors (or 'area' detectors), which make it possible to record simultaneously all the diffraction maxima arising from the crystal in the given orientation. Such detectors, which are as a rule complex electronic systems with simultaneous recording of a multiplicity of reflections, are the modern analogues of photographic films used previously at the dawn of X-ray diffraction analysis. The recording of a single diffraction pattern (with a large number of diffraction spots) for a specified orientation of the crystal may last several seconds or less, which, together with a powerful radiation source (synchrotron), diminishes the duration of the X-ray diffraction experiment by several orders of magnitude.

Table 8 presents certain results of the X-ray diffraction analysis of proteins, the diffraction patterns of which were obtained both with the aid of synchrotron radiation (Nos. 1–8 and 17–20) and the radiation from X-ray tubes with rotating copper anodes (Nos. 9–16). The table reflects only a small proportion of the publications from the end of 1993 until the first half of 1994 devoted to the solution of the three-dimensional structures of protein molecules and their complexes. If the advantages of the two methods are judged on the basis of the resolutions and the divergence factors (R), then one must conclude that the nature of the radiation source hardly affects the final result. With the aid of synchrotron radiation and an X-ray tube, it has been possible to elucidate the three-dimensional structures of protein molecules with a record resolution, having overcome in both cases the one angstrom barrier [Table 8, bacterial trypsin (No. 2) and crambin (No. 13)] and having attained at the same time a divergence factor R of about 10%—a value close to that of the factor R for the refined structures of small organic molecules.

The methods also do not differ appreciably as regards the size of the irradiated crystal and the diameter of the focussed spot. Thus, in the determination of the three-dimensional structure of the antibody Fab 17/9 (Table 8, No. 16) by means of an X-ray tube with a rotating anode, the size of the specimen was 0.30 × 0.04 × 0.02 mm and the size of the focussed spot was only 0.1 mm. These parameters are not inferior to the experimental conditions when a synchrotron is employed.

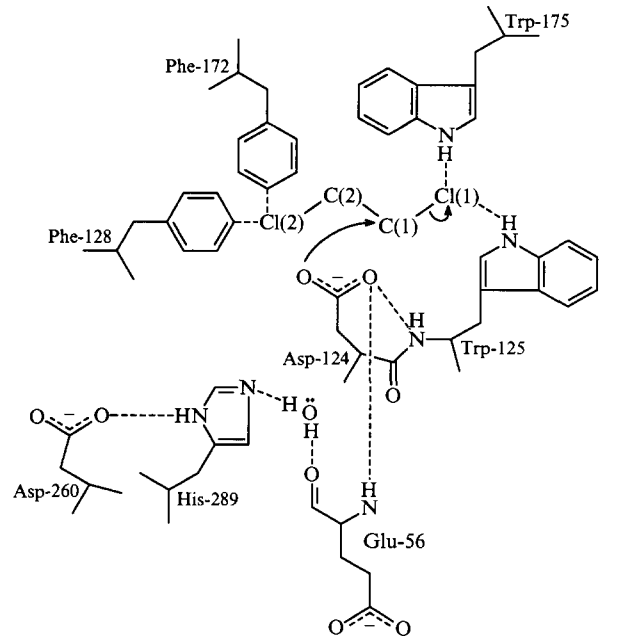
However, one can assume that the powerful synchrotron radiation and its sharp focus are somewhat preferable, since it is then possible to use smaller crystals. Nowadays the problem of the crystallisation of proteins is in both cases just as acute as decades ago. As already mentioned, the situation is particularly complex in the crystallisation of membrane proteins (for a description of the efforts made in this connection and of the relative successes, see Refs 233 and 236–238).

Comparison of the data presented in Table 8 leads to the conclusion that the X-ray diffraction methods employing synchrotron radiation and the radiation from an X-ray tube have no appreciable advantage relative to one another in the study of the native conformations of protein molecules and their stable complexes, i.e. in all those cases where the static problem of the determination of atomic three-dimensional structures is being solved. Until recently, it has been assumed that, in principle, X-ray diffraction analysis cannot be applied to the consideration of problems involving the dynamics of proteins. The use of synchrotron radiation and of modern systems for the simultaneous rapid measurement of the intensities of multiple reflections made it necessary to question the incontrovertible nature of this view if not demand its complete reversal. As can be seen from Table 8, it is possible to shorten the exposure time from many tens of hours (No. 9), days (No. 16), and even weeks (No. 11) to fractions of a second (Nos 3 and 5). According to Thomas,[277] the diffraction reflections from protein crystals exposed to synchrotron radiation may be measured over a period of 100 ps (i.e. 10^{-10} s). The appreciable shortening of the exposure not only makes it possible to shorten significantly the duration of the analysis of the three-dimensional protein structure but also leads to a fundamentally new prospect for the study of the mechanisms of the processes occurring in protein crystals by investigating the structures of the intermediates, when their lifetimes are fairly long or can be prolonged by altering the external conditions. The possibilities which have arisen render the X-ray diffraction method still more unique. One may postulate that the employment of synchrotron radiation promotes the direct monitoring of the kinetics of the conformational and chemical changes in the structures of proteins at the atomic level in the course of, for example, enzymic reactions. A study has been carried out (discussed below) in which an attempt has been made to solve this kind of problem.

1. The mechanism of the functioning of haloalkane dehalogenase

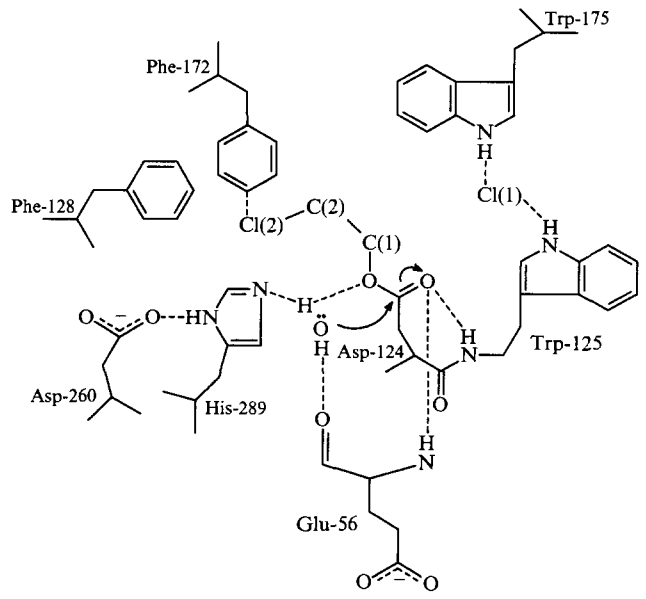
Verschueren and coworkers[175,265] applied X-ray crystallography to the study of the mechanism of the catalytic step involving haloalkane dehalogenase (Table 8, No. 10). The structures of the enzyme, a single crystal of which was kept permanently in the mother liquor, were solved both in the absence and in the presence of the substrate (1,2-dichloroethane) in the solution. At pH 5 and $T = 4$ °C, i.e. far from the optimum conditions (pH 8.2 and 22 °C, the substrate was bound to the active centre, but the catalytic reaction did not develop. The nonvalence enzyme–substrate Michaelis complex remained stable indefinitely and its structure could therefore be determined with the aid of the radiation from an X-ray tube, for an exposure time of 48 h, and with retention of all other conditions in the analysis of the native enzyme. The observed disposition of the substrate in the active centre is illustrated schematically in Scheme 7. One of the chlorine atoms [Cl(1)] in the complex is located at distances of 3.6 and 3.2 Å from the nitrogen atoms of the Trp-125 and Trp-175 side chains and interacts with the hydrogen atoms of two N–H bonds. The other chlorine atom [Cl(2)] is stabilised by dispersion interactions with the Phe-128 and Phe-172 benzene rings. In the observed conformation of the substrate in the active centre, the C(1) carbon atom has been brought closer to the $O^{\delta 1}$ oxygen atom of the Asp-124 side chain (3.8 Å), which is in fact the main reason for the productivity of the nonvalence complex.

Scheme 7



When a crystalline specimen is heated to room temperature, the C(1)–C(1) bond dissociates, which is accompanied by the formation of the $Cl(1)^-$ ion and the alkylation of the $O^{\delta 1}$ oxygen atom of the Asp-124 residue. Such a change in the complex is in fact indicated by the solved three-dimensional structure, which arises and remains stable at pH 5 and 22 °C (Scheme 8). Finally, at pH 6.2 and 22 °C, the alkylated fragment is hydrolysed by a water molecule activated by the side chains of the His-289 and Asp-260 residues interacting with one another. The reaction products are removed and the enzyme returns to the initial state, which is in fact revealed by the X-ray diffraction analysis.

Scheme 8



Thus the two-step mechanism of the reaction involving haloalkane dehalogenase, proposed previously,[278] has been confirmed experimentally.[265] In the catalytic reaction involving this enzyme and occurring under in vivo conditions, the lifetime of the intermediates is too short for crystallographic study. By varying the pH and the temperature, the authors were able to slow down the process, separate it into two stages, and investigate

Table 8. Certain X-ray diffraction data for proteins obtained with the aid of synchrotron radiation and radiation from X-ray tubes with a rotating anode.

No.	Protein	Source	Molecular mass/kDa	Structural data	Resolution/Å	*R* factor (%)	Remarks	Ref.
1	Haemaglutinin	*Influenza virus*	60	Homotrimeric complexes of glycoprotein with receptor analogues	2.15	21.6	Crystal dimensions $0.70 \times 0.70 \times 0.70$ mm; synchrotron radiation with $\lambda = 0.905$ Å; temperature 108 K	257
2	Bacterial trypsin	*Noncardiopsis*	20	Monomer	0.96	10.7	Homotrimeric complexes of glycoprotein with receptor analogues. Tube, CuK_α	258
3	Cytochrome *c* peroxidase (CCP)	Yeast	34	Haem(Fe)-containing enzyme	2.2	15.8	Crystal dimensions $0.40 \times 0.40 \times 1.0$ mm; polychromatic synchrotron radiation (Laue diffraction); single exposure time 300–400 ms; temperature 279 K	259
4	Transketolase	*Saccharomyces cerevisiae*	148	Homodimer	2.0	15.7	Synchrotron radiation	260
5	*p*-Guanidinobenzoyl-substituted trypsin	Bull	24	Monomer	2.0	22.1	Crystal dimensions $1.0 \times 0.40 \times 0.40$ mm; polychromatic synchrotron radiation (Laue diffraction); single exposure time 800 ms; pH 5.5–8.5	261
6	β-Galactosidase	*Escherichia coli*	465	Homotetramer	2.5	19.3	Synchrotron radiation	262
7	Glucose dehydrogenase	*Thermoplasm acidophilum*	160	Homotetramer	2.9	12.4	Crystal dimensions $1.50 \times 0.30 \times 0.20$ mm; tube, CuK_α and synchrotron radiation	263
8	Renin	Mouse	40	Enzyme–inhibitor complex	2.0	18.0	Tube CuK_α (resolution 3.0 Å) and synchrotron radiation resolution 2.0 Å)	264
9	Haloalkane dehydrogenase	*Xanthobacter autotrophicus*	36	Monomer	1.9	16.6	Crystal dimensions $0.40 \times 0.40 \times 0.15$ mm; tube, CuK_α; exposure time 48 h	265
10	Growth hormone	Man	22	Monomer	2.0	18.5	Crystal dimensions $0.25 \times 0.25 \times 0.15$ mm; tube, CuK_α	266
11	Aconitase	Bull, pig	83	Enzyme–*trans*-aconitate and enzyme–nitrocitrate complexes	2.05	17.0	Crystal dimensions $0.70 \times 0.70 \times 0.20$ mm; tube, CuK_α; exposure time 12–18 days	267
12	Pyruvate oxidase	*Lactobacillus plantarum*	270	Homotetramer	2.1	16.2	Crystal dimensions $0.70 \times 0.70 \times 0.70$ mm; tube CuK_α and synchrotron radiation; temperature 277 K	268
13	Crambin	*Crambe abyssinica*	5.5	Monomer	0.83	10.5	Tube, CuK_α; temperature 130 K	269
14	Toxin II	*Androctonus australis*	7	Monomer	1.3	14.8	Tube, CuK_α	270
15	Oncomodulin	Tumour cells	12	Monomer	1.3	16.9	Crystal dimensions $0.20 \times 0.60 \times 0.80$ mm; tube, CuK_α	271
16	Fab 17/9 antibody	IgG2 *a*, *k*	26	Complex between Fab 17/9 and the 101–107 peptide of the influenza virus haemagglutinin	2.8	19.0	Minimum crystal dimensions $0.30 \times 0.04 \times 0.02$ mm; tube, CuK_α; temperature 123 K; exposure time in excess of 10 days	272

Table 8 (continued)

No.	Protein	Source	Molecular mass/kDa	Structural data	Resolution/Å	*R* factor (%)	Remarks	Ref.
17	GH-5 domain of the linker histone H5 (24–96 fragment)	Bird erythrocytes	8.5	Monomer	2.5	25.0	Synchrotron radiation at the three wavelengths 0.9802, 0.9795, and 0.9150 Å corresponding to the Se absorption band. Phase determination by the MAD method. Recombinant [Se-Met]-GH5 sequence produced by *E. coli* plasmids	273
18	BamH1 endonuclease (native and Se-Met)	*Bacillus amiloliqueta-ciens*	25	Homodimer	1.95	19.0	Tube CuK_α and synchrotron radiation at the wavelengths corresponding to the Se absorption edge (0.979 Å), the absorption peak (0.978 Å), and at a point remote from the absorption region (0.900 Å); temperature 278 K	274
19	Gonadotropin (native and Se-Met)	Human embryo	28	Heterodimer (αβ)	2.6	19.9	Synchrotron radiation; anomalous diffraction at four Se wavelengths (MAD); temperatures 277, 293, and 110 K	275
20	Glutamine-5-phosphoribosyl-1-pyrophosphate (PRPP)-amidotransferase	*Bacillus subtilis*	210	Homotetramer	3.0	22.4	Synchrotron radiation; anomalous diffraction at the three wavelengths corresponding to the Fe atoms in the four [4Fe–4S]-clusters of the tetramer (MAD)	276

the atomic three-dimensional structures of the corresponding enzyme–substrate complexes with a resolution of 2.0–2.4 Å. It was shown that the central role is assumed by the carboxy-group of the Asp-124 residue as the nucleophile in the first (alkylation) stage and by a water molecule, attacking the central carbon atom of the ester group of the covalent intermediate, in the second (dealkylation) stage.

2. Deacylation of trypsin

A similar study has been carried out with a classical object in enzymology — trypsin.[261] The Laue method for the recording of synchrotron radiation with time resolution was used in the above study.

The chemical mechanism of the catalytic step in the reactions involving serine proteases, including trypsin, presented below has been known for a fairly long time.[279–281]

$$\underset{\text{I}}{E+S} \rightleftharpoons \underset{\text{II}}{ES} \rightleftharpoons \underset{\text{III}}{ES^*} \rightleftharpoons \underset{\text{IV}}{EA + P_1} \rightleftharpoons \underset{\text{V}}{EA^*} \rightleftharpoons \underset{\text{VI}}{EA} \rightleftharpoons \underset{\text{VII}}{E+P_2}$$

E = enzyme, S = substrate, A = acylenzyme, P_1 and P_2 = hydrolysis products.

According to the proposed scheme, the mechanism of the tryptic hydrolysis includes a consecutive chain of chemical interrelations between the enzyme and the substrate via covalent intermediates. The catalytic process begins with the formation of a nonvalence Michaelis complex (II) in which the hydroxyl of Ser-195 and the imidazole ring of His-57 in the enzyme are respectively close to the carbonyl and amide groups of the peptide or ester bond of the substrate to be cleaved. As a result of their concerted interactions, the nonvalence enzyme–substrate bonding is converted into covalent bonding with the initial formation of a relatively unstable intermediate — the so called tetrahedral adduct (III). The latter decomposes into the acylenzyme and the amine (IV), while on hydrolysis of the ester it decomposes into the acylenzyme and the alcohol. Next follows deacylation, which proceeds similarly in principle, but in the opposite sequence and with participation of a water molecule as the nucleophile and not the O^γ atom of the Ser-195 side chain. A metastable tetrahedral adduct (V) is again formed and then decomposes, via the nonvalence complex (VI) stage, into the initial enzyme and the second reaction product (VII). The chemical mechanism for the proteolytic serine enzymes was developed before the results of the X-ray diffraction analysis of the three-dimensional structure of the molecules became available.

The crystal structure of native trypsin has been established[282–287] with a resolution of 1.8 Å and refined to within 1.5 Å. The geometry of the active centre was identified on the basis of the results of X-ray diffraction analysis of complexes of trypsin with protein inhibitors of animal and plant origin[288–290] and with irreversible synthetic inhibitors.[291] It was shown that the hydroxy-group of the Ser-195 residue and the imidazole ring of His-57, located on the surface of the protein globule and forming the $N^{\varepsilon 2}\ldots H-O^\gamma$ hydrogen bond, participate directly in the interaction with the substrate and in the formation of intermediate products of the catalytic reaction. The His-57 residue is also close to Asp-102, the $N^{\delta 1}-H\ldots O^{\delta 2}$ interaction occurring between them.

We shall now return to the study[261] in which the mechanism of action of trypsin in the second stage of the catalytic step (IV–VII) was investigated by X-ray diffraction with synchrotron radiation. The study began with the preparation of a stable intermediate of the enzymic reaction — the acylenzyme

(VI) — by the addition of *p*-guanidinobenzoate (GB) to the Ser-195 residue of trypsin present in the crystalline state in the mother liquor at pH 5.5. On rapid increase in the pH to 8.5, the process, monitored by three-dimensional Laue diffraction, was initiated. The diffraction of X-rays was detected in three series of irradiations of various sections of the crystalline specimen with a five-second exposure for one photograph in each series. The first series of exposures (t_0) was carried out before injecting a buffer solution at pH 8.5 into the flow cell, while the second and third series were carried out after 3 and 90 min respectively (t_3, t_{90}). The three-dimensional structures of three enzyme–substrate complexes were solved with a resolution of 1.8 Å and *R* factors of ~20%. Comparison of their structures before and after increasing the pH showed that one of the water molecules in the active centre of the enzyme is predisposed to attack the acyl group in the stage involving the initiation of hydrolysis of the acylenzyme and exhibits a tendency to approach the carbonyl carbon atom during the reaction. Thus the claim that water is involved in the deacylation of the trypsin intermediate is transformed from an extremely probable hypothesis into an experimental fact.

3. The structure of the intermediate compound in the first stage of the reaction of cytochrome *c* peroxidase with hydrogen peroxide

According to existing idea, cytochrome *c* peroxidase (CCP) catalyses the reduction of peroxides via a mechanism consisting of the following three stages:[292–295]

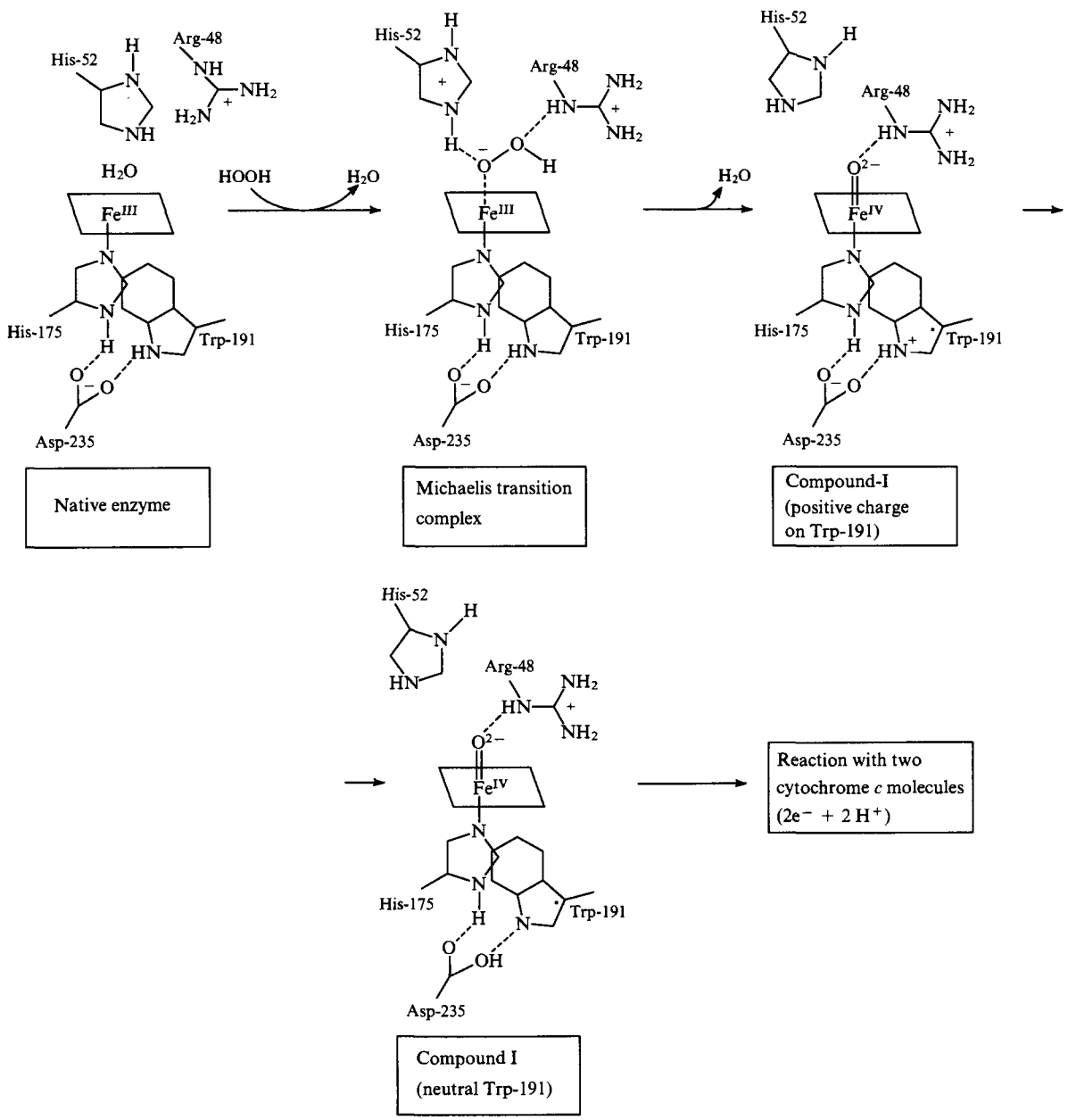
$$CCP(Fe^{III}) + H_2O_2 \rightarrow \text{compound-I } (Fe^{IV}O^{2-}, \text{Trp-191}^{*}) + H_2O \quad (1)$$

$$\text{Compound-I } (Fe^{IV}O^{2-}, \text{Trp-191}^{*}) + \text{Cyt-}c(Fe^{II}) + H^{+} \rightarrow \text{compound-II } (Fe^{IV}O^{2-}) + \text{Cyt-}c(Fe^{II}) \quad (2)$$

$$\text{Compound-II } (Fe^{IV}O^{2-}) + \text{Cyt-}c(Fe^{II}) + H^{+} \rightarrow CCP(Fe^{III}) + \text{Cyt-}c(Fe^{III}) + H_2O \quad (3)$$

In the first stage of the reaction of cytochrome *c* peroxidase with hydrogen peroxide, a doubly oxidised intermediate, which has been called 'compound-I', is formed. The three-dimensional structures of the native enzymes and of compound-I as well as

Scheme 9



the conformational changes in CCP, occurring on formation of the intermediate in the first stage of the catalytic reaction, have been described.[259]

Compound-I was obtained in a crystalline form from yeast cytochrome *c* peroxidase on reaction of the crystalline enzyme, placed together with the mother liquor in a flow cell, with hydrogen peroxide, also in the mother liquor. The reaction between the enzyme and H_2O_2, the occurrence of which was detected with the aid of absorption spectra in the visible region (550–750 nm), was almost completed after several minutes at 6 °C. The concentration of compound-I formed then remained virtually constant (90%–95%) for at least 30 min. The three-dimensional structures of the native enzyme and of its first intermediate were solved by three-dimensional Laue diffraction with a resolution of 2.2 Å and a divergence factor $R \sim 15.8\%$ (Table 8, No. 3). The size of the crystalline specimens was 0.4 × 4.0 × 1.0 mm. Polychromatic synchrotron radiation was employed; the duration of one exposure was ~0.3 s. Altogether, four series of independent experiments were performed on four crystals for four different orientations of the specimens (four for the native enzyme and four for compound-I).

On comparing the geometries of the observed structures, the authors[259] noted changes induced by the conversion of CCP into compound-I. They concerned only the region of the active centre and principally its distal part (Scheme 9). In the native state of the enzyme, the ligand-binding pocket over the iron atom is filled with three water molecules. On formation of the enzyme–substrate complex, two of them are eliminated, while the third is slightly displaced but still remains bound to the Trp-51 residue and the Fe-containing haem group. After the formation of compound-I and the heterolytic cleavage of the peroxide bond, the substrate oxygen atom is bound to the iron, altering its oxidation state from the high-spin ferri-state to the low-spin ferro-state ($Fe^{III} \rightarrow Fe^{IV}$). Having formed a Fe–O bond ~1.7 Å long, the iron atom is displaced by 0.3 Å from the plane of haem in the direction of the distal His-52. The Arg-47 side chain, located somewhat to one side, is displaced by 1.3 Å towards the ferro-oxygen atom and forms a hydrogen bond with the latter. The distances between the ferro-oxygen atom, on the one hand, and the N^{ε} atom of the Arg-48 residue, the $N^{\varepsilon 1}$ atom of the Trp-51 residue, and the $N^{\varepsilon 2}$ atom of the His-52 residue are 2.8, 2.7, and 3.6 Å respectively, and are too large for the formation of a hydrogen bond.

On formation of compound-I, the indole ring of the proximal Trp-191 residue is oxidised by giving up an electron to ferro-oxygen. The resulting radical-cation, bearing a charge on the indole nitrogen atom, interacts via the $N^+-H\ldots O^{\delta 1}$ hydrogen bond with the oxygen of the charged carboxy-group of the Asp-235 side chain; the second oxygen atom of this residue ($O^{\delta 2}$) is bound to the N–H group of the His-175 residue. Since there is no appreciable change in the geometry of the active centre in this region, the above considerations concerning the distribution of electron density in the proximal residues constitute merely one of the possible versions.

4. Photolysis of the myoglobin – carbon monoxide (Mb – CO) complex

Two structural studies on this complex, which in experimental terms can be regarded as the greatest advances in modern protein crystallography, have been published recently.[296,297] Both investigations were devoted to the mechanism of the photodissociation of the carbon monoxide-inhibited myoglobin.

$$Mb-C + h\nu \rightarrow Mb^*OC \rightarrow Mb + CO$$

The aim of both studies was to determine the position of the CO molecule in the transition state and to elucidate the response of the protein active centre to the dissociation of the Fe–O bond. The experimental solution of both problems required the determination of the three-dimensional structure of the short-lived intermediate Mb* and its comparison with the structures of the native myoglobin and its inhibitor complex.

Schlichting et al.[296] chose as the object of study a mutant myoglobin forming a hexagonal lattice. The specimen was cooled to ~20 K and irradiated with visible light from the usual source to initiate and maintain the photolysis; the X-ray diffraction pattern was obtained with the aid of synchrotron radiation (Fig. 21). The second experiment mentioned was formulated in accordance with a similar scheme.[297] The differences consisted in the employment in the latter case of native myoglobin (from whale sperm), the crystals of which have a monoclinic and not a hexagonal lattice; the specimen was cooled to ~40 K and was irradiated with light from a powerful laser source.

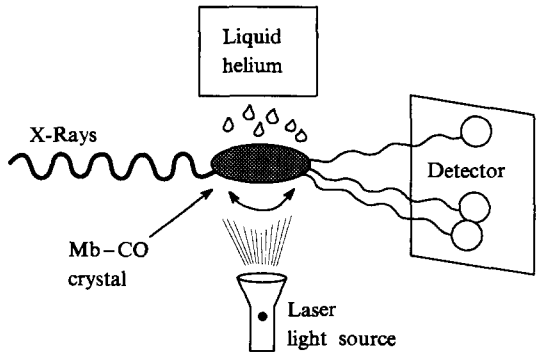


Figure 21. Schematic illustration of the experimental apparatus for X-ray diffraction by Mb–CO crystals during photolysis.[296–298]

Apart from certain quantitative discrepancies in the estimation of the conformational changes in the myoglobin active centre, the results of both investigations agreed. It was found in both cases that, on photodissociation of the complex, the CO molecule is removed from the Fe atom but remains in the active centre and is located parallel to the plane of the haem group at a distance of ~3.6 Å. The Fe atom shifts simultaneously in the same direction over a distance of 0.2 Å (data of Schlichting et al.[296]). In addition, on photolysis, changes were noted in the positions of the side chains of the distal His and Arg residues and of the proximal His residue and also of the α-helix F. Teng et al.[297] did not observe such changes, which apparently cannot be accounted for by the different packing of the crystals in the native and mutant myoglobin. It had been shown earlier that the mutation of the specimen employed by Schlichting et al.[296] does not entail conformational changes in the three-dimensional structure of the protein and does not affect it physiological properties.[299] The structural changes noted on photolysis agree with spectroscopic data[300,301] and the results of a molecular dynamics calculation.[302,303]

The results of the X-ray diffraction studies on the mechanisms of the functioning of proteins, carried out using synchrotron radiation and published towards the end of 1994, have been examined in this section. So far there have been few such investigations, but there is no doubt that they reflect the fundamental trend in the development of the method. Whereas only a few years ago, its purpose might have been formulated as concerning only the study of the three-dimensional structures of protein molecules and their stable complexes, nowadays the three-dimensional structures of the intermediates at the same atomic level have become accessible to investigation. Thus X-ray diffraction analysis has passed from the study of the molecular morphologies of the starting materials and final products of physiological reactions to the molecular morphologies of the intermediates. This finding denotes a jump in the development of the method — a qualitative change in its possibilities for the solution of an enormous number of new problems in molecular biology.

VIII. Multiwave anomalous diffraction

The most complex problem in X-ray crystallography is undoubtedly the phase problem. It has in fact held back the elucidation of diffraction patterns and the determination of three-dimensional molecular structures.

In the case of proteins, a solution to the phase problem was found by introducing into the X-ray diffraction analysis isomorphous derivatives — nonvalence complexes of the protein with heavy atoms (Au, Pb, Hg, Ag, Tl, etc.), the addition of which should not distort the three-dimensional structure of the protein molecule and the crystal lattice. The differences between the intensities of the beams diffracted by the crystals of the native protein and its derivatives can be used to determine the phases, provided that one establishes beforehand the positions of the heavy atoms. There are several different ways of solving this problem.[5,304]

The method for the determination of phases with the aid of heavy atoms, which has been called multiplet isomorphous substitution (MIS), was first tested in 1954 in a study of the crystal structure of haemoglobin.[305] Since then and almost until the very latest time, it remained virtually the only approach to the calculation of the required phase angles. However, throughout all these years the search for an alternative approach did not cease, because the MIS method is far from perfect.

Another solution to the phase problem became possible by employing the anomalous X-ray scattering effect. The classical theory of this phenomenon was developed by Honl as early as 1933.[306]

According to diffraction theory, the atomic scattering amplitude f is a complex quantity and can be formulated as follows:

$$f = f^0 + f^\Delta e^{ik} = f^0 + f' + f'' ,$$

where f^0 is the amplitude of the elastic 'normal' scattering, whilst $f^\Delta e^{ik}$ is the 'anomalous' correction formulated as the sum of the real dispersion (f') and imaginary absorption (f'') components. The correction f^Δ depends greatly on the radiation wavelength λ, whereas the usual scattering amplitude (f) is largely a function of the Bragg scattering angle θ.

The absolute value of f'' is proportional to the absorption coefficient. It therefore acquires great importance when the frequency of the X-ray quantum is close to the absorption edge of the atom.

The crystals of compounds containing no anomalous centres scatter X-rays in the normal manner. There is no anomalous scattering in this case, since the frequencies of the intrinsic vibrations of the H, C, N, O, and S atoms are far too remote from the frequency of the K emission for resonance to occur. The overall diffraction by a crystal (including a protein crystal) having anomalously scattering centres is described for each measured reflection by the structure factor ${}^\lambda F_T$. It includes the normal component ${}^0F_T$, consisting of the scattering components due to all the atoms in the protein structure, and the anomalous component. The latter is equal to the product of the normal components for the anomalously scattering centres ${}^0F_A$ and the ratio of the anomalous and normal scattering factors $f^\Delta(\lambda)/f^0(\theta)$. Consequently

$${}^\lambda F_T = {}^0F_T + {}^0F_A \cdot f^\Delta(\lambda)/f^0(\theta) .$$

Karle in 1980 [307] and later Hendrickson[308] showed that precise measurements of the intensities of all the diffraction reflections from a single crystalline protein specimen with anomalous scattering, obtained for several (3–5) X-ray wavelengths, make it possible to calculate from the set of experimental ${}^\lambda I$ data the real components of the factors $|{}^0F_T|$, $|{}^0F_A|$, and $\Delta\Phi^0 = \Phi_T^0 - \Phi_A^0$. The values of $|{}^0F_A|$ are then used to determine the positions in space of the anomalous scattering centres. Initially the values of Φ_A^0 and then, knowing $\Delta\Phi^0$, those of Φ_T^0 are calculated on this basis.

Thus the phase problem may also be solved without resorting to the multiplet isomorphous substitution method. However, the cost of such a solution remained for a long time too high and at least two conditions, fairly difficult to fulfill, had to be observed. Firstly, the test specimen must contain anomalously scattering atoms, which may not be present in the native protein. Secondly, in order to optimise the anomalous scattering effect, it is necessary to have a source of X-rays, such as the radiation from a synchrotron, continuously tuned to different wavelengths with a high accuracy and over a wide spectral range. Currently, the above difficulties of the multiwave anomalous diffraction (MAD) method have been largely overcome and its evident advantages over the traditional approach to the solution of the phase problem (MIS) have begun to play a decisive role.

The monopoly of the isomorphous substitution method in the X-ray crystallography of proteins was first broken in 1981[309] when it became possible to establish the three-dimensional atomic structure of crambin from the diffraction pattern of a single crystalline specimen. The phase problem was solved by the MAD method employing three wavelengths of the synchrotron radiation and the anomalous scattering by the sulfur atoms in the methionine residues forming part of the aminoacid sequence of the protein. It became evident that synchrotron radiation may render MAD a powerful instrument in the study of protein structures. However, the use of sulfur as the anomalously scattering centre was not entirely satisfactory. The dispersion (f') and absorption (f'') components of the anomalous scattering factor for this atom are much smaller than the normal component of the structure factor and are many times smaller than the corresponding values of the components of the anomalous scattering by heavier atoms. In the subsequent X-ray diffraction analysis of proteins with the aid of MAD, the use of sulfur as the anomalously scattering atom had to be abandoned. Proteins containing metal atoms (Fe, Zn, Cu, etc.) in the native state and isomorphous heavy atom derivatives of proteins became the objects of study, as in the MIS method. After crambin, the structures of parvalbumin,[310] cytochrome c',[311] azurin,[312] haemoglobin,[313,314] ferroxin,[314] selenolanthionine,[315] and selenobiotinyl-streptavidin[314] were solved by using anomalous scattering.

The experience gained in studies involving MAD made it possible to improve many experimental and mathematical procedures of the resonance method,[316] as a result of which the calculations of the phases with the aid of MAD are just as accurate as in the multiplet isormorphous substitution procedure. The solution to the phase problem based on the anomalous scattering effect has become universal and is applicable to any crystalline protein specimens containing anomalously scattering centres. The method for the introduction of diffraction labels, necessary in connection with the use of MAD, has also become general.[317]

The accuracy of the X-ray diffraction data obtained with the aid of MAD and MIS evidently improves the closer the isomorphism of the protein derivatives with resonance centres (for MAD), and with heavy atoms (for MIS). In this respect, the situation is preferable in the case of anomalous scattering, because here all the necessary data for the determination of the three-dimensional structure of the protein molecule can be obtained by irradiating a single crystal at several wavelengths. In order to make use of this advantage, it is necessary to have a method which would guarantee the reduction to a minimum of the probability of the breakdown of iso-morphism when resonance labels are employed in situ, which would be sufficiently simple, and which could be used in the X-ray diffraction analysis of any protein. The method used to obtain selenomethionine protein preparations, giving rise to anomalous scattering, is extremely close to satisfying these requirements.[317]

As early as 1957, it was established that auxotrophic [auxoheterotrophic? (Ed. of Translation)] *E. coli* cells, which have lost the ability to synthesise methionine, can develop successfully and can give rise to at least 100 generations after the addition of selenomethionine to the nutrient medium.[318]

It was shown thereby that the proteins required for the maintenance of the life of *E. coli*, in which all the Met residues have been replaced by Se-Met, continue to function normally. Later these results were confirmed by the deliberate creation of a clone auxotrophic in relation to methionine by damaging the MetA gene.[319] It became possible to synthesise the aminoacid sequences of *E. coli* in which all the sites designated for the Met residues contain the Se-Met residues. Developing further this aspect of the research, Hendrickson et al.[317] devised a method for the incorporation of Se-Met residues into recombinant proteins produced by the *E. coli* plasmids. The authors' preceding studies on the three-dimensional structures of the selenolanthionine[315] and selenobiotinylstreptavidin[314] molecules with the determination of the phases by the MAD method showed that the Se atom is an extremely effective anomalous scattering centre. One can therefore assume that the proposed method for the incorporation of selenomethionine residues in the methionine positions will become a universal approach for proteins, especially those which do not contain natural resonators in the native state.

The authors of the method used it to obtain two thioredoxins of the T4 cells of *E. coli* with 100% replacement of methionine by selenomethionine. The crystals of [Se-Met]-substituted thioredoxins proved to be fully isomorphous with the crystals of the natural recombinant proteins. The diffraction measurements were performed at three selected synchrotron radiation wavelengths. One wavelength corresponded to minimum anomalous scattering (f'_{min}), the second corresponded to the maximum absorption energy (f''_{max}), and the third wavelength was remote from the band due to the electronic transitions in the Se atom and hence corresponded to the normal scattering factor (f^0). Fig. 22 presents the dependence of the anomalous scattering factors f' and f'' on the irradiation wavelength obtained for a single orientation of the *E. coli* [Se-Met]-thioredoxin crystal. The high sensitivity of f' and f'' to changes in the wavelength in the region of 0.98 Å and the distinct edge effect indicate the considerable possibilities of the MAD method in the solution of the phase problem: the phases are initially found for several anomalously scattering centres and then, on this basis, for all the nonhydrogen atoms of the protein (for further details, see Hendrickson[320]).

Thus, towards the beginning of the 1990s the internal problems of the multiwave anomalous diffraction method were largely solved. Hendrickson's method for the preparation of selenomethionine derivatives of proteins rapidly gained recognition. In the studies of recent years, the crystals of such proteins have frequently served for the measurement of the diffraction patterns arising from both anomalous (using the resonance wavelengths) and normal scattering (considering selenium as a heavy atom). The study of Ramakrishnan et al.,[273] in which the three-dimensional structure of the globular domain of the linker histone H5 was determined with a resolution of 2.5 Å, is precisely of this kind.[273] The [Se-Met]-derivative of the domain was synthesised by genetic engineering methods. The crystals grown from it were fully isomorphous with the crystals of the native protein. The phases were determined by means of the MAD and MIS methods. The authors noted that treatment of the results by the traditional method combined with the recently proposed procedure for the refinement of the heavy atom parameters, called the maximum entropy or maximum similarity method,[321,322] led to somewhat preferable electron density maps compared with the procedure called the algebraic method.[316]

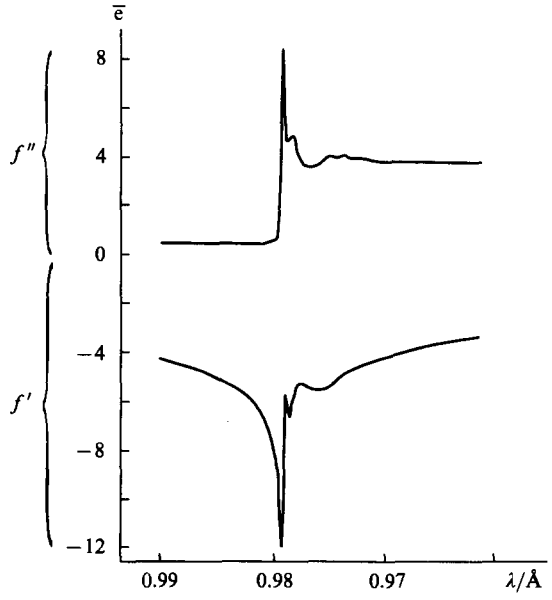


Figure 22. Anomalous scattering factors f' and f'' for crystals of *E. coli* selenomethionine thioredoxin measured in the vicinity of the absorption edge of selenium.

Newman et al.[323] established with a resolution of 1.95 Å the crystal structure of restriction endonuclease Bam HI, consisting of 213 aminoacid residues. The authors resorted to the use of the selenomethionine version after the failure of attempts to interpret the Patterson map constructed from measurements for several heavy atom protein derivatives. The [Se-Met]-endonuclease was expressed in the auxotrophic *E. coli* cells grown in a medium incorporating selenomethionine instead of methionine together with 19 standard aminoacids.[317] The object of study thus obtained had the same activity as the native enzyme and its crystals were fully isomorphous with those of the latter. The novel feature of the above investigation is the fact that the three-dimensional structure of the endonuclease was determined by the combination of the phase information, contained in the anomalous diffraction data, obtained by the maximum entropy and algebraic methods.[316,321,322] Both methods lead to approximately the same phase errors in relation to the phases of the refined model. The authors suggest that the averaged phases are appreciably closer to reality than those obtained by one of the methods. The [Se-Met]-BamHI crystals were irradiated at 5 °C at three wavelengths corresponding to the Se absorption edge (0.979 Å) and peak (0.978 Å) and the remote region of the spectrum (0.900 Å).

A human embryo gonadotropin, the structure of which has been described,[324] is a glycoprotein of the placenta hormone (237 aminoacid residues) stimulating the secretion of the steroid progesterone, which maintains the pregnancy. Like the recombinant [Se-Met]-protein, it was synthesised in the cells of the hamster ovary. This somewhat unexpected finding shows that the eukaryotic mammalian cells can be just as highly tolerant as the prokaryotic *E. coli* cells as regards the complete substitution of methionine by selenomethionine. The level of substitution in the above study was 92%. The structure of gonadotropin after partial deglycosylation was identified with a resolution of 2.6 Å. Diffraction data obtained by the MAD method were employed. The crystalline specimen was irradiated at four synchrotron radiation wavelengths. Two of them (~0.98 Å) were at the Se absorption edge and peak, whilst the other two were to one side of the absorption band. The approximate values of the anomalous scattering components f' and f'' were found for each wavelength.

The MAD method has been used[276] to determine the three-dimensional structure of the allosteric regulator enzyme glutamine–5-phosphoribosyl-1-pyrophosphate (PRPP) amidotransferase.[276] The protein consists of 465 aminoacid residues and an Fe atom, which is an anomalously scattering centre on irradiation at three wavelengths from a synchrotron (1.7425, 1.7390, and 1.5000 Å). The crystalline form of PRPP amidotransferase was obtained in the form of a homotetramer with a molecular mass of ~200 kDa. In the preceding X-ray diffraction analyses by the anomalous diffraction method, the objects of

study were proteins whose molecular masses did not exceed 30 kDa. The above study indicates the major possibilities of MAD in the determination of the three-dimensional structures of cumbersome protein complexes.

IX. Conclusion

The studies examined clearly leave no doubt that during the 1990s the X-ray diffraction analysis of proteins was applied to the solution of new problems of primary interest for molecular biology whilst retaining the previous high rate of extensive development. The main cause of the qualitative change which has arisen in the possibilities of the crystallography of macromolecules is associated with the employment of synchrotron radiation and new methods for the measurement of the diffraction pattern. Firstly, the transition to a new source of X-rays weakens the requirements which must be met by the size of the crystals, which is especially important in the structural analysis of high-molecular-mass proteins and their complexes with large unit cells. Secondly, the continuous synchrotron radiation spectrum and the ease of selecting any wavelength of the monochromatic radiation permitted a new approach to the solution of the phase problem and the development of the multiwave anomalous diffraction method, in which only one crystalline specimen is required for the determination of the phases. The procedure for the recombinant formation in auxotropic cells of proteins in the aminoacid sequences of which all the methionine residues have been replaced by selenomethionine supplemented significantly the MAD method. The use of [Se-Met]-proteins not only frees the X-ray diffraction analysis from the prolonged routine procedure involving the preparation of several isomorphous heavy atom protein derivatives but virtually eliminates the very problem of isomorphism.

Finally, the most important feature—the application in protein crystallography of synchrotron radiation and of new coordinate detectors—reduces the exposure time by at least 2–3 orders of magnitude. It is difficult to overestimate the importance of this fact, since the determination of the three-dimensional structures at the atomic level of intermediates in the processes involved in vital activity becomes possible. Whereas until recently, X-ray diffraction analysis was in fact the only direct method for the investigation of the native conformations of protein molecules with atomic resolution, nowadays, literally in front of our very eyes, it is becoming a source (also the only one available) of just as detailed information about the three-dimensional structures of intermediates.

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Iron compounds and the mechanisms of the homogeneous catalysis of the activation of O_2 and H_2O_2 and of the oxidation of organic substrates

A Ya Sychev, V G Isak (deceased)

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Abstract. Experimental data on the homogeneous catalysis by iron compounds of the activation of O_2 and H_2O_2 and of their oxidation of organic substances, and the current ideas on this subject are described. Data concerning the formation of various intermediate species and of their role in these processes are analysed. A series of catalytic systems simulating the functional activity of certain enzymes are considered at a model level. The bibliography includes 338 references.

I. Introduction

The activation of O_2 and H_2O_2 by aquoiron ions and iron complexes in biological, environmental, and industrial oxidation–reduction processes has been the subject of numerous publications. The experimental results available on this question have been partly surveyed in monographs and reviews.[1–5] The mechanisms of model and real processes have been investigated mainly at a qualitative level and only rarely at a semi-quantitative level. This situation is due to the complexity of the systems investigated, the multivariability of the possible routes followed by the processes, and the dependence of the latter on many parameters. Molecular oxygen and hydrogen peroxide, which are ecologically ideal oxidants, are reduced in the presence of iron compounds, generating highly reactive superoxide and hydroxyl radicals as well as species of the ferryl type $LFe^{IV}=O^{2+}$. The rapid reaction of these species in biological or nonbiological processes, the difficulty of their identification, their specific and nonspecific activity, and the influence of various parameters (temperature, the nature of the solvent and the ligand L, pH, the ratio of the ligand and iron ions, the characteristics of the oxidant, the concentrations of the components, etc.) create significant difficulties in the study of the mechanisms of the catalytic processes in which they participate. Nevertheless, during the last 10–15 years vigorous studies have been performed on the mechanisms of catalytic reactions involving the oxidation of various substrates by environmentally pure oxygen and hydrogen peroxide, on the mode of these reactions, and in particular on the elucidation of the role of iron compounds as catalysts in these reactions. Conditions have been developed for the optimisation of the processes and foundations have been laid for the prediction of the paths in the reactions of the substrates. The role played by iron compounds in the manifestation of toxicity by the products of the conversion of O_2 in vivo has been explained at a model level.

In order to establish the mechanisms of the catalytic oxidation of the various organic substances, it is important to have information about the radical and nonradical intermediates formed under these conditions, for example the ferryl complexes. The experimental data concerning the latter refer mainly to the 1980s.

II. Iron compounds and the mechanisms of catalytic decomposition of H_2O_2

1. Catalysis by Fe^{2+} and Fe^{3+} aquo-ions

After the demonstration of the catalytic activity of aquoiron ions in the H_2O_2 decomposition reactions (see the relevant reviews[1,3]), a detailed study was made of the $Fe^{2+}-H_2O_2$ system (the Fenton reagent)[2] and the mechanism of this process was analysed and discussed.[1–3,6–14] Numerous studies have been devoted to the kinetics of the decomposition of H_2O_2 by the Fe^{3+} aquo-ions.[1,3,6,7,9,15–19, etc.]

The study of the $Fe^{2+}-H_2O_2$ system (and also the $Fe^{2+}-H_2O_2$–substrate systems) made it possible to develop mechanisms for the decomposition of H_2O_2 catalysed by aquoiron(II) ions. All the reactions considered in this respect are compiled in Table 1. The question of the generation of the $^{\bullet}OH$ radicals in the $Fe^{2+}-H_2O_2$ system is of fundamental importance. It has now been demonstrated unambiguously that such radicals are formed in this process. The experimental data obtained (surveyed in a monograph[3] and partly presented in Scheme 1 and in Table 1) made it possible to determine the elementary stages in the decomposition of H_2O_2 by Fe^{2+} aquo-ions and their sequence depending on the experimental conditions.

Scheme 1 (p. 1107) presents the reactions involved solely in the H_2O_2 decomposition process in the $Fe^{2+}-H_2O_2$ system.[3]

A Ya Sychev, V G Isak Department of Physical Chemistry, State University of the Republic of Moldova, ul. Mateevicha 60, 277009 Kishinev, Moldova. Fax (7-042) 224 06 55

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Table 1. The rate constants for the elementary reactions and the acid–base equilibrium constants in the $Fe^{2+}-H_2O_2$ system.

Reaction	Constant[a]	Ref.	Reaction	Constant[a]	Ref.
$Fe^{2+}+H_2O_2 \longrightarrow Fe^{3+}+{}^{\bullet}OH+OH^-$	68	20	$(H_2O)_4(OH^-)Fe^{2+}(H_2O_2) \longrightarrow$	3×10^5	47
	76.5	21	$\longrightarrow (H_2O)_4(OH^-)FeO^{2+}+H_2O$		
	62	22			
	53	8, 23			
	58	24	$(H_2O)_5Fe(H_2O_2)^{2+} \longrightarrow$	2.8×10^3	47
	66	25	$\longrightarrow (H_2O)_5(OH^-)Fe^{3+}+{}^{\bullet}OH$		
	79	26			
	49.5	27			
	73	28	$(H_2O)_5Fe(H_2O_2)^{2+}+Fe^{2+}(H_2O)_6 \longrightarrow$	3×10^5	47
	76	29	$\longrightarrow 2\,(H_2O)_5Fe^{3+}(OH^-)+H_2O$		
	56.2	30			
	41.7	31			
	61.7	32	$Fe^{2+}+O_2^{\bullet-} \xrightarrow{H^+} Fe^{3+}+HO_2^-$	7.3×10^5	45
	60.3	33			
	50.1	34, 35	$Fe^{3+}+H_2O_2 \longrightarrow Fe^{2+}+HO_2^{\bullet}+H^+$	9.1×10^{-7}	48
$Fe^{2+}+{}^{\bullet}OH \longrightarrow Fe^{3+}+OH^-$	2.6×10^8	36			
	5.1×10^8	37	$Fe^{3+}+H_2O_2 \rightleftharpoons FeHO_2^{2+}+H^+$	2×10^{-3}	49
	3×10^8	29, 40			
	5×10^8	38	$Fe^{3+}HO_2^- \longrightarrow Fe^{2+}+HO_2^{\bullet}$	2×10^{-3}	50
	3.2×10^8	38, 39, 41		1.6×10^{-3}	20
	2.5×10^8	42	$FeHO_2^{2+}+FeOH^{2+} \longrightarrow$	5	20
	2.7×10^8	43	$\longrightarrow 2\,Fe^{2+}+H_2O+O_2$		
	3.3×10^8	44			
$Fe^{2+}+HO_2^{\bullet} \longrightarrow Fe^{3+}+HO_2^-$	7.2×10^5	45	$Fe^{3+}+HO_2^{\bullet} \longrightarrow Fe^{2+}+H^++O_2$	7.3×10^5	45
	1.5×10^6	46		2.1×10^6	51
				3.3×10^5	30
$Fe^{3+}+{}^{\bullet}OH \longrightarrow Fe^{4+}+OH^-$	7.9×10^7	3, 42	$Fe^{3+}+O_2^{\bullet-} \longrightarrow Fe^{2+}+O_2$	4×10^8	52
				1.29×10^9	51, 53
${}^{\bullet}OH+H_2O_2 \longrightarrow HO_2^{\bullet}+H_2O$	4.5×10^7	36		1.1×10^9	50
	1.7×10^7	37		5×10^7	30
	3×10^7	42		1.9×10^9	46
${}^{\bullet}OH+{}^{\bullet}OH \longrightarrow H_2O_2$	5.3×10^9	29	$H_2O_2 \rightleftharpoons HO_2^-+H^+$	2.63×10^{-12}	58
	5.02×10^9	54			
	8×10^9	36	$HO_2^{\bullet} \rightleftharpoons H^++O_2^{\bullet-}$	3.55×10^{-5}	59
	6×10^9	52			
${}^{\bullet}OH+O_2^{\bullet-} \longrightarrow OH^-+O_2$	1×10^{10}	3, 42	$HO_2^{\bullet}+H^+ \rightleftharpoons H_2O_2^+$	$(3.16-3.98)\times10^{-5}$	55, 56
${}^{\bullet}OH+HO_2^{\bullet-} \longrightarrow H_2O+O_2$	1.4×10^{10}	3, 42	${}^{\bullet}OH \rightleftharpoons O^{\bullet-}+H^+$	1.02×10^{-12}	60
$HO_2^{\bullet}+HO_2^{\bullet} \longrightarrow H_2O_2+O_2$	1.9×10^6	55	$Fe^{2+}+OH^- \rightleftharpoons FeOH^+$	$K=3.63\times10^5$	61
	2.2×10^6	56			
	8.1×10^5	57	$Fe^{3+} \rightleftharpoons FeOH^{2+}+H^+$	2×10^{-3}	62
				1.4×10^{-3}	63
$O_2^{\bullet-}+O_2^{\bullet-} \xrightarrow{H^+} O_2+HO_2^-$	< 0.35	38		1.83×10^{-3}	64
$HO_2^{\bullet-}+O_2^{\bullet-} \longrightarrow HO_2^-+O_2$	8.5×10^7	38	$(H_2O)_5Fe^{2+}(H_2O)+H_2O_2 \rightleftharpoons$	1.8×10^{-2}	47
$HO_2^{\bullet}+H_2O_2 \longrightarrow H_2O+O_2+{}^{\bullet}OH$	0.2	3	$\rightleftharpoons (H_2O)_5Fe(H_2O_2)^{2+}+H_2O$		
	3.7	3			
			$(H_2O)_5Fe(H_2O_2)^{2+} \rightleftharpoons$	6×10^{-5}	47
			$\rightleftharpoons (H_2O)_4(OH^-)Fe(H_2O_2)^{2+}+H^+$		
			$Fe^{2+}+HO_2^{\bullet} \rightleftharpoons FeHO_2^{2+}$	2.1×10^6	51

[a] The rate constants are expressed in litre $mol^{-1}\ s^{-1}$, the decomposition constants in s^{-1}, and the equilibrium constants in mol $litre^{-1}$.

The following set of consecutive reactions in the $Fe^{2+}-H_2O_2$ system is nowadays regarded as generally accepted.

Scheme 2

1. $Fe^{2+}+H_2O_2 \longrightarrow Fe^{3+}+HO^{\bullet}+OH^-$
13. $Fe^{2+}+{}^{\bullet}OH \longrightarrow Fe^{3+}+OH^-$
20. ${}^{\bullet}OH+H_2O_2 \longrightarrow HO_2^{\bullet}+H_2O$
18. $Fe^{3+}+HO_2^{\bullet} \longrightarrow Fe^{2+}+H^++O_2$
19. $Fe^{3+}+O_2^{\bullet-} \longrightarrow Fe^{2+}+O_2$
14. $Fe^{2+}+HO_2^{\bullet} \longrightarrow Fe^{3+}+HO_2^-$

This series of stages occurs under the following conditions: $0.5 < [H_2O_2]/[Fe^{2+}] < 200$, pH > 2. The catalytic decomposition of H_2O_2 by Fe^{2+} aquo-ions proceeds in accordance with a radical-ion cyclic mechanism (a characteristic feature of this mechanism is the equality of the rates of the chain initiation and propagation stages) when $0.5 < [H_2O_2]/[Fe^{2+}] < 3\times10^6$ and in accordance with a radical-chain mechanism {only in this case it is possible to differentiate clearly the chain initiation [reaction (1)], propagation [reactions (20) and (21)], and termination [reaction (18) and/or (19)] steps} when $[H_2O_2]/[Fe^{2+}] > 3\times10^6$.

Scheme 1

A. Processes with participation of Fe^{2+}

1. $Fe^{2+} + H_2O_2 \longrightarrow Fe^{3+} + {}^{\bullet}OH + OH^-$
2. $Fe^{2+} + H_2O_2 \longrightarrow FeO^{2+} + H_2O$
3. $Fe^{2+} + H_2O_2 \longrightarrow Fe^{4+} + 2OH^-$
4. $FeOH^+ + H_2O_2 \longrightarrow Fe^{3+} + {}^{\bullet}OH + 2OH^-$
5. $FeOH^+ + H_2O_2 \longrightarrow FeO^{2+} + H_2O + OH^-$
6. $(H_2O)_5Fe(H_2O)^{2+} + H_2O_2 \rightleftharpoons (H_2O)_5Fe(H_2O_2)^{2+} + H_2O$
7. $(H_2O)_5Fe(H_2O_2)^{2+} \xrightarrow[-H^+]{} (H_2O)_4(OH^-)FeO^{2+} + H_2O$
8. $(H_2O)_5Fe(H_2O_2)^{2+} \xrightarrow[-H^+]{} (H_2O)_5(OH^-)Fe^{3+} + {}^{\bullet}OH$
9. $(H_2O)_5Fe(H_2O_2)^{2+} + Fe^{2+}(H_2O)_6 \longrightarrow 2\,(H_2O)_5Fe^{3+}(OH^-) + H_2O$
10. $Fe^{2+} + HO_2^- + H_2SO_4 \longrightarrow Fe(SO_4H)(OOH) + H^+$
11. $Fe^{2+}SO_4 + H_2O_2 \longrightarrow FeSO_4(H_2O_2)$
12. $Fe(SO_4H)(OOH) + H_2O_2 \longrightarrow Fe(SO_4H)(OH) + H_2O + O_2$
13. $Fe^{2+} + {}^{\bullet}OH \longrightarrow Fe^{3+} + OH^-$
14. $Fe^{2+} + HO_2^{\bullet} \longrightarrow Fe^{3+} + HO_2^-$
15. $Fe^{2+}(H_2O_2)(HO_2) \rightleftharpoons Fe^{2+}(HO_2^{\bullet})(HO^+) + OH^-$
16. $Fe^{2+}(HO_2^{\bullet})(HO^+) \rightleftharpoons Fe^{3+}(HO_2^{\bullet})(HO^{\bullet})$
17. $[Fe_2(OH)_2]^{2+} + H_2O_2 \longrightarrow [Fe_2(OH)_2]^{4+} + 2OH^-$

B. Processes with participation of Fe^{3+}

18. $Fe^{3+} + HO_2^{\bullet} \longrightarrow Fe^{2+} + H^+ + O_2$
19. $Fe^{3+} + O_2^{\bullet-} \longrightarrow Fe^{2+} + O_2$

C. Processes with participation of ${}^{\bullet}OH$, $HO_2^{\bullet}$ ($O_2^{\bullet-}$)

(in addition to those listed above)

20. ${}^{\bullet}OH + H_2O_2 \longrightarrow HO_2^{\bullet} + H_2O$
21. $HO_2^{\bullet} + H_2O_2 \longrightarrow O_2 + H_2O + {}^{\bullet}OH$

D. Processes with participation of Fe^{4+}

22. $FeO^{2+} + H_2O_2 \longrightarrow Fe^{2+} + O_2 + H_2O$
23. $Fe^{4+} + OOH^- \longrightarrow Fe^{2+} + O_2 + H^+$
24. $Fe^{4+} + HO_2^- \rightleftharpoons FeOOH^{3+} \longrightarrow Fe^{3+} + HO_2^{\bullet}$
25. $(H_2O)_4(OH^-)Fe^{2+}O + H_2O \longrightarrow (H_2O)_4(OH^-)_2Fe^{3+} + {}^{\bullet}OH$
26. $(H_2O)_4(OH^-)Fe^{2+}O + Fe^{2+} \longrightarrow 2\,Fe^{3+}(OH^-)(H_2O)_5$
27. $Fe^{4+} + Fe^{2+} \longrightarrow 2\,Fe^{3+}$
28. $FeO^{2+} + H_2O_2 \longrightarrow HO_2^{\bullet} + OH^- + Fe^{3+}$

E. Acid–base equilibria

29. $Fe^{2+} + H_2O \rightleftharpoons FeOH^+ + H^+$
30. $2\,Fe^{2+} + 2\,H_2O \rightleftharpoons Fe_2(OH)_2^{2+} + 2\,H^+$
31. $H_2O_2 \rightleftharpoons HO_2^- + H^+$
32. $HO_2^{\bullet} \rightleftharpoons H^+ + O_2^{\bullet-}$
33. $(H_2O)_5Fe(H_2O_2)^{2+} \rightleftharpoons (H_2O)_4(OH^-)Fe(H_2O_2)^{2+} + H^+$

According to a series of data,[16,20,46,50,65–73] the decomposition of H_2O_2 by Fe^{3+} aquo-ions (Ruff's system)[74,75] in an acid medium (at pH $\leqslant$ 2) proceeds via a radical-chain mechanism. A different mechanism of this process has sometimes been suggested.[45,49,51–53,57,76–81] All the possible steps of the process occurring in the $Fe^{3+}-H_2O_2$ system, proposed by various investigators, are presented in a monograph.[3]

Of the principal experimental evidence in support of the operation of a radical-chain mechanism of the decomposition of H_2O_2 in the $Fe^{3+}-H_2O_2$ system, we shall mention the following: (a) evidence based on the inhibiting effects of various organic substances;[16,17,20,50,66–73,82] (b) evidence indicating (directly or indirectly) the generation of the ${}^{\bullet}OH$ radicals[72,73,83–89] and/or $O_2^{\bullet-}$ radical-ions[16,50,66–68,82,90] in the system; (c) evidence confirming the existence of one-electron transfer steps which include the oxidation-reduction cycle

$$Fe^{3+} \underset{-\bar{e}}{\overset{\bar{e}}{\rightleftharpoons}} Fe^{2+},$$

(the assumption[91,92] of the formation of Fe^{2+} has been confirmed[16,20,85,92]).

The question arises of the evidence used by the supporters of the ion-molecule mechanism. The principal evidence is believed to be[49,76–79,81,93–95] the formation in the reaction medium of active intermediate compounds and primarily peroxo-complexes. Indeed the peroxo-complex $FeHO_2^{2+}$ is formed in the system.[49,51,76–79,81,94–98] However, it has been shown[3] that this does not conflict with the occurrence of the process by a radical-chain mechanism.

Purmal'[16] demonstrated qualitatively and quantitatively that, among all the possible reactions considered in the literature as steps in the H_2O_2 decomposition by Fe^{3+} aquo-ions,[3] only the series of consecutive steps presented in Scheme 3 actually occur. This scheme is nowadays generally accepted to be the description of the mechanism of the decomposition of H_2O_2 by Fe^{3+} aquo-ions.

Scheme 3

Initiation

$FeHO_2^{2+} \longrightarrow Fe^{2+} + HO_2^{\bullet}$

$FeHO_2^{2+} + FeOH^{2+} \longrightarrow 2\,Fe^{2+} + O_2 + H_2O$

Chain propagation

$Fe^{2+} + H_2O_2 \longrightarrow Fe^{3+} + {}^{\bullet}OH + OH^-$

${}^{\bullet}OH + H_2O_2 \longrightarrow HO_2^{\bullet} + H_2O$

$O_2^{\bullet-} + Fe^{3+} \longrightarrow Fe^{2+} + O_2$

Chain termination

$Fe^{2+} + HO_2^{\bullet} \longrightarrow Fe^{3+} + HO_2^-$

$Fe^{2+} + {}^{\bullet}OH \longrightarrow Fe^{3+} + OH^-$

$HO_2^{\bullet} + HO_2^{\bullet} \longrightarrow H_2O_2 + O_2$

Acid–base equilibria

$H_2O_2 \rightleftharpoons H^+ + HO_2^-$

$HO_2^{\bullet} \rightleftharpoons H^+ + O_2^{\bullet-}$

$Fe^{3+} + H_2O \rightleftharpoons FeOH^{2+} + H^+$

$Fe^{3+} + H_2O_2 \rightleftharpoons FeHO_2^{2+} + H^+$

Analysis of the literature devoted to studies of the kinetics and mechanisms of catalytic decomposition of H_2O_2 by Fe^{2+} and Fe^{3+} aquo-ions demonstrated, firstly, the complexity of the reactions occurring in the $Fe^{2+}-H_2O_2$ and $Fe^{3+}-H_2O_2$ systems; secondly, it demonstrated the possibility of kinetic studies on such systems and the limitations of this possibility; thirdly, it made it possible to devise procedures for the determination, discrimination, and justification of the reaction mechanisms in complex systems including a set of a large number of consecutive elementary stages.

When iron ions are replaced as catalysts by their coordination compounds, the decomposition of H_2O_2 is in many cases accelerated.[1,3,16,99,106] The catalytic activity of the Fe^{3+} complexes is in many cases higher than that of aquoiron ions. Among the iron complexes with a catalase-like activity, the coordination compounds of Fe^{3+} with triethylenetetramine ('inorganic catalase') exhibit the highest activity in the hydrogen peroxide decomposition reaction.[3]

Complex formation promotes the occurrence of the process by different mechanisms depending on the nature of the ligand. This can be seen from the data presented in Table 2.

The oxidation-reduction decomposition of H_2O_2 by iron(III) complexes can also proceed via different mechanisms: radical-chain (I), ion-molecule (II), and chain-nonradical (III). A general scheme for the reactions occurring in the Fe^{3+} – ligand – H_2O_2 systems is presented in Scheme 4.

Cycle I. The free radical species $O_2^{\cdot-}(HO_2^{\cdot-})$ and $^{\cdot}OH$ are generated during the process and the one-electron transfer stages

$$L''Fe^{3+} \underset{-\bar{e}}{\overset{\bar{e}}{\rightleftharpoons}} L'''Fe^{2+}$$

occur. The rate of gas evolution (w_{O_2}) appreciably exceeds the rate of initiation (w_i). This mechanism operates in the Fe^{3+}–2,2′-Bipy – H_2O_2,[3,15,107] Fe^{3+} – EDTA – H_2O_2,[117–119] Fe^{3+} – H_2LM – H_2O_2[3,113,120] Fe^{3+} – Acid Chrome Dark-Blue – H_2O_2,[2] Fe^{3+} – ethylenediamine – H_2O_2,[119,121] Fe^{3+} – glutamic acid – H_2O_2,[122,123] and certain other systems.

Cycle II. The main process does not include the reactions of the $^{\cdot}OH$ and $O_2^{\cdot-}$ radical species. The two-electron transfer stage

$$L'Fe^{2+} \underset{-2\bar{e}}{\overset{2\bar{e}}{\rightleftharpoons}} L'Fe^{4+}$$

takes place. As in cycle I, $w_{O_2} \gg w_i$.

This mechanism operates, in particular, in the decomposition of H_2O_2 by the coordination compounds of Fe^{3+} with triethylenetetramine[3,104–106] and histidine.[3,111,124–126]

Cycle III. The catalytic process proceeds via the formation of mono- and di-peroxo-complexes. In the course of the reaction, the oxidation state of the central ion in the complex catalyst remains unchanged and the $^{\cdot}OH$ and $HO_2^{\cdot}$ ($O_2^{\cdot-}$) radical species are not generated in the reaction medium. It has been shown that the decomposition of H_2O_2 by the coordination compounds of Fe^{3+} with 4′,4″,4‴-tetrasulfophthalocyanine (PTS),[116] *N,N′*-bis-(2-methylpyridyl)ethylenediamine,[127] and quaterpyridyl[127] proceeds in accordance with this mechanism.

Analysis of published data[3] made it possible to arrange systematically the factors determining the catalytic activity of the Fe^{2+} and Fe^{3+} ions on complex formation and the characteristic features of the catalytic processes in the presence of coordination compounds of iron. The hydrolytic stability of iron ions, their electrochemical properties, and the lability of the coordination sphere change on complex formation. All this leads ultimately to a change in the catalytic activity of the aquoiron ions.

2. Oxidation of organic substrates by the $Fe^{2+}(LFe^{2+})$–H_2O_2 system

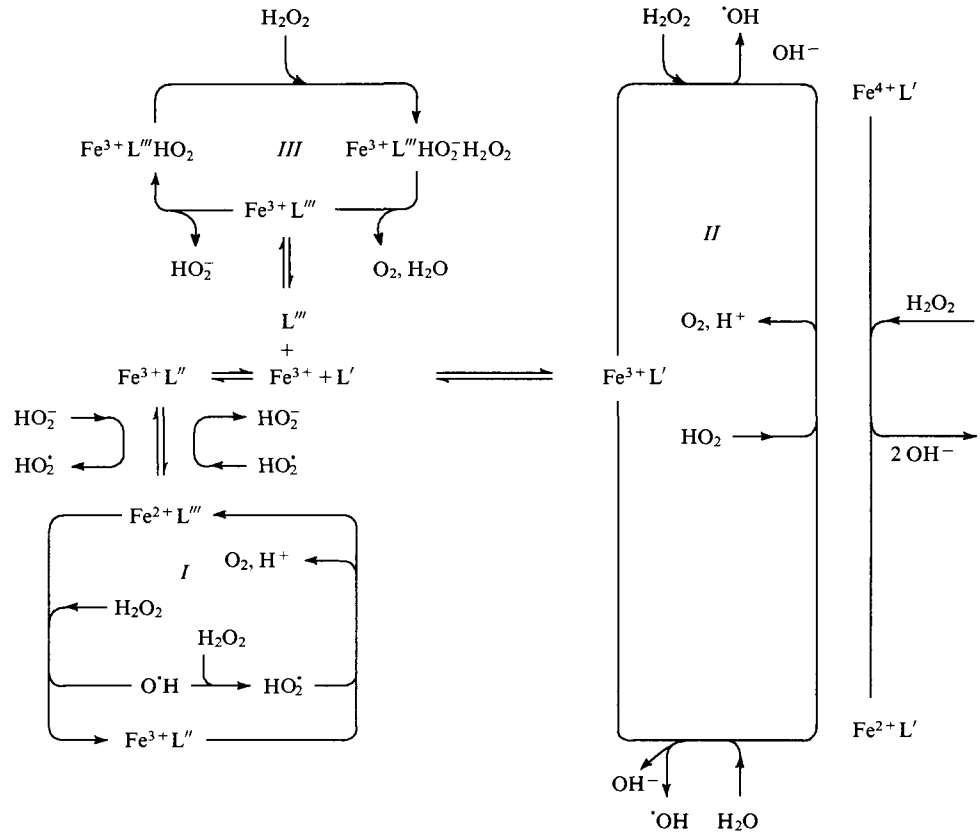
The results of the numerous studies devoted to the elucidation of the mechanisms of the oxidation of organic substrates by the Fe^{2+} – H_2O_2 system have been arranged systematically to the fullest extent by Walling.[29] However, the scheme which he presented does not embrace the entire wide variety of such mechanisms. The question of the nature of the substrate (S) is considered to only a limited extent in his communication,[29] the influence of the formation of a complex between the substrate

Table 2. The mechanisms of the interaction of the iron(II) complexes with H_2O_2.

System[a]	Elementary mechanism of the interaction with H_2O_2	Process mechanism	pH of medium	Ref.
$Fe^{2+}-Bipy-H_2O_2$	$FeBipy_n^{2+} + H_2O_2 \longrightarrow FeBipy_n^{3+} + {}^{\cdot}OH + OH^-$	radical-chain	4–6	107
$Fe^{2+}-Phen-H_2O_2$	$FePhen^{2+} + H_2O_2 \rightleftharpoons FePhenH_2O_2^{2+} \longrightarrow$ $\longrightarrow FePhen^{3+} + O^{\cdot}H + OH^-$	radical-ion	4–5	108
	$FePhen_n^{2+} + H_2O_2 \longrightarrow FePhen_n^{3+} + {}^{\cdot}OH + OH^-$	"	2–5	109
$Fe^{2+}-His-H_2O_2$	$Fe(His)_2 + H_2O_2 \longrightarrow Fe(His)_2^+ + {}^{\cdot}OH + OH^-$	"	2–5	110
	$Fe^{2+}(His)_2 + H_2O_2 \longrightarrow Fe^{4+}(His)_2 + 2\,OH^-$	ion-molecule	7–8	111
$Fe^{2+}-H_4T-H_2O_2$	$H_2TFe^{2+} + H_2O_2 \longrightarrow H_2TFe^{3+} + {}^{\cdot}OH + OH^-$	radical-ion	2–4	112
$Fe^{2+}-DFH_4-H_2O_2$	$FeDFH_3^+ + H_2O_2 \longrightarrow FeDFH_3^{2+} + {}^{\cdot}OH + OH^-$	cyclic radical-ion	2–4	112
	$FeDFH_2 + H_2O_2 \longrightarrow FeDFH_2 + {}^{\cdot}OH + OH^-$	"	2–4	112
$Fe^{2+}-H_3Cit-H_2O_2$	$FeHCit + H_2O_2 \longrightarrow FeHCit^+ + {}^{\cdot}OH + OH^-$	radical-ion	2–4	112
$Fe^{2+}-H_2LM-H_2O_2$	$Fe^{2+}HLM + H_2O_2 \longrightarrow Fe^{4+}HLM + 2\,OH^-$	radical-chain	2–5	113
$Fe^{2+}-EDTA-H_2O_2$	$EDTAFe^{2+} + H_2O_2 \longrightarrow EDTAFeO^{2+}$	ion-molecule	4–6	2, 114
$Fe^{2+}-TETA-H_2O_2$	$TETAFe^{2+} + H_2O_2 \longrightarrow TETAFe^{4+} + 2\,OH^-$	"	7–8	106
$Fe^{2+}-CN^--H_2O_2$	$[Fe(CN)_5H_2O]^{3-} + H_2O_2 \longrightarrow [Fe(CN)_5(H_2O)]^{2-} + {}^{\cdot}OH + OH^-$	radical-ion	3–5	115, 116

[a] The following notation has been adopted: Bipy = α,α′-bipyridyl, Phen = 1,10-phenanthroline, His = histidine, H_4T = tartaric acid, DFH_4 = dihydroxyfumaric acid, H_3Cit = citric acid, H_2LM = lumomagneson, EDTA = ethylenediaminetetraacetic acid, and TETA = triethylenetetramine.

Scheme 4



L', L'', and L''' are ligands of different kinds.

and Fe^{2+} on the oxidation mechanism is not considered, and no account is taken of the fact that the oxidation proceeds under aerobic conditions (under the influence of oxygen), as usually happens in real systems involving the use of the Fenton reagent and in other similar systems. The problem of the change in the mechanism of the oxidation of organic substrates following the introduction of an additional ligand into the system also requires special consideration. In order to take into account the above factors, it is essential to analyse the results obtained in typical ferroperoxide systems, which are listed below.

1.	$Fe^{2+} - H_2O_2 - S(S_1)$	$S(S_1)$ = noncomplex-forming or weakly complex-forming substrate. In contrast to S, the substrate S_1 has pronounced reducing properties
2.	$Fe^{2+} - H_2O_2 - S - O_2$	Aerobic system
3.	$Fe^{2+} - L - H_2O_2 - S$	The additional ligand L has been introduced into the system
4.	$Fe^{2+} - L - H_2O_2 - S - O_2$	Aerobic system with additional ligand
5.	$Fe^{2+} - H_2O_2 - S_L$	S_L = substrate which functions simultaneously as a ligand
6.	$Fe^{2+} - H_2O_2 - S_L - O_2$	Aerobic system with S_L
7.	$Fe^{2+} - L - H_2O_2 - S_L$	System incorporating L and S_L
8.	$Fe^{2+} - S_L - H_2O_2 - S$	System incorporating S_L and S
9.	$Fe^{2+} - S_L - H_2O_2 - S - O_2$	Aerobic system incorporating S_L and S

These systems can be divided into two groups. In the first group (systems 1–4), the substrate being oxidised does not form a complex with Fe^{2+} or forms it very ineffectively. Here there is little overlap of the electron orbitals of Fe^{2+} and S. The oxidation reaction in systems of this group should proceed via an outer-sphere route (outside the first coordination sphere of Fe^{2+}, i.e. in the reaction volume). In the second group (systems 5–9), the substrate is also a ligand. Here one should expect the formation of intermediate compounds with the substrate and inner-sphere electron transfer. Such subdivision into two groups reflects only the extreme manifestations of complex-forming properties and there is a possibility of a series of intermediate versions.

We shall analyse briefly the data obtained in the study of some typcial systems.

a. The $Fe^{2+} - H_2O_2 - S(S_1)$ system

Organic substances (S and S_1) without a chelating capacity towards iron ions or forming relatively unstable complexes with the latter are oxidised by the Fenton reagent.[3,128–134] Analysis of the results shows that, when the chosen substrate (S) or the substrate radical formed (R$^{\cdot}$) has no reducing properties (and the latter also has oxidising properties), the process mechanism includes the following stages:

Scheme 5

1. $Fe^{2+} + H_2O_2 \xrightarrow{k_1} Fe^{3+} + {}^{\cdot}OH + OH^-$
2. ${}^{\cdot}OH + S \xrightarrow{k_2} R^{\cdot}$
3. ${}^{\cdot}OH + H_2O_2 \xrightarrow{k_3} HO_2^{\cdot} + H_2O$
4. $Fe^{3+} + HO_2^{\cdot} \xrightarrow{k_4} Fe^{2+} + H^+ + O_2$
5. $Fe^{2+} + HO_2^{\cdot} \xrightarrow{k_5} Fe^{3+} + HO_2^-$
6. $Fe^{2+} + {}^{\cdot}OH \xrightarrow{k_6} Fe^{3+} + OH^-$

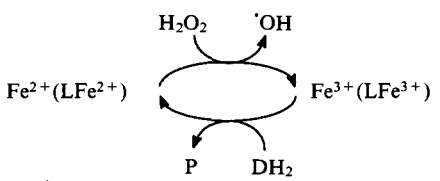
It is not difficult to demonstrate that, when $[S]/[H_2O_2] \geqslant 0.01$ (recalling that k_2 is 2–3 orders of magnitude higher than k_3), only the first two stages will occur in the system — in this case, because $k_6 = 3 \times 10^8$ litre mol^{-1} s^{-1}, $[S]/[Fe^{2+}]$ should be greater than

unity.[29] Consequently the rate of oxidation of the substrate under such conditions is defined by the following expression:

$$w_S = k_1[Fe^{2+}][H_2O_2][S]^{1\to 0}.$$

In this case, Fe^{2+} and S are actually oxidised in the system by hydrogen peroxide via a radical and not a chain mechanism. After the conversion of the initial Fe^{2+} into Fe^{3+}, the oxidation of the substrate also ceases. Since the rate constants for all the elementary stages in Scheme 4 are known, it is possible to calculate theoretically the necessary Fe^{2+}, H_2O_2, and S concentrations in each specific case for the catalytic process to occur via the radical-ion cyclic mechanism. Only when this mechanism operates can one expect the effective oxidation by the Fenton reagent of substrates of the type considered. The effectiveness of the oxidation may be increased also by the additional introduction into the reaction medium of a substance capable of reducing Fe^{3+} to Fe^{2+}, i.e. of regenerating the initial form of the catalyst. The addition of the appropriate reductant (DH_2) leads to the appearance of an oxidation-reduction (OR) cycle in which the $^{\cdot}OH$ radicals, oxidising the substrate, are generated.

Scheme 6



P = product.

Similar OR cycles arise also in the $Fe^{3+}(LFe^{3+}) - H_2O_2 - S$ systems. Such systems, containing $Fe^{2+}(LFe^{2+})$ ions (or other transition metal ions, for example Cu^{2+}),[47] hydrogen peroxide, and the reductant, have been called 'reversible' and have been described, in particular, in the monographs of Dolgoplosk and Tinyakova.[11,13] Various sugars, dienols, rongalite, hydrazine, cysteine, and a series of other organic and inorganic compounds are used as reductants. For example, ascorbic acid (AH_2) increases appreciably the effectiveness of the oxidation of ethyl alcohol by the Fenton reagent[135] ($Fe^{2+} - S_L - H_2O_2 - S - O_2$ is a typical system).[3]

The oxidation reactions of substrates with reducing properties are of greatest interest in the analysis of systems of the type considered because they play a decisive role in the formation of a reversible OR cycle incorporating the following reactions:

Scheme 7

1. $Fe^{2+} + H_2O_2 \longrightarrow Fe^{3+} + {}^{\cdot}OH + OH^-$
2. $^{\cdot}OH + S_1 \longrightarrow R_1^{\cdot}$
3. $Fe^{3+} + S_1 \longrightarrow R_1^{\cdot\prime} + Fe^{2+}$

$R_1^{\cdot\prime}$ = substrate radical.

As a consequence of this, the substrate undergoes effective catalytic oxidation.

When the reactivity of the substrate radicals (including the reactivity with respect to O_2) is low, the oxidation mechanism (Scheme 7) does not include additional stages. It does not change under aerobic conditions either—conditions are considered where $[S_1]/[H_2O_2] \geqslant 0.1$, since otherwise it is also necessary to take into account the possible occurrence of stages 3–6 (Scheme 5). A similar mechanism has been adopted also in the anaerobic and aerobic oxidation of indigocarmine (IC), indigotetrasulfonate (ITS) and Methylene Blue (MB) by the Fenton reagent.[136] Since the ability of these substrates to form complexes with Fe^{2+} (the OR potential of the Fe^{3+}/Fe^{2+} couple hardly changes when the dye is added), one may assume that the catalyst in the $Fe^{2+} - H_2O_2 - IC(MB, ITS)$ systems is the Fe^{2+} aquo-ion.

A more complex picture is observed (and a greater variety of products are accordingly formed) when the substrate radical in the $Fe^{2+} - H_2O_2 - S(S_1)$ systems is reactive (it possesses mainly reducing properties).

The mechanism of the oxidation of type $S(S_1)$ substrates under anaerobic conditions in the typical $Fe^{2+} - H_2O_2 - S(S_1)$ systems has been investigated in numerous studies, which have been surveyed in the monograph of Sychev and Isak.[3] It has been most fully elucidated, justified qualitatively, and generalised in the publications of Walling and coworkers.[137–140] It has been suggested that the $^{\cdot}OH$ radical formed in the system as a consequence of the interaction of Fe^{2+} with H_2O_2.

Analysis of the possible steps occurring in the $Fe^{2+} - H_2O_2 - S(S_1)$ systems under anaerobic conditions, where the reactive substrate radical is formed, combined with allowance for other data[29,139,140] leads to the following series of consecutive steps:[3]

Scheme 8

Step	Reaction	k_i/litre mol^{-1} s^{-1}
1	$Fe^{2+} + H_2O_2 \rightarrow Fe^{3+} + {}^{\cdot}OH + OH^-$	53
3	$^{\cdot}OH + H_2O_2 \rightarrow HO_2^{\cdot} + H_2$	3×10^7
4	$Fe^{3+} + HO_2^{\cdot} \rightarrow Fe^{2+} + H^+ + O_2$	2.1×10^6
5	$Fe^{3+} + HO_2^{\cdot} \rightarrow Fe^{3+} + HO_2^-$	1.5×10^6
6	$Fe^{2+} + {}^{\cdot}OH \rightarrow Fe^{3+} + OH^-$	4×10^8
7	$Fe^{3+} + S_1 \rightarrow Fe^{2+} + R_1^{\cdot}$	–
8	$^{\cdot}OH + R_\alpha H^* \rightarrow R_\alpha^{\cdot} + H_2$	$\sim 10^9$
9	$^{\cdot}OH + R_\beta H^* \rightarrow R_\beta^{\cdot} + H_2$	$\sim 10^9$
10	$^{\cdot}OH + R_\gamma H^* \rightarrow R_\gamma^{\cdot} + H_2$	$\sim 10^9$
11	$R_\alpha^{\cdot} + Fe^{3+} \rightarrow Fe^{2+} + P$	$\sim 10^8$
12	$R_\alpha^{\cdot} + H_2O_2 \rightarrow ROH + {}^{\cdot}OH$	1.6×10^5
13	$R_\alpha^{\cdot} + {}^{\cdot}OH \rightarrow ROH$	$\sim 10^{10}$
14	$R_\gamma^{\cdot} + Fe^2 \rightarrow RH + Fe^{3+}$	–
15	$2R_\beta^{\cdot} \rightarrow$ products (dimers)	–
16	$RH + HO_2^{\cdot} \rightarrow R^{\cdot} + H_2O_2$	–
17	$R^{\cdot} + O_2 \rightarrow RO_2^{\cdot}$	$\sim 10^9$

Organic compounds (hydrocarbons, alcohols, aldehydes, acids, etc.), the interaction of which with $^{\cdot}OH$ in the positions indicated (α-, β-, or γ-) results in the abstraction of a hydrogen atom, are designated by an asterisk (RH*).

If the rate constants for the elementary stages presented and the concentrations of the corresponding species are known, it is possible to estimate which reactions make the main contribution to the process under consideration. It is easy to demonstrate that, in a specific instance involving certain concentrations, Scheme 8 reduces to Walling's scheme, which is well known in the literature and has been proposed for the oxidation of organic compounds of different classes under anaerobic conditions.[29] If account is taken of data[29,130,137,138,141–145] indicating the addition of $^{\cdot}OH$ to the substrate and the formation of 'adhesion' radicals, the following additional steps must be included in the mechanism:

Scheme 9

8. $R_iH + {}^{\cdot}OH \longrightarrow R_i^{\cdot}HOH$
10. $R_kH + {}^{\cdot}OH \longrightarrow R_k^{\cdot}HOH$
11. $R_i^{\cdot}HOH + Fe^{3+} \longrightarrow R_i^{\prime}HO + Fe^{2+} + H^+$
14. $R_k^{\cdot}HOH + Fe^{2+} \xrightarrow{H^+} R_k^{\prime}H_2OH + Fe^{3+}$
17. $R_j^{\cdot}HOH + R_jH \longrightarrow R_j{-}R_j + H_2O$

R_i = substrate radical with reducing properties, R_k = oxidant radical, and R_j = radical tending to dimerise.

The mechanism in each specific case must be determined by specified concentration conditions with allowance for the established reaction kinetics, the data concerning the types of

substrate radicals formed in the systems and their reactivities, as well as information about the intermediates obtained and the rate constants for elementary reactions. The problem of obtaining complete information for a particular system is difficult to solve: it is rare to achieve an unambiguous experimental determination of all the types of substrate radicals formed and it is as a rule impossible to detect the intermediates; the rate constants for any elementary stages of the oxidation process are frequently unknown. For this reason, the mechanisms of oxidation of organic substrates by the Fenton reagent under anaerobic conditions have been at the present time justified only at a qualitative level. Nevertheless the overall mechanism (Schemes 8 and 9) makes it possible to describe more fully and adequately the mechanism of the oxidation of organic substrates than Walling's scheme.

b. The $Fe^{2+}-H_2O_2-S-O_2$ system

The process mechanism under aerobic conditions becomes even more complicated when molecular oxygen is involved in the oxidation. In this case, the amount of H_2O_2 consumed in the presence of O_2 on the oxidation of a specific amount of S diminishes, while the amount of the accumulated product of the oxidation of S in the presence of O_2 exceeds the theoretical maximum value established from the amount of H_2O_2 consumed.

The question arises how molecular oxygen influences the oxidation process. It has been established experimentally that the aerobic oxidation of substrates in the absence of Fe^{2+} and H_2O_2 hardly occurs (although iron ions are a universal contaminant and it is virtually impossible to get rid of them).

The available data on the activation of O_2 by Fe^{2+} aquo-ions indicate that the process includes the reactions[2]

$$18.\ Fe^{2+} + O_2 \underset{k_{-18}}{\overset{k_{18}}{\rightleftharpoons}} (FeO_2)^{2+},$$

$$\left(K = \frac{k_{18}}{k_{-18}} = 10^{-10}\ \text{litre mol}^{-1}\right),$$

$$19.\ (FeO_2)^{2+} + Fe^{2+} \overset{k_{19},\,2H^+}{\rightleftharpoons} 2Fe^{3+} + H_2O_2,$$

$$(k_{19} = 10^6\ \text{litre mol}^{-1}\ \text{s}^{-1}).$$

However, the influence of O_2 is exerted via the intermediates formed in the $Fe^{2+} - H_2O_2 - S$ system and not via the initial components (the last two stages may be neglected[3]). The primary product of the oxidation of organic substances by the Fenton reagent is the substrate radical R$^{\bullet}$, which possesses mainly reducing properties. Consequently, it can react effectively with O_2. Thus, in the typical systems considered, the radicals R$^{\bullet}$ formed may be consumed via the reactions with H_2O_2, Fe^{3+}, and O_2. If the interaction of $^{\bullet}OH$ with ethanol results in the formation of the alkoxy-radical $CH_3C^{\bullet}HOH$ ($R^{\bullet}_{\alpha}$), i.e.

$$20.\ C_2H_5OH + {}^{\bullet}OH \xrightarrow{k_{20}} CH_3C^{\bullet}HOH + H_2O,$$

$$(k_{20} = 1.6 \times 10^9\ \text{litre mol}^{-1}\ \text{s}^{-1}),$$

then the following reactions involving its consumption may be considered:

Step	Reaction	k_i/litre mol^{-1} s^{-1}	Ref.
12	$R^{\bullet}_{\alpha} + H_2O_2 \xrightarrow{k_{12}} ROH + {}^{\bullet}OH$	$k_{12} = 1.6 \times 10^5$	146
21	$R^{\bullet}_{\alpha} + Fe^{3+} \xrightarrow{k_{21}} P + Fe^{2+} + H^+$	$k_{21} = 2.7 \times 10^8$	147
22	$R^{\bullet}_{\alpha} + O_2 \xrightarrow{k_{22}} RO^{\bullet}_2$	$k_{22} = 4.6 \times 10^9$	148

Comparative analysis of stages 12, 21, and 22 permits the conclusion that under aerobic conditions the radicals $R^{\bullet}_{\alpha}$ are almost fully consumed on the interaction with O_2. Consequently, in contrast to the mechanism operating under anaerobic conditions (Scheme 7) and also Walling's general mechanism,[29] the above scheme should include new elementary stages involving the formation and further reactions of the peroxyl radical $CH_3C^{\bullet}H(OO)OH$ ($RO^{\bullet}_2$) derived from the alcohol. The complete mechanism of the oxidation of ethanol under aerobic conditions (an example of a typical $Fe^{2+} - H_2O_2 - S - O_2$ system), put forward by Sychev et al.,[149] is given in Scheme 10.

Scheme 10

$$1.\ Fe^{2+} + H_2O_2 \longrightarrow Fe^{3+} + {}^{\bullet}OH + OH^-$$

$$20.\ {}^{\bullet}OH + C_2H_5OH \longrightarrow R^{\bullet}_{\alpha} + H_2O$$

$$22.\ R^{\bullet}_{\alpha} + O_2 \longrightarrow RO^{\bullet}_2$$

$$23.\ RO^{\bullet}_2 \longrightarrow CH_3CHO + HO^{\bullet}_2$$

$$24.\ RO^{\bullet}_2 + ROH \longrightarrow CH_3CH(OOH)OH + R^{\bullet}_{\alpha}$$

$$25.\ RO^{\bullet}_2 + Fe^{2+} \xrightarrow{H^+} Fe^{3+} + CH_3CH(OOH)OH$$

$$26.\ HO^{\bullet}_2 + C_2H_5OH \longrightarrow R^{\bullet}_{\alpha} + H_2O_2$$

$$5.\ HO^{\bullet}_2 + Fe^{2+} \xrightarrow{H^+} Fe^{3+} + H_2O_2$$

$$4.\ HO^{\bullet}_2 + Fe^{3+} \longrightarrow Fe^{2+} + O_2 + H^+$$

$$27.\ CH_3CH(OOH)OH \longrightarrow CH_3CHO + H_2O_2$$

On the basis of this scheme, it is possible to derive an expression for the initial rate of formation of acetaldehyde on the assumption that $k_{25}[Fe^{2+}] \leqslant k_{23} + k_{24}[ROH]$ and $k_{26}[ROH] \ll k_5[Fe^{2+}] + k_4[Fe^{3+}]$:

$$w_{o,A} = \frac{k_1[Fe^{2+}][H_2O_2]}{(1 + k_{27}[H_2O_2])(1 + k_{24}[ROH]/k_{23})}.$$

It is consistent with the experimentally observed features.[149]

The participation of oxygen in the aerobic oxidation of organic substrates by the Fenton reagent and the complication of the reaction mechanism under these conditions has also been noted in other studies.[2, 3, 144, 150–153]

A similar mechanism operates in the oxidation of substrates also in the typical $Fe^{2+}-S_L-H_2O_2-O_2$ and $L-Fe^{2+}-H_2O_2-S-O_2$ systems with the sole difference that the coordination compounds of Fe^{2+} with S_L and L respectively function as catalysts in this case.[3]

The following features should be included in the experimental evidence for the occurrence of the process under aerobic conditions according to Scheme 10:

(1) the difference between the rates of oxidation of the substrate in the aerobic and anaerobic systems;

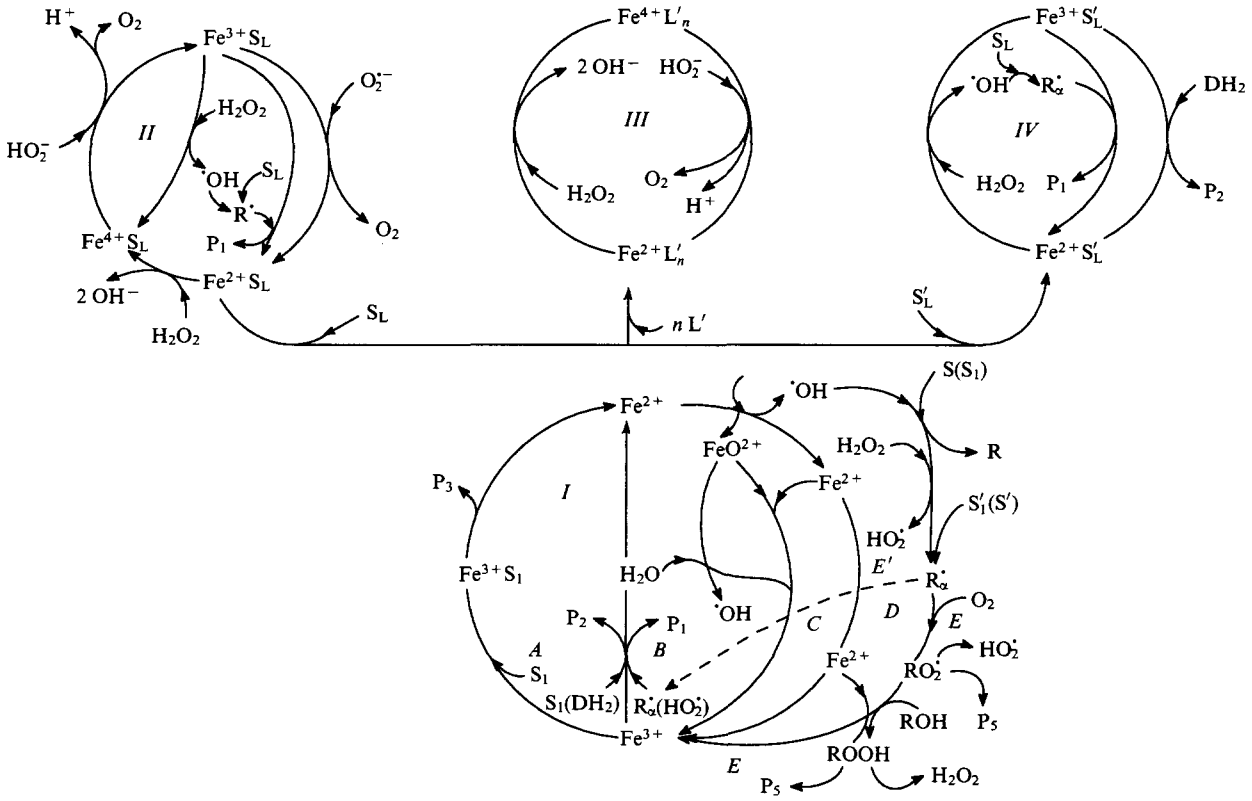
(2) the greater amount of the substrate oxidation product compared with the amount of disproportionated H_2O_2;

(3) the generation of $^{\bullet}OH$ radicals, the decrease in the Fe^{2+} concentration during the reaction, and the accumulation of Fe^{3+}.

Thus one may postulate that the mechanism of the oxidation of organic substrates under aerobic conditions by the $^{\bullet}OH$ radicals generated by ferroperoxide systems in cases where an active radical (of the type $R^{\bullet}_{\alpha}$) is formed can be described by Scheme 10. Consequently the role of H_2O_2 in the aerobic oxidation of organic substrates (especially alcohols) reduces to the preparation of the latter for their subsequent oxidation by oxygen (in the case of alcohols, for the conversion of ROH into $R^{\bullet}_{\alpha}$).

On the basis of the analysis of literature data, the mechanisms of the decomposition of H_2O_2 and of the oxidation of substrates can be represented by the generalised Scheme 11.[3]

Scheme 11



If iron(II) coordination compounds serve as the catalyst, the general mechanism assumes as a rule a form (mainly in acid and weakly acid media) analogous to fragment *I* of Scheme 11 ($Fe^{2+}L_n$ participates in the reaction instead of Fe^{2+}).

For simplicity, not all possible reactions of the $^{\bullet}OH$ radicals generated have been included in fragments *II*, *IV*, and also *I* (sequence *C*) (they are all analogous to the reactions presented in sequence *E* of fragment *I*).

The ferroperoxide systems may be classified in terms of different features: in terms of the effectiveness of their action, in terms of the complex-forming capacity of the substrate relative to Fe^{2+}, and in terms of the mechanisms of the disproportionation of H_2O_2 and the oxidation of the substrate.

If the substrate S introduced and the substrate radical $R^{\bullet}$ formed have no reducing properties, then the oxidation process decays as a function of time and reaches completion after the conversion of all the Fe^{2+} into Fe^{3+} (sequence *D* or *C* occurs — see Scheme 11). If the substrate S_1 and/or the substrate radical $R^{\bullet}_{\alpha}$ formed are effective reductants, then quantitative oxidation of the substrate takes place under anaerobic conditions, the process being more effective the higher the reducing 'strength' of the latter (or of the corresponding substrate radical). Such processes include the reaction sequences *D* (or *C*), *E*, and *B* (Scheme 11). The formation of an active substrate radical increases the effectiveness of the oxidation of the substrate also under aerobic conditions as a consequence of the realisation of sequences *D* (or *C*), *E*, and *B*. In such cases, the role of hydrogen peroxide consists merely in preparing the substrate (via the formation of $R^{\bullet}_{\alpha}$) for the subsequent interaction with O_2. It is possible to infer which of the mechanisms operates in the oxidation of a particular substrate by ferroperoxide systems, provided that the rate constants for the elementary stages of the interaction of the substrate and substrate radicals with $^{\bullet}OH$ and O_2 are known.

The role of the added inert ligand consists in enhancing the oxidising capacity of the ferroperoxide systems and of ensuring their operation in weakly acid and neutral media. This occurs as a consequence of the change in the OR potential of the Fe^{3+}/Fe^{2+} couple and the stabilisation of a particular oxidation state of iron at higher pH. If one-electron transfers from the complex catalyst to the substrate are preferred in the system, then the fundamental process mechanism is as a rule similar to that operating in the $Fe^{2+} - H_2O_2 - S$ system (Scheme 11, fragment *I*) with the sole difference that the catalyst is a Fe^{2+} ion bound in a complex. If two-electron transfers are preferred, then the mechanism as a rule changes (fragments *II* and *III* in Scheme 11). Consequently, in order to increase the effectiveness of the ferroperoxide systems, it is necessary to choose a suitable ligand and to establish conditions under which cyclic or radical-chain H_2O_2 disproportionation and substrate oxidation processes take place. If the reducing 'strength' of the substrate (or the substrate radical) is low, effective reductants (of the type of ascorbic and dihydroxyfumaric acids, etc.), capable of regenerating the active form of the catalyst (Fe^{2+}), must be introduced into the system.

The substrates S which do not form complexes are oxidised in the reaction volume by the $^{\bullet}OH$ radicals (sequences *D* or *C* in Scheme 11), while those which possess a reducing capacity (S_1) are oxidised in sequences *D* (or *C*), *E*, and *B* (Scheme 11) and also by Fe^{3+} ions (or complexes).

The substrates S_1 which form complexes with Fe^{2+} alter the OR potential of the catalyst, which may increase the catalytic activity of the latter and the fundamental mechanisms of the disproportionation of H_2O_2 and the oxidation of substrate may remain virtually unaltered under these conditions (fragment *IV* in Scheme 11) or may undergo some changes (fragment *II*). Depending on the mechanism operating, such substrates may be oxidised via an inner-sphere route (via the transfer of one or two electrons) and also in the reaction volume by the $^{\bullet}OH$ or $O_2^{\bullet-}$ radical species generated. If S_L forms complexes only with Fe^{3+}, the process mechanism includes sequence *A* instead of sequence *B* (Scheme 11).

All the ferroperoxide systems can be divided into two groups in terms of the H_2O_2 and substrate oxidation mechanisms: a radical-ion mechanism (cyclic or radical-chain) mechanism operates in the first group and is described by fragments *I*, *II*, and *IV*, while an ion-molecule mechanism operates in the second group (fragment *III* in Scheme 11).

3. Oxidation of organic substrates by the $Fe^{3+}(LFe^{3+})-H_2O_2$ system

As observed already in an early investigation,[74,75] the Fe^{3+} aquo-ions also catalyse the decomposition of H_2O_2. The disproportionation of the Fe^{3+} ions proceeds via a radical-chain mechanism,[1,3,16,85,154,155] which includes stages involving the generation of $^{\cdot}OH$ free radicals. Since the formation of radicals actually ensures the high reactivity of the Fenton reagent in the oxidation reactions of organic substrates, one may expect that the substrates will be oxidised effectively also in the Ruff system, i.e. this system may be used for hydroxylation. Indeed, it has been shown[154] that acetone, *tert*-butyl alcohol, methanol, acetic acid, and other substrates are oxidised by the Ruff system.

The data concerning the influence of the type of substrate radical on the mechanism of the decomposition of H_2O_2 and on the oxidation of the substrate in the $Fe^{3+} - H_2O_2 - S_x$ system (and hence also on the composition of the oxidation products) [3] agree almost fully with those which have been obtained in the study of the oxidising activity of the Fenton reagent. The principal postulates and conclusions concerning the oxidation of S in the $Fe^{2+} - H_2O_2$ system are therefore applicable also to the oxidation of organic substrates by the Ruff system.

The mechanism of the oxidation of S by Fe^{3+} ions, as well as certain coordination compounds of trivalent iron, in the course of the catalytic disproportionation of H_2O_2, has been considered from similar standpoints.[70,85,89,142,156–162]

The reactions involving the oxidation of organic dyes by the Ruff system (and also by the Fenton reagent) are used widely in the kinetic methods for the determination of microamounts of iron ions in weakly acid aqueous media.[3,163–168]

The set of consecutive stages occurring in each specific case in the oxidation of substrates in the $Fe^{3+} - H_2O_2$ systems depends on the type of substrate, the properties of the substrate radical formed, and the experimental conditions (primarily on the concentrations of the reactants and on the occurrence of the process under aerobic or anaerobic conditions). All the factors noted above affect the process mechanism in the given system, as in the $Fe^{2+} - H_2O_2$ system. In planning the experiment and in considering the mechanism of the oxidation of substrates by the Ruff system, one may be guided by the generalised Scheme 11, which has been developed for the Fenton reagent and ferroperoxide systems.

III. Intermediates of the type of ferryl ions and complexes in the catalysis of oxidation processes

The fundamental mechanisms of the activation of oxygen, the catalytic decomposition of hydrogen peroxide, and the oxidation by the latter of organic substrates in the presence of iron ions or coordination compounds of iron were examined above. The role of the intermediate reactive species formed on reduction of O_2 or decomposition of H_2O_2 — the superoxide ($HO_2^{\cdot}$) and especially hydroxyl ($^{\cdot}OH$) radicals — was fairly widely dealt with in this connection.

Since the beginning of the 1930s, the nature and role of the reactive species formed in the interaction of iron ions or complexes with hydrogen peroxide has been the subject of numerous publications and discussions. Since the investigations of Haber and Weiss,[169,170] the view that the initial activation of H_2O_2 by Fe^{2+} ions is accompanied by the formation of the $^{\cdot}OH$ radical has been quite firmly established.

$$Fe^{2+}(aq) + H_2O_2 \longrightarrow Fe^{3+}(aq) + OH^- + {}^{\cdot}OH \qquad (1)$$

This was confirmed by the experimental observation of the acceleration of the polymerisation of various monomers when H_2O_2 and Fe^{2+} ions are introduced into the reaction medium, by the analysis of the products of the hydroxylation of numerous organic compounds by the Fenton system, and by comparing the rate constants for the elementary stages in the interaction of various substrates with hydroxyl radicals (generated in the radiolysis of water), and also by the results of the study of the catalytic decomposition of H_2O_2 by the Fe^{2+} aquo-ions.[3]

However, the question arises whether reaction (1) is elementary. If it is not, then what are the reactive species which precede the appearance of the $^{\cdot}OH$ radical and what are their properties? Many investigators postulate that the generation of Fe^{3+} ions and the hydroxyl radicals $^{\cdot}OH$ by the $Fe^{2+}(aq.) - H_2O_2$ system does not constitute unambiguous proof that reaction (1) is elementary and that these species are merely the detectable products of a complex process.

Since the study of Bray and Gorin[171] up to the present time, there has existed also another point of view, according to which the hydrogen peroxide decomposition process in the $Fe^{2+}(aq.) - H_2O_2$ system proceeds with formation of the ferryl

$$Fe^{2+} + H_2O_2 \longrightarrow Fe^{IV}{=}O^{2+} + H_2O \qquad (2)$$

ion $(Fe^{IV} = O)^{2+}$:

$$L_nFe^{2+} + H_2O_2 \longrightarrow (L_nFe^{IV}{=}O)^{2+} + H_2O\,. \qquad (3)$$

At a higher pH, a complex is formed:

The occurrence of stage (2) requires the simultaneous transfer of two electrons from the catalyst to H_2O_2. Although direct experimental evidence for the formation of the ferryl ion FeO^{2+} in the given system has not been obtained, nevertheless this idea has been supported by many investigators,[2,116,172–177] who used it to account for the mechanism of the activity of the Fenton reagent. Subsequently the possibility of the formation of the ferryl species as a constituent of complexes at pH 7 and not in an acid medium, where only the $Fe^{2+}(aq.) - H_2O_2$ system may exist, was also considered.[178] Be it as it may, one cannot rule out the possibility of the formation of the ferryl ion in ferroperoxide systems. It may be that the interaction of Fe^{2+} with H_2O_2 results in the initial formation of an intermediate complex, where electron transfers lead to the generation of the ferryl ion, giving

$$Fe^{2+} + H_2O_2 \underset{-H^+}{\rightleftharpoons} Fe^{2+}(HO_2^-) \xrightarrow{H^+} \qquad (4)$$

$$\longrightarrow FeO^{2+} + H_2O \longrightarrow Fe^{3+} + HO^- + {}^{\cdot}OH$$

rise to the $^{\cdot}OH$ radicals as a result of the reaction with water.

If the contribution of the inner-sphere electron transfer in the intermediate complex, leading to the formation of FeO^{2+}, is large and the ferryl ion interacts rapidly with a water molecule, then only the $^{\cdot}OH$ radicals and Fe^{3+} ions are detected in the system. This explains the impossibility of the experimental detection of the FeO^{2+} species in the Fenton system. This problem has been analysed in detail in the monograph of Sychev and Isak.[3]

In more complex systems (metal complexes, enzymes and their models which incorporate iron at the active centre of the enzyme, as well as hydrogen peroxide and dioxygen), there is an increase in the likelihood of the generation of the ferryl species bound in a complex as a consequence of the greater probability of the transition of iron to the Fe(IV) oxidation state and the stabilisation of the latter by the surrounding ligands (L). The number of examples of this kind has been increasing recently.

There is experimental proof that at a low pH the $^{\cdot}OH$ radicals are generated by reaction (1) in the Fenton system, whereas at a high pH, where the iron ion is bound in a complex, there is an increase in the probability of the appearance, instead of the $^{\cdot}OH$ radical, of the less reactive ferryl complex species $L_nFe^{IV}{=}O^{2+}$ via reaction (3). This species acts more specifically as an oxidant.

The mechanisms of reactions (1) and (3) apparently include the formation of the intermediate Fe^{II} and Fe^{III} peroxo-complexes.[178] However, it is not entirely clear which oxidising species are formed in the course of these reactions. The proof of the formation at different pH of oxidising species differing from one another is provided by the characteristic features of the product distribution in the reactions of a series of substrates. In acid media, the distribution is close to that attained when the $^{\bullet}OH$ radicals, generated by radiolysis, are employed whereas in neutral and alkaline media it is more stereospecific. In other words, in the latter case the oxidant is not the $^{\bullet}OH$ radical but another species, tentatively ferryl iron.[29,179-183] Different experimental methods have been used in experiments of this kind:[184,185] pulse radiolysis, the stopped flow method, the generation of iron(IV) compounds as a result of the oxidation of iron(III) salts or complexes by $^{\bullet}OH$ free radicals, and the reduction of the ferrate ion (FeO_4^{2-}) to the perferryl ion (FeO_4^{3-}) by the hydrated electron or the $CO_2^{\bullet-}$ radical. Ferryl (Fe^{IV}) and perferryl (Fe^{V}) forms of iron have different spectroscopic characteristics. On the other hand, in terms of their chemical behaviour they are very similar and this is why perferryl can sometimes be used as a model for the investigation of the interaction of ferryl with organic substrates. Thus iron in the +4 oxidation state has been detected in the presence of inorganic ligands (OH^-, $P_2O_7^{4-}$, and HCO_3^-/CO_3^{2-}) or their mixtures.[185]

$$^{\bullet}OH + Fe(OH)_4^- \longrightarrow Fe^{IV} + H_2O \quad (k = 10^8 \text{ litre mol}^{-1} \text{ s}^{-1})$$

$$^{\bullet}OH + HCO_3^-/CO_3^{2-} \longrightarrow H_2O/OH^- + CO_3^{\bullet-} \quad (k = 4 \times 10^8 \text{ litre mol}^{-1} \text{ s}^{-1})$$

$$CO_3^{\bullet-} + L_nFe^{III} \longrightarrow L_nFe^{IV} + CO_3^{2-} \quad (k = 2.4 \times 10^8 \text{ litre mol}^{-1} \text{ s}^{-1})$$

$$^{\bullet}OH + [Fe^{III}OH(P_2O_7)_2]^{6-} \longrightarrow [Fe^{IV}(OH)(P_2O_7)_2]^{5-} + OH^- \quad (k = 5 \times 10^7 \text{ litre mol}^{-1} \text{ s}^{-1})$$

Although the different iron(IV) complexes have very similar spectroscopic characteristics ($\lambda_{max} \approx 430$ nm, $\varepsilon = 900 \pm 100$ litre $mol^{-1} s^{-1}$), the kinetics of their reactions depend on the pH and the nature of the ligand (the half-reaction time $\tau_{1/2}$ varies from 0.1 to 1.0 s).[184-186] The iron(V) compounds are relatively stable in alkaline solutions ($\tau_{1/2} \approx 170$ ms) and their UV spectra have a shoulder between 260 and 300 nm [$\varepsilon = (4 - 5) \times 10^3$ litre $mol^{-1} s^{-1}$].[185] The iron(V) complexes are much more reactive than the iron(VI) complexes: the ratio of the rate constants for the oxidation of formate is

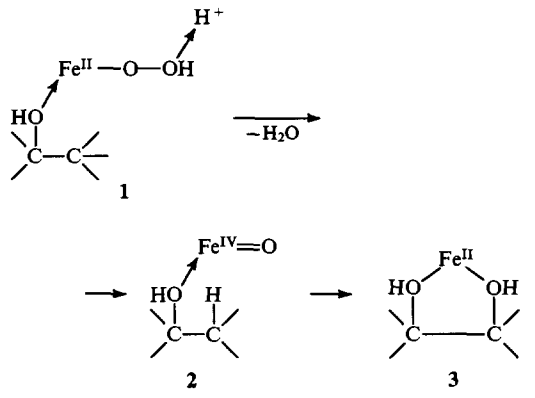
$$\frac{k_{Fe^V + HCOO^-}}{k_{Fe^{VI} + HCOO^-}} = 10^5 .$$

Such or an even greater increase in reactivity is observed on passing from iron(V) to iron(IV) complexes.

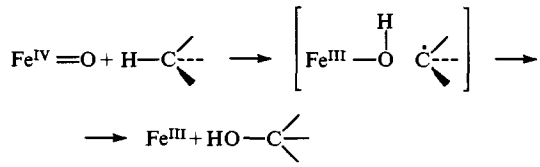
In systems of the Fenton type under the conditions involving the formation of superoxidised iron states, the latter may exhibit a greater specificity (stereospecificity) in oxidation and hydroxylation reactions.[186] Such specificity is especially important when the reactions proceed in biological systems.

One of the first fairly convincing experimental pieces of evidence for the generation of the ferryl ion in oxidation-reduction catalytic reactions has been obtained by Groves.[187] In the oxidation of cyclohexanol by hydrogen peroxide in the presence of iron(II) salts and perchloric acid in acetonitrile, in addition to cyclohexanone, the products included cyclohexane-diols, 72% of which comprised *cis*-cyclohexane-1,3-diol. Such regioselectivity was explained by the appearance of an iron(IV) intermediate capable of subsequently transferring an oxygen atom. This view has been confirmed by the existence of a whole series of salts and other compounds in which the oxidation state of iron is +4.

The above regioselectivity might have been the result of the formation of an iron(II) complex **1** with the OH group of cyclohexanol and the peroxide ion. The reaction is accompanied by the heterolysis of the peroxide, which leads to the formation of complex **2**, and the insertion of oxygen in the substrate (complex **3**).



The transfer of oxygen from the ferryl intermediate to the carbon atom of cyclohexanol, accompanied by the formation of the corresponding diol, most probably proceeds in accordance with the mechanism



Somewhat later, the iron in the 'ultrahigh' oxidation state was detected in the reaction of hydrogen peroxide with the water-soluble iron(III)-porphyrin.[188] The compound formed, in which the iron atom is in the same oxidation state, is characterised by an appreciable lifetime in aqueous solution.[184] The reduction potential of the ferryl/ferriporphyrin couple is ~ 0.9 V, which is lower by 1.3 V than for the $^{\bullet}OH/H_2O$ couple at pH 7.[178] The maximum (FeO^{2+} – chelate)/(Fe^{3+} – chelate) potential is approximately 2 V, i.e. the ferryl complex is a weaker and more selective oxidant than the $^{\bullet}OH$ radical.

Yet another piece of experimental evidence for the possibility of the formation of a ferryl complex is provided by the results obtained in the study of the interaction of the coordination compound Fe^{II}EDTA with H_2O_2 and the way the system is acted upon by various alcohols, aminoacids, and acids. The reaction of Fe^{II}EDTA with H_2O_2 may involve the formation of either the $^{\bullet}OH$ radical or the ferryl complex of EDTA, the latter being more probable. Indeed, it has been shown that this process can be described by the following equations:[189]

$$Fe^{II}EDTA + H_2O_2 \xrightarrow{k_1} I_1 \xrightarrow{Fe^{II}EDTA} Fe^{III}EDTA$$

$$I_1 + H_2O_2 \xrightarrow{k_2} I_2 \xrightarrow{Fe^{II}EDTA} Fe^{III}EDTA$$

I_1 and I_2 = intermediates

where $k_1 = 1.75 \times 10^4$ and $k_2 = 3.2 \times 10^3$ litre $mol^{-1} s^{-1}$. It has been suggested that the intermediate I_1 is most probably the ferryl-EDTA complex and not the hydroxyl radical, while the intermediate I_2, capable of reacting with ferricytochrome *c*, is the $^{\bullet}OH$ radical. The difference between I_1 and I_2 is manifested by their different reactivities towards *tert*-butyl alcohol and ethanol ($^{\bullet}OH$ radical-fixing agents). The intermediate I_1 is not fixed by *tert*-butyl alcohol, whereas the intermediate I_2 is fixed. I_1 is much less reactive towards the benzoate ion, *tert*-butyl alcohol, the acetate ion, arginine, and serine than the $^{\bullet}OH$ radical, but it is fixed by compounds with easily oxidisable functional groups such

as ethanol and isopropyl alcohol. All this indicates that the intermediate I_1 does not effect reactions characteristic of the hydroxyl radical and as an oxidant has a reactivity closer to that of the metal ion, i.e. it resembles the complex (FeO^{2+})EDTA.[189]

Although the formation of the 'OH radical in the Fe^{2+}–EDTA – H_2O_2 systems has been confirmed by various methods (the spin trapping method,[190] the hydroxylation of aromatic compounds,[191] and comparison of the rate constants for the interaction of certain substances with the above radicals and the 'OH radicals obtained by radiolysis),[192] nevertheless there exists the view, based on the dehydration of cytochrome *c* in the given system, according to which the reactive species is more likely to be the ferryl complex and not the 'OH radical. The formation of the ferryl complex may precede the formation of 'OH radicals. Indeed, two oxidising species are generated in the reactions of haemoglobin with H_2O_2, one of which hydroxylates aromatic compounds (the 'OH radical), while the other cannot effect this reaction.[193] It has been suggested that this second species is the ferryl complex. Thus there are two possibilities for the formation of reactive species in vivo.[194–201] The predominance of one or other possibility depends on the biological target to which the iron ions bind.[193]

The generation of the ferryl group on protonation of plant peroxidases has been confirmed with the aid of resonance Raman spectroscopy. A hydrogen bond, in which the oxygen atom bound to the ferryl ion of the peroxidase participates, arises in this process.[202–204] The formation of the ferryl group has been confirmed also by the study of the interaction of peroxidases and catalases with peroxides.[205] Two intermediates are formed (green and red compounds), the first of which is formally $Fe^{V}O^{3+}$, or more precisely a $[P^{\cdot+}Fe^{IV}O]^{3+}$ haem (one electron is transferred to iron by the porphyrin ligand), while the other is an Fe^{IV} haem. Indeed, bands characteristic of the vibrations of the $Fe^{IV}=O$ groups have been noted in the resonance Raman spectra of the second haem intermediate. The frequencies of these vibrations are extremely sensitive to the effect of the environment. Peroxidase exhibits an enzyme activity only when the $Fe^{IV}=O$ group binds the hydrogen of a remote aminoacid group.

The interaction of ferrimyoglobin with H_2O_2 has also been examined as a possible model of the activity of catalase. It was postulated that the structure of the intermediate includes the ferryl ion (FeO^{3+}).[206]

The presence of the ferryl group in model systems simulating the peroxide oxidation of lipids has been demonstrated experimentally.[207] Whereas it had been suggested previously that the 'OH radical is the initiator of the peroxide oxidation (peroxidation) of lipids, later this role began to be attributed to an ionic complex of adenosine diphosphate ($ADP.Fe^{2+}.O_2$). Initiation by the 'OH radical is more likely in the absence of appreciable amounts of iron chelates. Otherwise (for example, in biological systems) the peroxidation of lipids apparently proceeds without the involvement of the hydroxyl radical. Two additional electrons convert the initial complex into the ferryl complex. This reaction resembles reaction (2).[187] It has been postulated that the ferryl ions are formed preferentially in the reaction of the

$$ADP\cdot Fe^{2+}\cdot O_2 \xrightarrow{2H^+,\,2\bar{e}} ADP\cdot(FeO_2)^{2+} + H_2O$$

adenosine diphosphate complex of iron(II) with hydrogen peroxide. The principal evidence for the absence of the hydroxyl radicals from the $ADP\cdot Fe^{2+}\cdot O_2$ system is the fact that, after the addition of a strong acceptor (mannitol), the rate of peroxidation of lipids remains almost unchanged. Thus the oxidation is promoted by the ferryl ions forming part of the ADP complex and not by the 'OH radicals.

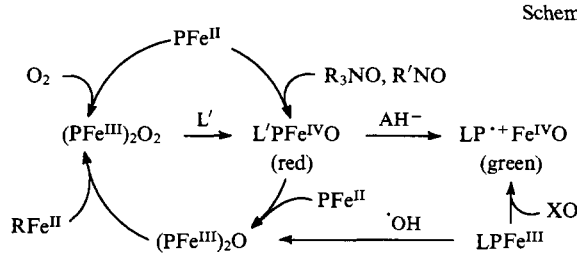
The involvement in the process of 'OH radicals or ferryl complexes depends to some extent on the hydrogen peroxide concentration in the system, which has been observed in the reaction involving the membrane peroxidation of lipids.[208] At low H_2O_2 concentrations and in the presence of haemoproteins (myoglobin, haemoglobin), lipids are oxidised mainly by ferryl species, whereas at high concentrations they are oxidised by hydroxyl radicals.

The epoxidation of alkenes and the hydroxylation of alkanes by various oxidants in the presence of iron-porphyrin complexes can proceed via different mechanisms.[5,209] The mechanism of the epoxidation of alkenes by iodosobenzene, hydrogen peroxide, and hydroperoxides (the catalysts are various porphyrin complexes of iron) includes the formation of the $P^{\cdot+}Fe^{IV}=O$ oxoporphyrin π-radical-cation as the oxidant. This species has not been isolated, but its existence has been confirmed by the presence in the resonance Raman spectrum of an intense band at 852 cm^{-1} (~ 15 K), which appears during the irradiation by a laser of the oxygenated iron complex of *meso*-tetraphenylporphyrin $Fe(TPP)O_2$.[210] This species may be formed in the presence

$$Fe(TPP)Cl + XO \longrightarrow Fe^{IV}O(TPP^{\cdot})Cl + X\,.$$

of an oxidant (XO) in accordance with the mechanism
The length of the Fe=O bond is ~ 1.60 – 1.66 Å.[211] Examination of the molecular orbitals in the $FeO(P)H_2O$ complex (P = porphyrin) shows that the ferryl group has the electronic configuration $\sigma^2\pi^4\pi^{*2}$, i.e. it contains the Fe=O double bond.[212] The paths leading to the formation of such species at temperatures below −50 °C have been examined in fair detail. Depending on the source of oxygen, the nature of the axial ligand (L′ or L), the way in which these species are obtained, the solvent, and the temperature, the oxo-transfers occur with formation of different intermediates.[213]

Scheme 12

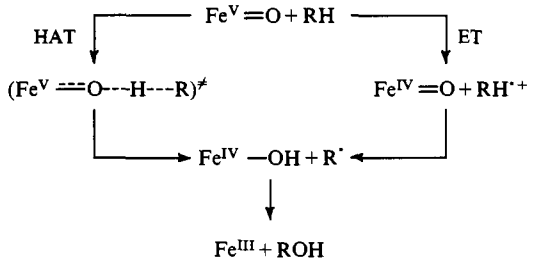


Here PFe^{II} is the porphyrin complex of iron(II), $L'PFe^{IV}O$ is the complex with the additional ligand L′ = methylimidazole or pyridine), $LP^{\cdot+}Fe^{IV}O$ is a similar complex with $L = ClO_4^-$, $LPFe^{III}$ is the iron(III) complex, $(PFe^{III})_2O$ is the dinuclear oxoiron(III) complex, $(PFe^{III})_2O_2$ is the μ-peroxo-dimer, AH^- is the electron acceptor, and XO is the oxidant (R_3NO or R′NO). The $Fe^{IV}O$ species cannot be detected in aqueous solutions or isolated in the form of the corresponding porphyrin complex. It can be more easily detected in a nonaqueous medium. The different routes to its formation are presented in Scheme 12.

When alkanes are hydroxylated by dioxygen in the presence of the same catalyst, the oxoiron(IV)-porphyrin participates in the process. The mechanism of the hydroxylation by iodosobenzene is radical in character. When this reaction proceeds with participation of hydrogen peroxide, the oxidising species is the 'OH radical, whereas in the case where hydroperoxides participate in the reaction, two oxidation mechanisms are possible: with formation of RO' (free-radical reactions) and with generation of high-valence oxoferryl species.

The hydroxylation of the substrate RH by an oxygen donor (iodosobenzene, peroxy-acids, etc.) in the presence of iron(III)-porphyrin has been discussed.[214] Two possible mechanisms were postulated: with hydrogen atom transfer (HAT) and with electron transfer (ET) from RH to the perferryloxygen atom ($Fe^{IV}=O$) formed in the system.

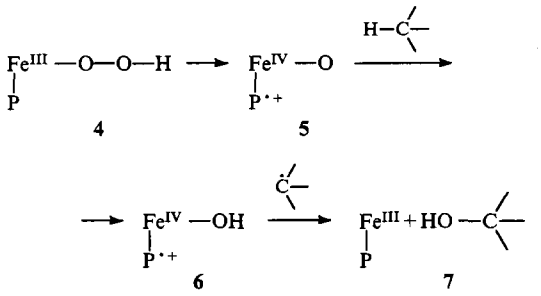
Scheme 13



The electron transfer path predominates when the hydroxylation substrates are electron-rich substances. An oxoferryl compound and a substrate radical-cation are formed in this case. The latter is deprotonated and affords the same pair of substances as in the transfer of a hydrogen atom. The interaction of this pair leads to the formation of a hydroxylated substrate. If the process is carried out in solvents with a low polarity and with the participation of substrates with an oxidation potential below 1.2–1.4 V, the HAT mechanism is preferred. In more polar solvents and with the participation of a substrate with an oxidation potential of 1.2–1.8 V, the ET mechanism predominates.

The formation of the oxoiron(IV)-porphyrin radical-cation is postulated in the hypothetical model of the generation of the active catalyst in hydroxylation reactions effected by cytochrome P-450.[215,216] The mechanism of this process provides for the heterolytic dissociation of the O–O bond in the hydroperoxoiron complex **4** with formation of the iron-porphyrin **5**, which has undergone one-electron oxidation and is an active oxidant. On reaction with the substrate, this complex accepts a hydrogen atom and gives rise to the hydroxoiron(IV) complex **6**. The radical centre of the substrate then recombines with the OH group of the hydroxoiron(IV) complex, which leads to the formation of the hydroxylated substrate and the initial ferri-form **7** of cytochrome P-450. The mechanism of this process can be represented in the following form:[217]

Scheme 14

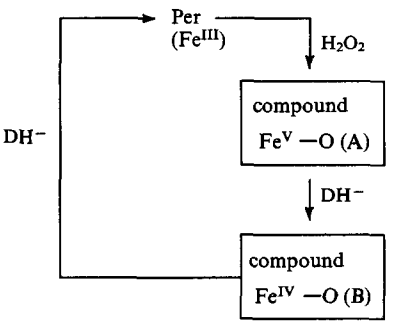


The interaction of various peroxidases (Per) with hydrogen peroxide results in the formation of outer- and inner-sphere intermediates and then of the compound PerO of the ferryl type ($Fe^{V}-O$ or more precisely $P^{\cdot+}Fe^{IV}O$):[218]

$$Per + H_2O_2 \rightleftharpoons (PerH_2O_2) \rightleftharpoons PerH_2O_2 \longrightarrow PerO + H_2O.$$

The formation of the Fe–O bond and other rearrangements do not require that a high energy barrier be overcome (the activation energy for this process is approximately 14.7 kJ mol^{-1}). The rates of formation of compounds of the type $Fe^{V}O$ are similar for different haemoproteins. The addition of an oxygen atom to the Fe^{III} atom of the native enzyme converts the latter formally into the Fe^{V} state but, in the presence of a suitable reductant (DH^-) or of an additional electron, the source of which may be some kind of haemoprotein, the final product becomes a compound of the type $Fe^{IV}O$, which can be in its turn reduced to the Fe^{III} state of the initial peroxidase.

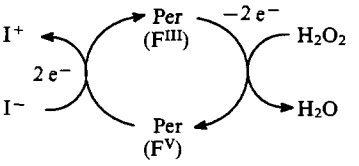
Scheme 15



This reaction cycle is characteristic, in particular, of horse peroxidase (the data on the magnetic susceptibilities of compounds A and B have been interpreted as referring to the Fe^{V} and Fe^{IV}states respectively). In the case of other peroxidases (chloroperoxidase, cytochrome *c* peroxidase), approximately the same reactions with some deviations have been observed.

The reactions of a type $Fe^{V}O$ compound can be demonstrated in relation to the interaction of the native horse peroxidase with the iodide ion.

Scheme 16



The same two-electron mechanisms of the interaction of the enzyme with hydrogen peroxide and of compound A with the iodide ion is characteristic also of chloroperoxidase. When nitrous acid (or the nitrite anion) participates in the usual enzymic cycle, compound A undergoes one-electron reduction to compound B and the latter is reduced to the initial peroxidase.

The reactions of a type $Fe^{IV}O$ compound have been investigated in particular detail in relation to horse peroxidase. Compounds A and B may compete with one another for the reductant. At a low pH, this competition is won by compound B, whilst at pH 9 it is won by compound A. Under such conditions, the yield of compound B may be made quantitative and the conversion of $Fe^{IV}O$ into PFe^{III} may be observed spectrophotometrically at the wavelength $\lambda = 425$ nm. In the general case, the interaction of various peroxidases with hydrogen peroxide affords compounds A and B in a similar way, although these processes also differ somewhat from one another.

The details of the oxidation of iron(III) porphyrinate by hydrogen peroxide or by organic peroxides in the catalytic cycle involving peroxidases and catalases were refined in subsequent studies. Thus it has been demonstrated by electronic and Mössbauer spectroscopy and also by EPR spectroscopy that compound A is the oxoiron(IV)-porphyrin π-radical-cation,[219] i.e.

$$P^{\cdot+}F^{III} + H_2O_2 \longrightarrow P^{\cdot+}Fe^{IV}{=}O,$$

whereas compound B is formed as a result of the one-electron reduction of compound A:

$$P^{\cdot+}Fe^{IV}{=}O + DH^- \longrightarrow PFe^{IV}{=}O + {}^{\cdot}DH.$$

The formation of compound A in the cytochrome P-450 cycle has also been postulated.

The better understanding of the mechanisms of the interaction of H_2O_2 or of the hydroperoxides ROOH with peroxidases, catalases, and cytochrome P-450 considered here is assisted by the study of model systems of the type $PFe^{III} - X - H_2O_2(ROOH)$. Evidence has been obtained[220]

that the peroxide (hydroperoxide) O–O bond is dissociated homolytically in the $(Ph_4P)Fe^{III}Cl - H_2O_2(ROOH)$ systems (Ph_4P = 5,10,15,20-tetraphenylporphyrinate) in methanol. This results in the formation of highly oxidised forms of iron porphyrinate of the oxoferryl type.

$$(Ph_4P)Fe^{III}(Cl) + ROOH \longrightarrow [(Ph_4P)Fe^{IV}O(Cl)RO^{\cdot}] \longrightarrow \begin{cases} [(Ph_4P^{\cdot+})Fe^{IV}O(Cl)] + RO^- \\ [(Ph_4P)Fe^{IV}O(Cl)] + RO^{\cdot} \end{cases}$$

It is much more difficult to investigate the catalytic decomposition of H_2O_2 in model systems of the type $PFe^{III}X - H_2O_2$ and to demonstrate the formation in this process of oxoferryl complexes in aqueous solutions, because in this instance it is necessary to create conditions preventing the appearance of the inactive dinuclear iron(III) porphyrinates and the stabilisation of oxoferryl species. The use of the $(TDSP)Fe^{III}(H_2O) - H_2O_2 - ABTS - H_2O$ model systems (30 °C), where $(TDSP)Fe^{III}(H_2O)$ = 5,10,15,20-tetra(2,6-dimethyl-3-sulfophenyl)porphyrinatoiron(III) hydrate and ABTS = 2,2′-azinodi(3-ethylbenzothiazoline-6-sulfonate), a trapping agent for the highly oxidised form of iron, made it possible to avoid the formation of dinuclear complexes and to stabilise the oxoiron(IV) porphyrinate species.[188] Depending on the pH (in the range 1–12), iron(III) complexes of different composition are formed initially: $(TDSP)Fe^{III}(H_2O)(H_2O_2)$ at a low pH, $(TDSP)Fe^{III}(OH^-)(H_2O_2)$ at an intermediate pH, and $(TDSP)Fe^{III}(OH^-)(HO_2^-)$ at a high pH. The homolytic or heterolytic dissociation of the peroxide O–O bond in the intermediate leads to the formation of $(TDSP)Fe^{IV}O$ and $^{\cdot}OH$ and of $(TDSP^{\cdot+})Fe^{IV}O$ and H_2O respectively.

Thus very numerous pieces of experimental evidence have been obtained in recent years for the generation of ferryl ions, their complexes, and enzyme compounds of types A and B, which are strong and at the same time specific oxidants for organic substrates (in hydroxylation, epoxidation, etc. reactions), competing with $^{\cdot}OH$ radicals. The $(Fe^{IV}=O)^{2+}$ species and $^{\cdot}OH$ radicals are highly reactive: the former can be converted into the latter under the conditions of the catalytic oxidation of any kind of substrate, for example in the $Fe^{2+}(aq.) - H_2O_2 - S$, $L_nFe^{2+} - H_2O_2 - S$, and enzyme $-Fe^{2+} - O_2(H_2O_2) - S$ systems. Hence it follows that the experimental identification of the ferryl species is in general fairly difficult and the question of the generation of such 'ultra-oxidised' iron states in the specific systems investigated is not yet clear. Even in the case where the formation of such species has been demonstrated by some kind of experimental method (with varying degrees of reliability), the information obtained is factual in character and does not account for the differences between the catalytic activities (for example in the decomposition of hydrogen peroxide) of different transition metal ions and of the different effects on the latter by the ligands and also for the appearance of different intermediate species (peroxo-complexes, free radicals) in the initiation steps.

Hence arises the need for the theoretical estimation of the possibility of the generation of ferryl species in the step involving the initiation of the decomposition of H_2O_2, starting with the simplest Fenton system $Fe^{2+}(aq.)-H_2O_2$ (working in weakly acid media) and ending with more complex $L_nFe^{2+} - H_2O_2$ systems.

It has been suggested that the initiation stage in the decomposition of hydrogen peroxide in the Fenton system is elementary.[1] According to an alternative view, the generation of the $^{\cdot}OH$ radical and the Fe^{3+} ion is not unambiguous evidence that this stage is elementary. It may be that the two-electron transfer from the catalyst to the substrate results in the initial formation of the ferryl ion.[171]

$$[(H_2O)_5Fe^{II}(H_2O)]^{2+} + H_2O_2 \xrightarrow[-H_2O,\ -H^+]{} [(H_2O)_5Fe^{IV}O]^{2+} \xrightarrow{H_2O} [(H_2O)_5Fe^{III}(OH^-)]^{2+} + {}^{\cdot}OH$$

It was later suggested[177] that a peroxo-complex is generated intially and a complex with a ferryl ion is formed from it as a consequence of intramolecular electronic transitions. The latter complex is then converted into an iron(III) complex and $^{\cdot}OH$.

$$[(H_2O)_5Fe^{II}(H_2O)]^{2+} + H_2O_2 \xrightarrow{-H_2O} [(H_2O)_5Fe^{II}(H_2O_2)]^{2+} \xrightarrow{-H^+} [(H_2O)_4(OH^-)Fe^{IV}O]^{+} \xrightarrow{H_2O} [(H_2O)_4(OH^-)_2Fe^{III}]^{+} + {}^{\cdot}OH$$

However, as already stated above, there is no convincing experimental evidence in the literature for the proposed mechanisms of the initiation of the decomposition of H_2O_2. On the contrary, according to the data of Koppenol and Liebman,[178] $^{\cdot}OH$ radicals are formed in this system in acid media and the possibility of the appearance of ferryl complexes increases only in neutral and alkaline media (where the iron ions are bound in complexes). Nevertheless, the idea that a ferryl species is formed in ferroperoxide systems has been discussed in numerous investigations.[3]

For a theoretical consideration of the possibility of the initial formation of ferryl species in the Fenton system, quantum-chemical calculations of the electronic structure of $Fe(H_2O)_6^{n-}$ and of a series of hypothetical complex compounds, postulated[171,177] as intermediates, have been performed. Calculations have also been carried out for all the peroxide species (H_2O_2, HO_2^-, $HO_2^{\cdot}$, and $^{\cdot}OH$) by the LCAO-MO SCF method in terms of the Mulliken–Wolfsberg–Helmholtz (MWH) approximation.[221] Self-consistent atomic charges and orbital populations as well as the electronic energy levels and the coefficients of the LCAO of the corresponding MO were found from these calculations (Fig. 1). Furthermore, the electron transfer from the MO of the complex to the MO of the peroxide species has been assessed quantitatively and the amounts of charge transferred (δq) have been found.

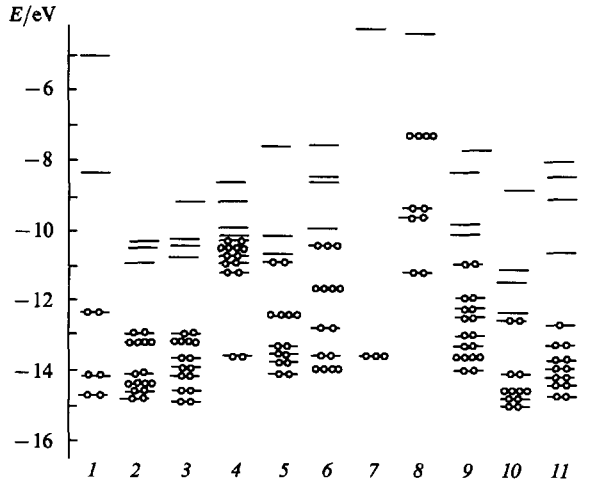


Figure 1. Energy level diagram for the molecular orbitals of the active regions of the molecules: (*1*) H_2O_2; (*2*) $[Fe^{II}(H_2O)_6]^{2+}$; (*3*) $[Fe^{II}(H_2O)_5.(H_2O_2)]^{2+}$; (*4*) $[Fe^{II}(OH^-)(H_2O)_4(H_2O_2)]^{+}$; (*5*) $[Fe^{IV}O(H_2O)_4(OH^-)]^{+}$; (*6*) $[Fe^{III}(OH)_2(H_2O)_4]^{+}$; (*7*) $^{\cdot}OH$; (*8*) HO_2^-; (*9*) $[Fe^{II}(H_2O)_5(HO_2^-)]^{+}$; (*10*) $[Fe^{IV}O(H_2O)_5]^{2+}$; (*11*) $[Fe^{III}(OH^-)(H_2O)_5]^{2+}$.

Analysis of the energy levels of the complexes indicates a low probability of the formation of the peroxo-complex $[Fe^{II}(H_2O)_5(H_2O_2)]^{2+}$ (energy level set *3*) and the impossibility of the occurrence of intramolecular transformations in which $[Fe^{II}(OH^-)(H_2O)_4(H_2O_2)]^+$ (*4*) and $[Fe^{IV}O(H_2O)_4(OH^-)]^+$ (*5*) are generated, because the levels of the highest occupied molecular orbitals (HOMO) and the lowest unoccupied orbitals (LUMO) of these species are much higher than the corresponding levels of both $[Fe(H_2O)_6]^{2+}$ (*2*) and $[Fe^{II}(H_2O)_5(H_2O_2)]^{2+}$ (*3*). Thus the formation of the ferryl ion in a very acid medium is impossible, in agreement with the experimental data.

However, as the pH increases, the intermediate peroxo-complex $[Fe^{II}(H_2O)_5(HO_2^-)]^+$ may be formed, which is indicated by analysis of the nature of the HOMO and LUMO levels of the species $[Fe(H_2O)_6]^{2+}$ (*2*) and HO_2^- (*8*) and of the hypothetical complex $[Fe^{II}(H_2O)_5(HO_2^-)]^+$ (*9*) and also by calculation of the charge transfer from the aquoiron(II) complex to H_2O_2 and from HO_2^- to the aquo-complex ($\delta q = -0.05$ e and 0.76 e respectively). Comparison of the energy levels of the MO of the peroxo-complex $[Fe^{II}(H_2O)_5(HO_2^-)]^+$ (*9*), on the one hand, and the MO of the complexes $[Fe^{IV}O(H_2O)_5]^{2+}$ (*10*) and $[Fe^{III}(OH^-)(H_2O)_5]^{2+}$ (*11*), on the other, indicates the possibility of a multistage course for the process.

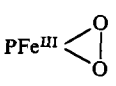
$$[Fe^{II}(H_2O)_6]^{2+} + H_2O_2 \xrightarrow[-H^+]{} [Fe^{II}(H_2O)_5(HO_2^-)]^+ \xrightarrow{H^+}$$

$$\longrightarrow [Fe^{IV}O(H_2O)_5]^{2+} \xrightarrow{H_2O} [Fe^{III}(H_2O)_5(HO^-)]^{2+} + {}^{\cdot}OH$$

Thus, quantum-chemical calculations have confirmed the possibility of the formation of the peroxo-complex $[Fe^{II}(H_2O)_5(HO_2^-)]^+$ and the ferryl ion $[Fe^{IV}O(H_2O)_5]^{2+}$ as intermediates. If the reactions considered are rapid, then it is in fact impossible to detect these species at the present level of experimental technique and only $[Fe^{III}(H_2O)_5(OH^-)]^{2+}$ and the radical ·OH can be detected in the system. This indicates the limits of the existing experimental possibilities and confirms the importance of the quantum-chemical calculations.

IV. Porphyrin and other iron complexes in the catalysis of epoxidation and hydroxylation reactions

Numerous studies (see, for example, Refs 222–229, etc.) have been devoted to the mechanisms of the oxidation of alkenes, alkanes, and other organic substrates by dioxygen under the influence of various monooxygenases (cytochrome P-450 and others) and these problems will not be specially considered here. It is sufficient to note that the prosthetic group in monooxygenases is the iron(III) complex of the porphyrin (P), which in the course of the interaction with O_2 is converted into the highly reactive ferryl species $P^{\cdot+}Fe^{IV}=O$ or $PFe^{IV}=O$ (compounds A and B), which selectively epoxidise or hydroxylate alkenes or alkanes. When these reactions take place only with participation of iron complexes of porphyrin, which may be regarded as the closest structural model of monooxygenases, similar oxoferryl species are also formed. The mechanisms of the epoxidation and hydroxylation by these model compounds have their characteristic features, determined by the nature of the oxidant transferring oxygen to the iron atom of the porphyrin complex, the characteristics of the catalyst and the solvent, and the temperatures.[230–232] Thus the introduction of individual substituents into the porphyrin can prevent the transition of the monomeric peroxoiron(II) complex of the porphyrin[233–236]



into the μ-oxodimer $(PFe^{III})_2O$.[237] Under conditions where the peroxoiron(III) complex of tetramesitylporphyrin (TMP) was acylated by acetic anhydride (Ac_2O) at low temperatures (−45 °C), the product was $TMP^{\cdot+}Fe^{IV}=O$.[238,239] The same reactive species was generated in a series of other model systems[239,240] and in the interaction of peroxidase with H_2O_2.[241] The formation of a similar species from the acylated iron complex (TMPFeOOAc) is the rate-determining stage of the entire process.[242] On this basis, the catalytic model system[242]

$$T_{piv}PPFeBr - Zn(Hg) - MV^{2+} - Ac_2O - O_2 ,$$

was developed. Here $T_{piv}PP$ = tetra(α,α,α,α-*o*-pivaloylaminophenyl)porphyrin, whose complex with iron is not converted into the μ-oxodimer,[243] while the dioxygen complex $T_{piv}PPFe(O_2)$ is stable at room temperature,[244,245] Zn(Hg) is zinc amalgam, which plays the role of the reductant, and MV^{2+} is methylviologen, which facilitates electron transfer from the reductant to $T_{piv}PPFe(O_2)$. The oxidation by this system of substrates (RH) such as cyclohexene, cyclohexane, and 1,2-dimethylcyclohexane was investigated.[242] The reactions occurring in this process are presented in Scheme 17.

Scheme 17

1. $Zn(Hg) + MV^{2+} \longrightarrow MV^{\cdot+}$
2. $Zn(Hg) + PFe^{III} \longrightarrow PFe^{II}$
3. $MV^{\cdot+} + PFe^{III} \longrightarrow PFe^{II} + MV^{2+}$
4. $PFe^{II} + O_2 \longrightarrow PFeO_2$
5. $PFeO_2 + MV^{\cdot+} \longrightarrow PFeO_2^-$
6. $PFeO_2^- + Ac_2O \longrightarrow P^{\cdot+}Fe^{IV}=O + 2\,AcO^-$
7. $P^{\cdot+}Fe^{IV}=O + RH \longrightarrow PFe^{III} + ROH$
8. $P^{\cdot+}Fe^{IV}=O + MV^{2+} \longrightarrow PFe^{III} + \text{products}$
9. $MV^{\cdot+} + O_2 \longrightarrow MV^{2+} + O_2^{\cdot-}$
10. $O_2^{\cdot-} + Ac_2O \longrightarrow AcO_2^{\cdot} + AcO^-$
11. $AcO_2^{\cdot} + RH \xrightarrow[-AcOOH]{} R^{\cdot} \xrightarrow{O_2} ROH + R'O$
12. $P^{\cdot+}Fe^{IV}=O + PFe^{III} \longrightarrow \text{products}$

The following equation can be written for the rate of formation of cyclohexanol (ROH):[246]

$$\frac{d[ROH]}{dt} = \frac{k_7[RH](k_1[MV^{2+}] + k_2[PFe^{III}])}{2\,(k_7[RH] + k_8[MV^{2+}] + k_{12}[PFe^{III}])} + \frac{k_9[O_2](k_1[MV^{2+}] - k_2[PFe^{III}])}{2\,k_3[PFe^{III}]} .$$

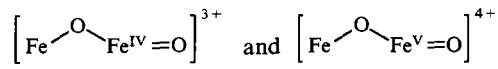
This equation agrees well with experimental data. The activity of the system may be greatly increased by immobilising the above catalyst on a solid polymeric support. The activation of O_2 in the hydrocarbon oxidation processes in the presence of metalloporphyrins can be achieved also by means of other systems.[247,248]

A wider range of iron-porphyrins in acetonitrile solutions was used in subsequent studies and the kinetics of the oxidation of cyclohexane by atmospheric oxygen (at 20 °C) in the presence of carboxylic acids (acetic and benzoic) and a reductant (zinc dust) were investigated both with and without the introduction of methylviologen.[249] The addition of methylviologen was accompanied by the accelerated absorption of O_2 and the generation of H_2O_2. On interaction with H_2O_2, the iron-porphyrins gave rise to a species of the type $P^{\cdot+}Fe^{V}=O$ or $P^{\cdot+}Fe^{IV}=O$ [250] and the oxidation mechanism resembles the 'shunted' mechanism involving the oxidation of hydrocarbons by cytochrome P-450. In the absence of methylviologen, the activation of O_2 in these systems is

apparently achieved almost in the same way as in the cytochrome P-450 system.[249]

In order to form an oxene (an oxygen atom) from O_2 and transfer it to iron, it is necessary to bind the water residue (O^{2-}) to acceptors of some kind (the most suitable acceptor is acetic anhydride). The latter interacts with O_2 and iron-porphyrin and gives rise to the complex PFe–O–O–Ac at −70 °C, which is converted into $P^{\cdot+}Fe{=}O$ at −50 °C.[251] Numerous pieces of evidence have been obtained for the involvement of precisely the $P^{\cdot+}Fe{=}O$ species (detected spectroscopically) in the interaction with alkenes and alkanes.[251–256,279] The ferryl complex with the radical-cation of a nonhaem ligand, which interacts with alkanes,[257] has recently been characterised for the first time, i.e. the study of the analogues of nonhaem monooxygenases has been initiated.

The possibility of the formation of a ferryl species, but this time as part of the composition of a dinuclear complex, has been postulated also in reactions involving the use of methane monooxygenase.[253,258,259] A general method of synthesis of complexes of this kind has been developed[260,261] and alkanes have been oxidised by hydrogen peroxide in acetonitrile with their participation. The postulated mechanism of the oxidation of alkanes includes the formation of a hydroxoperoxoiron complex, which decomposes heterolytically with formation of the ferryl species[253]

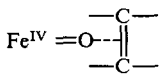


Apart from the haem and nonhaem[262–265] iron complexes, generating ferryl intermediates on treatment with oxenoids (O_2, H_2O_2, ROOH, PhIO, ClO^-, etc.), other active species may also be formed. Brief information about these has been published.[253,266]

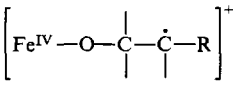
The possibility of the replacement of O_2 by other oxidants capable of transferring an oxygen atom to the metalloporphyrin and of generating the same oxoferryl species as those produced by dioxygen has been discussed in detail in a number of reviews.[5,242,267,268]

Oxidants such as iodosobenzene (PhIO), NaClO, H_2O_2, and hydroperoxides (ROOH) are usually employed in alkene epoxidation reactions catalysed by iron-porphyrin complexes. The epoxidation of alkenes in the FeTPP–PhIO catalytic system (H_2TPP = tetraphenylporphyrin) is stereospecific: only *cis*-epoxides are obtained from *cis*-alkenes. *cis*-Alkenes are much more reactive than their *trans*-isomers. The oxidant for the substrate is the oxoiron(IV)-porphyrin π-radical-cation $P^{\cdot+}Fe^{IV}{=}O$, which can react in different ways with the alkene, affording intermediates:

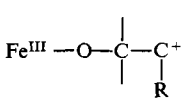
via the direct transfer of an oxygen atom,



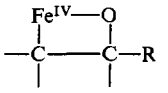
via the free-radical addition of the alkene,



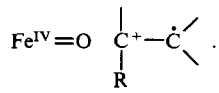
or its electrophilic addition,



via the formation of ferra(IV)oxetane,



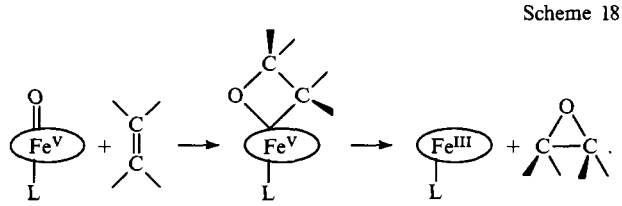
or via electron transfer with formation of an alkene radical-cation[5,269]



The decomposition of the ferra(IV)oxetane to the epoxide, electron transfer or partial charge transfer from the alkene to the oxoiron(IV)-porphyrin π-radical-cation, and other processes have been considered on the basis of kinetic data as the rate-determining stages of the reaction.[5,270]

It was postulated that the intermediate metallooxenes[271] are formed when oxygen is transferred from the highly oxidised oxoiron-porphyrins to the alkenes in the epoxidation reactions.[268,272–275] The following mechanism has been proposed for this process:[272,273]

Scheme 18



It has proved impossible to characterise the intermediate ion complex with the aid of EPR and NMR spectra.[274] The principal piece of evidence for its formation is the proportions of the reaction products. The involvement of the ferra(IV)oxetane in the epoxidation of *cis*-cyclooctene (as well as norbornene) in the presence of *meso*-[tetra(pentafluorophenyl)porphyrinato]-iron(III) chloride [$(F_{20}TPP)Fe^{III}(Cl)$] and C_6F_5IO has been reflected in the mechanism of this process developed on the basis of kinetic data.[276,277]

Scheme 19

$(F_{20}TPP)Fe^{III} + C_6F_5IO \rightleftharpoons (F_{20}TPP)Fe^{III}-OIC_6F_5$

$(F_{20}TPP)Fe^{III}-OIC_6F_5 \longrightarrow (F_{20}^{\cdot+}TPP)Fe^{IV}O + C_6F_5I$

$(F_{20}^{\cdot+}TPP)Fe^{IV}O + \text{alkene} \rightleftharpoons \text{Fe(IV)oxetane}$

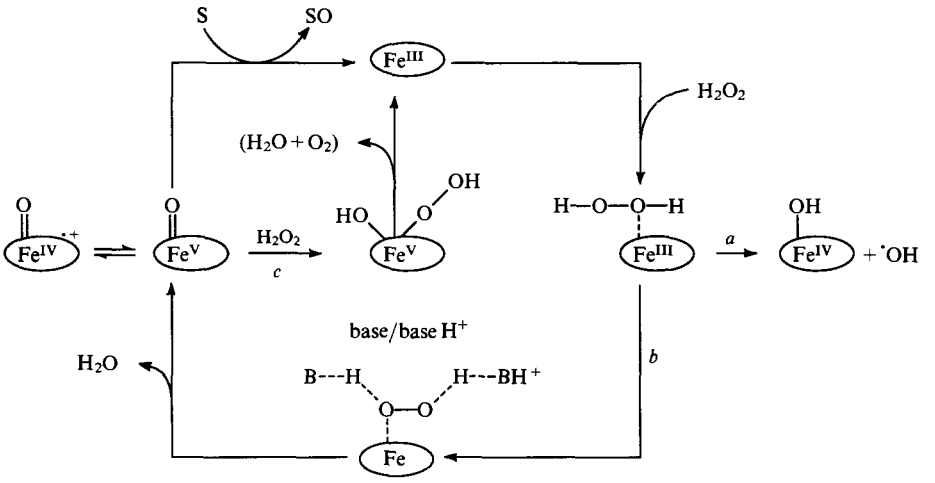
$\text{ferra(IV)oxetane} \longrightarrow (F_{20}TPP)Fe^{III} + \text{epoxide}$

The rate constants indicate that the rate of the process is determined by the stage involving the decomposition of ferra(IV)oxetane to the epoxide and the initial catalyst $(F_{20}TPP)Fe^{III}$.[277]

However, in the study of, for example, the oxidation of *trans*-cyclooctene and other alkenes in the presence of iron porphyrinates as catalysts, the idea of the formation of the ferraoxetane as an intermediate was rejected and the epoxidation was regarded as a result of electron transfer from the alkene to the highly oxidised iron intermediate.[278–281] In the case where the epoxidation substrate was ethene, a biradical intermediate was more likely to participate in the reaction than the ferraoxetane.[282] In the oxoiron-porphyrin systems, radical intermediates are formed preferentially in the reactions with alkenes. Thus one must take into account the possibility that the epoxidation reactions proceed not only via metallaoxetanes but also via other routes, especially since the evidence for the existence of metallaoxetanes is incomplete. This situation resembles somewhat that which has arisen in the study of the possibility of the existence of the oxoferryl ion. Indeed, if the ferraoxetane is highly reactive (this means that it is short lived), then it is difficult or impossible to detect it experimentally. Hence it follows that the question of the formation of metallaoxetanes in the epoxidation reaction remains controversial.[283]

The epoxidation of alkenes (S) by hydrogen peroxide in the presence of iron-porphyrin complexes may proceed via different reaction paths:[5] via a homolytic path with the generation of $^{\cdot}OH$

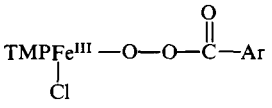
Scheme 20



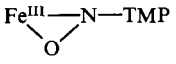
(path *a*, Scheme 20), via a heterolytic path with formation of oxoferryl species (path *b*), and via a catalase path, in which the addition of a second H_2O_2 molecule with formation of O_2 and H_2O is postulated (path *c*). Path *b* is the main one,[5,209] while path *c* is the second in importance.

The epoxidation by hydroperoxides involves their decomposition by iron(III)-porphyrins as a result of a homolytic process with formation of a complex between oxoiron(IV) and the alkoxyl radical RO·,[5,284] i.e. via a free-radical mechanism, although other paths are not ruled out.

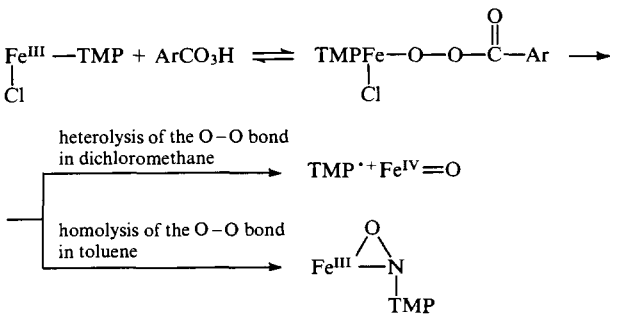
The nature of the solvent also exerts a significant effect on the nature of the intermediates formed and on the process selectivity. Thus, in the epoxidation of a 1 : 1 mixture of norbornylene and α-methylstyrene by chloroperbenzoic acid in the presence of the complex Fe^{III}TMP(Cl) [tetramesitylporphyrinatoiron(III) chloride] as the catalyst at −78 °C in dichloromethane, norbornylene is oxidised to a greater extent than α-methylstyrene (100 : 9).[285] In these reactions, the colour of the solution changed from brown to green after the addition to the system of $ArCO_3H$ as the source of oxygen, which indicates the formation of the oxoiron(IV)-porphyrin π-radical-cation ($TMP^{\cdot+}Fe^{IV}=O$) from the intermediate peracid complex of iron.



When the epoxidation is carried out in an aromatic solvent (toluene), the selectivity with respect to the alkenes changes significantly: comparable amounts of norbornylene and α-methylstyrene are oxidised. In this case, the active species in the epoxidation process is the *N*-oxide[286]



while the formation of the $TMP^{\cdot+}Fe^{IV}=O$ species is less probable.[285]

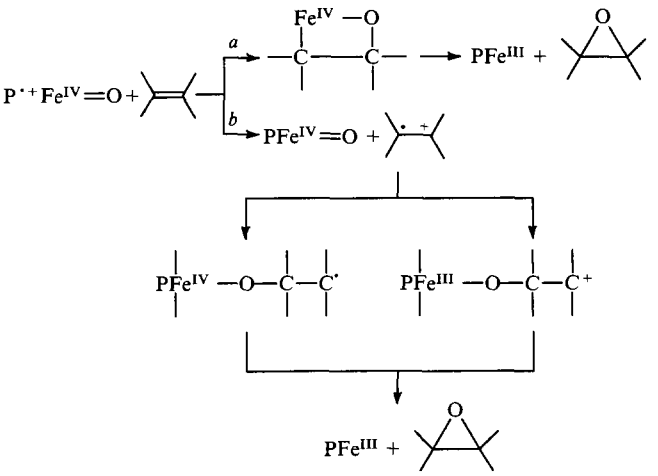


Hence the nature of the active intermediate species produced and the selectivity determined by this factor depend to a large extent on the choice of solvent.

The nature of the substituents in the porphyrin ring and of the axial ligand also influences the activity of the catalyst in the epoxidation reactions. It has been established that an increase in the number of electron-accepting substituents in the porphyrin ring and an increase in the electron-accepting capacity of the axial ligand increase the electrophilicity (oxidising power) of the intermediate oxoiron(IV)-porphyrin π-radical-cation, as a consequence of which the activity of this species increases.

The details of the formation of the type $P^{\cdot+}Fe^{IV}=O$ intermediates in living systems are not as yet entirely clear. One of the possible routes is the formation of a peroxide bridge. For example, in the interaction of the complex $[Fe^{III}(OH^-)(TMP)]^+$ with *p*-$NO_2C_6H_4CO_3H$, the intermediate Fe^{III}(TMP) peroxybenzoate is formed initially and its decomposition then affords $(TMP^{\cdot+})Fe^{IV}=O$, i.e. the same species as in the processes occurring under the influence of cytochrome P-450. It has been suggested that the mechanisms of the epoxidation of different alkenes (for example, norbornene) in the presence of iron(III)-tetraarylporphyrin and pentafluoroiodosobenzene by systems modelling cytochrome P-450 involve the formation of the $P^{\cdot+}Fe^{IV}=O$ intermediate, which interacts with alkenes at a rate close to that of a diffusion process, as a result of which it is impossible to isolate it at normal temperatures. It has been suggested in this connection[287] that electrocyclic addition (*a*) and electron transfer (*b*) mechanisms operate.

Scheme 21



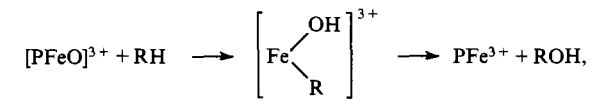
The first mechanism includes the electrolytic addition of the alkene to $Fe^{IV}=O$ with formation of a ferracyclooxetane and the second involves initial electron transfer with formation of a

radical-cation and the subsequent decomposition of the latter into either radical or cationic species. The idea of electron transfer (path *b*) agrees with all the available kinetic data and with the proportions of the reaction products. This is the most probable mechanism of the oxidation of alkenes in both model and enzyme systems.[287]

The characteristic features of processes involving the hydroxylation of alkanes as well as the epoxidation of alkenes depend on the source of oxygen, the nature of the catalyst, and other factors. Thus the oxidation of cyclohexane with the aid of PhIO and FeTTPCl [*meso*-(tetra-*o*-tolylporphyrinato)iron chloride] leads to the formation of cyclohexanol and cyclohexanone, hydroxylation proceeding via a radical mechanism.[5] It has been shown[288] that alkanes may be oxidised also in accordance with a cryptoradical mechanism via the formation of the $P^{\cdot+}Fe^{IV}=O$ active species.

The introduction of substituents into the porphyrin alters the regioselectivity of the oxidation of alkanes.[239,289–291] The regioselectivity of these reactions should depend on steric and electronic factors, which has in fact been demonstrated in a study of the oxidation of hexane by iodosobenzene, where a tetraphenylporphyrin complex of iron (TPPFeCl) was used as the catalyst.[242] The ratio of the oxidation products (2-hexanol and 3-hexanol) was then determined mainly by steric factors, while the ratio of 1-hexanol and 3-hexanol depended on both steric and electronic characteristics of the substituents. An increase in steric hindrance in the porphyrin molecule increased the proportions of both 1-hexanol and 2-hexanol relative to 3-hexanol because of the greater accessibility of the atoms of the first two alcohols. The introduction of electron-accepting substituents into the porphyrin molecule promotes the generation of a more electrophilic oxoferryl species, which also facilitates the formation of the primary alcohol. Thus the study of the steric and electronic effects in model systems made it possible to understand better the nature of similar effects generated by proteins in the monooxygenase enzyme systems.[242,292,293]

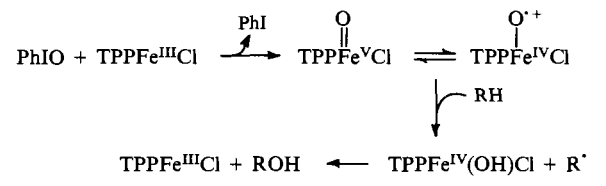
Insertion of an oxygen atom into a C–H bond of the alkane in model systems is apparently a two-electron process, which proceeds with the intermediate formation of an alkylhydroxocomplex,[242] i.e.



$$[PFeO]^{3+} + RH \longrightarrow \left[\begin{array}{c} OH \\ Fe \\ R \end{array}\right]^{3+} \longrightarrow PFe^{3+} + ROH,$$

although the preliminary formation of the $[PFeOH + R^{\cdot}]^{3+}$ couple cannot be ruled out in individual instances.

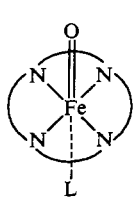
A similar mechanism of the hydroxylation of cyclohexane (RH) by iodosobenzene has been proposed on the basis of the analysis of spectroscopic and EPR data.[294]



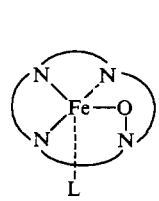
$$PhIO + TPPFe^{III}Cl \xrightarrow{PhI} TPPFe^{V}(O)Cl \rightleftharpoons TPPFe^{IV}(O^{\cdot+})Cl$$

$$TPPFe^{IV}(OH)Cl + R^{\cdot} \xrightarrow{RH} TPPFe^{III}Cl + ROH$$

As in many other investigations (see, for example, Refs 268 and 295–297), in this case the structure of the active catalyst (the oxoferryl species) was represented by formula **8**.

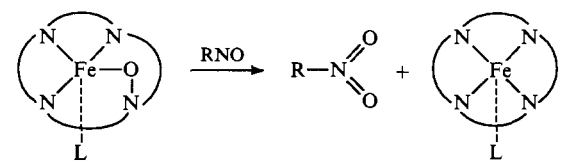


8



9

However, both experimental[298–300] and theoretical[212,301–303] points of view give rise to doubts about structure **8**. As a result, another structure (formula **9**) was proposed in which the oxygen atom was inserted in one of the iron–nitrogen bonds. This model of the oxoiron-porphyrin was used [304] to describe the oxidation of the nitroso-compounds RNO (R = Ar or Bu^t) to the nitro-compounds RNO_2. In the presence of PhIO and the very effective catalyst TPPFe(III)Cl at 0 °C and even at −78 °C (in dichloromethane), this reaction proceeds very rapidly, so that the yield of the nitro-compound reaches more than 90% after several minutes. The tentative mechanism of the formation of RNO_2 from the oxoferryl species **9** can be represented in the following way:[304]



In the presence of *meso*-[tetra(pentafluorophenyl)porphyrinato]iron (F_{20}TPP)Fe, isobutane is hydroxylated at a low temperature in Bu^{t}OH with a selectivity up to 95%. The hydroxylation can occur even at room temperature, but this requires *meso*-[tetra(pentafluorophenyl)-β-octabromoporphyrinato]iron as the catalyst. The proposed mechanism involves the reduction of the iron(III)-porphyrin complex to the iron(II) complex, the formation of an oxoiron μ-complex, and its subsequent conversion into the $Fe^{IV}=O$ form. The latter reacts with isobutane, abstracting a hydrogen atom.[5]

In the presence of hydrogen peroxide as the source of the oxygen, polyhalogenated iron-porphyrins, containing bromine, chlorine, or fluorine in the β-pyrrole positions, catalyse the hydroxylation of aromatic compounds (for example, benzene to phenol) at room temperature.[5]

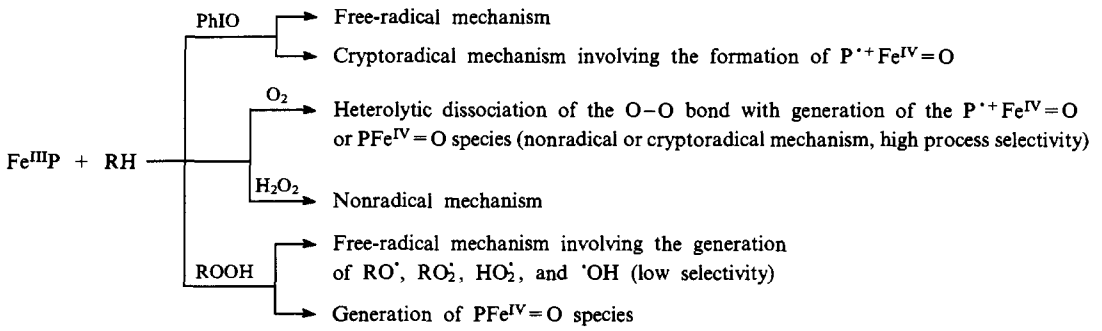
On the other hand, if the oxidants are alkyl hydroperoxides ROOH, then two paths leading to the activation of a C–H bond of the substrate are followed in the presence of iron-porphyrins: via the homolytic cleavage of the O–O peroxide bond with formation of a RO$^{\cdot}$ free radical or via the heterolytic dissociation of this bond with generation of oxoferryl species.[305] Thus the mechanisms of the hydroxylation of alkanes when different oxygen sources are employed can be represented in a general form as shown in Scheme 22.

These hydroxylation mechanisms predominate, although it has been suggested that, depending on the nature of the iron porphyrinates, the choice of the solvent, and temperatures, other mechanisms, differing in certain details, may also operate.[5]

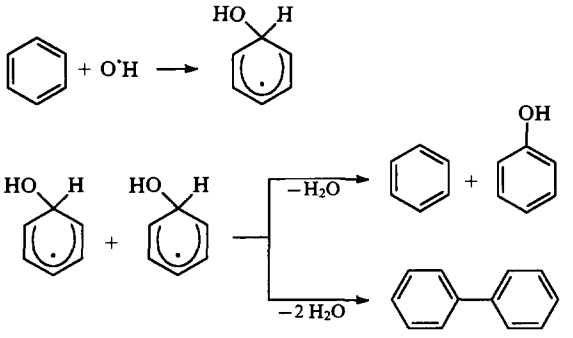
Despite the entire wide variety of the systems modelling monooxygenases and of the iron-porphyrin complexes employed in them, and also despite the dependence of the mechanisms of the oxidation of alkenes and alkanes on the surroundings of the catalyst active centre, one may say that, overall, the processes involving the epoxidation and hydroxylation of organic substrates proceed via the formation of highly reactive oxoferryl iron complexes, although one cannot fully exclude other paths.

Numerous studies have been devoted to the catalytic hydroxylation of the aromatic ring by the Fenton reagent ($Fe^{2+} + H_2O_2$).[130,306–311] Under these conditions, benzene, phenol, and their derivatives are hydroxylated in an aqueous medium via the generation of $^{\cdot}OH$ radicals, which interact with the corresponding substrates via the formation of various intermediate substrate radicals. For example, the hydroxylation of benzene involves the formation of the hydroxycyclohexadienyl radical, which, on subsequent disproportionation or dimerisation, is converted into phenol or biphenyl respectively.

Scheme 22

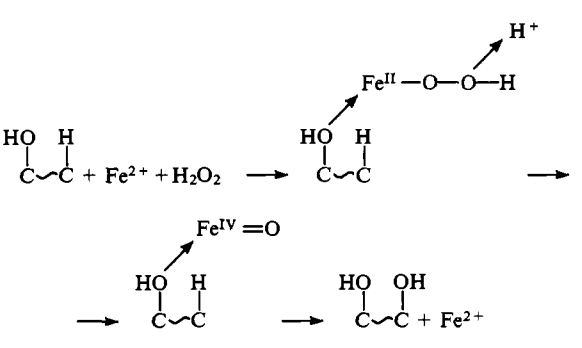


Scheme 23



The effectiveness of the hydroxylation of benzene by the Fenton reagent depends in many respects on the reactant ratios, the pH of the medium, and other factors. The selectivity of the hydroxylation of benzene and phenol derivatives is low and the reaction proceeds via a radical mechanism. It has been shown that, in the hydroxylation of the aromatic ring (especially in benzene) by the Fenton, Udenfriend [$Fe^{3+}-O_2(H_2O_2)$–EDTA–AH_2, where AH_2 = ascorbic acid], and Hamilton (Fe^{3+} – L – H_2O_2, where L = different ligands) systems, the highest yield of the product is observed in the last case.[130] However the selectivity and yields are nevertheless low in all the systems, although it is sometimes possible to increase them.[312]

In aqueous-aprotic or aprotic solvents, both the selectivity and the yield of the hydroxylation products increase in a number of instances and a series of physicochemical characteristics also change. It therefore becomes impossible to describe the hydroxylation reaction as a radical process involving the interaction of ·OH with substrates, and the formation of an oxoferryl species, which promotes the insertion of an oxygen atom in the C–H and C=C bonds and in the aromatic ring, is postulated in this instance. For example, in the oxidation of an alcohol by the Fenton reagent in acetonitrile, proportions of the isomers in the reaction products uncharacteristic of a radical process are observed, which can be accounted for by the fact that the active hydroxylating species is not the ·OH radical but an oxoferryl compound.[313]



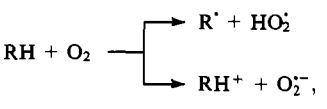
The formation of an oxoferryl intermediate in a process involving the Fenton reagent is also indicated by the extremely high NIH shifts (the migration of hydrogen isotopes on hydroxylation of labelled compounds), which are observed when an oxygen atom is inserted into the 4-deuteriochlorobenzene, 4-deuterioanisole, and 1,4-dideuterionaphthalene in nitromethane and acetonitrile (the NIH shifts are 38%, 30%, and 68% respectively). Small NIH shifts correspond to radical processes. Thus, in the hydroxylation of the first two compounds in water, the NIH shifts were 2% and 3% respectively.[314,315] The appreciable increase in the NIH shift on passing from aqueous to aprotic media shows that in the latter case the hydroxylation of aromatic compounds proceeds via the formation of oxoferryl intermediate.[315]

V. The role of iron compounds in the manifestation of toxicity by the products of the reduction of O_2 in vivo

Iron compounds as catalysts activate O_2 and H_2O_2, generating reactive species $O_2^{\cdot-}$, ·OH, and $LFeO^{2+}$) via the reduction of dioxygen and hydrogen peroxide. These species are responsible for the toxicity of the products of the reduction of O_2, participating both in the peroxide oxidation of lipids and in the decomposition (damage) of deoxyribonucleic acids (DNA) and other biological targets in vivo.[316]

Iron complexes play an important role in the peroxide oxidation of lipids, i.e. in a process where the substrates are aliphatic acids, especially polyunsaturated acids. This process exerts a significant effect on biological membranes, influences the toxicity of medicinal preparations, and contributes to carcinogenesis and other manifestations of the oxidative stress. A detailed survey of the lipid peroxidation processes may be found in many of the articles in a collected volume.[317] In the present section, attention is concentrated on the role of iron compounds in this process and on their interaction with oxygen species, especially with the superoxide radical-ion $O_2^{\cdot-}$.

The direct interaction of O_2 with organic compounds in vivo, i.e.



with formation of $O_2^{\cdot-}$ is extremely slow as a consequence of the endothermic nature of this reaction. However, in biological systems a number of reductants, for example the flavines (FH_2), may interact nonenzymically with O_2 via a radical mechanism to form the hydroperoxyl radical $HO_2^{\cdot}$.[318]



The hydroperoxyl radical is also generated in the autoxidation of cytochrome P-450[319] in the xanthine–xanthine oxidase system and in many other cases.[318]

The interaction of $O^{\cdot}_2^-$ with H_2O_2 affords the radical $^{\cdot}OH$:

$$O^{\cdot}_2^- + H_2O_2 \longrightarrow O_2 + OH^- + {}^{\cdot}OH.$$

However, in aqueous solution the rate constant for this reaction is close to zero and at low concentrations of the starting materials the interaction does not take place noncatalytically.

The presence in vivo of iron ions or compounds (under physiological conditions, at micromolar concentrations) makes this reaction catalytic (the Haber–Weiss reaction).

$$Fe^{3+} + O^{\cdot}_2^- \longrightarrow Fe^{2+} + O_2$$
$$Fe^{2+} + H_2O_2 \longrightarrow Fe^{3+} + OH^- + {}^{\cdot}OH$$
$$O^{\cdot}_2^- + H_2O_2 \xrightarrow{Fe^{III}} O_2 + OH^- + {}^{\cdot}OH$$

In aqueous solutions, $O^{\cdot}_2^-$ has reducing rather than oxidising properties. However, in vivo there are many other reductants (NADPH, NADH, cysteine, etc.), which may compete with $O^{\cdot}_2^-$. Hydrogen peroxide readily permeates through cell membranes, whereas $O^{\cdot}_2^-$ can pass only through special channels.[320] Furthermore, a ferryl species together with a suitable iron complex, similar to the active compounds A and B of peroxidase and cytochrome P-450 as regards the oxidation state of oxoiron, may be formed via the reaction

$$LFe^{3+} + {}^{\cdot}OH \longrightarrow (LFe^{IV}{=}O)^{2+} + OH^-,$$

and also via another route.

The human organism contains on average approximately 4 g of iron, 66% of which is present in haemoglobin, ~ 10% in myoglobin, a small amount in various iron-containing enzymes and in the transport protein transferrin, while the rest is present in storage tissues (ferritin and haemosiderin) and in certain other tissues, organs, and intercellular fluids.[320]

The presence of iron in the living organism makes possible the formation of ferryl species or $^{\cdot}OH$ radicals. The latter are capable of abstracting a hydrogen atom from the lipid (LipH) and of forming a hydrocarbon radical derived from polyunsaturated aliphatic acids (Lip$^{\cdot}$), which reacts rapidly with O_2 and generates a peroxyl radical ($LipO^{\cdot}_2$). This radical interacts with the lipid molecule, forming the lipid hydroperoxide (LipOOH), which is fairly stable under physiological conditions. One of the functions of compounds of iron (and certain other transition metals) consists in catalysing the decomposition of LipOOH. In vivo, such iron complexes may be formed by phosphates, phosphate esters (ADP), and porphyrins (haemoglobin, methaemoglobin, peroxidase, cytochrome P-450, other cytochromes, and nonhaem iron-proteins) and can participate in the propagation of the membrane lipid peroxidation chain with formation of alkoxyl and alkylperoxyl radicals (LipO$^{\cdot}$ and $LipO^{\cdot}_2$ respectively), which stimulate the given chain reaction. All these reactions can be represented as follows:[320]

$$LipH + {}^{\cdot}OH \longrightarrow Lip^{\cdot} + H_2O,$$
$$Lip^{\cdot} + O_2 \longrightarrow LipO^{\cdot}_2,$$
$$LipO^{\cdot}_2 + LipH \longrightarrow LipOOH + Lip^{\cdot},$$
$$LipOOH + LFe^{2+} \longrightarrow LFe^{3+} + OH^- + LipO^{\cdot},$$
$$LipOOH + LFe^{3+} \longrightarrow LFe^{2+} + H^+ + LipO^{\cdot}_2.$$

It is frequently assumed that the iron complexes initiate the peroxide oxidation of lipids. In reality, however, in most cases they also induce the decomposition of the lipid hydroperoxides formed previously and the generation of oxygen radicals ($O^{\cdot}_2^-$ and $^{\cdot}OH$).

$$LFe^{2+} + O_2 \rightleftharpoons LFe^{2+}O_2 \longleftrightarrow LFe^{3+}O^{\cdot}_2^- \rightleftharpoons LFe^{3+} + O^{\cdot}_2^-$$
$$2O^{\cdot}_2^- + 2H^+ \longrightarrow H_2O_2 + O_2$$
$$LFe^{2+} + H_2O_2 \longrightarrow LFe^{3+} + OH^- + {}^{\cdot}OH$$

Indeed the hydroperoxides formed on peroxidation are unstable and their subsequent decomposition to iron(II, III) compounds leads to the formation of numerous products, containing aldehyde, keto-, hydroxy-, epoxy-, and carboxy-groups. The aldehyde products formed are frequently responsible for the poor taste of many food products, in particular for the incipient bitter taste of fats and oils. It has been shown that highly reactive aldehydes, such as hydroxyalkenals (for example, 4-hydroxynonenal) are formed in vivo on peroxidation of liver microsomal lipids and that, by accumulating in the NADPH–Fe systems, they inhibit the syntheses of many substances important for cells.[321]

The available kinetic data also fail to confirm the hypothesis[322] that the peroxidation of lipids is initiated by species of the type $Fe^{2+}O_2 \leftrightarrow Fe^{3+}O^{\cdot}_2^-$ or $O^{\cdot}_2^-$. The $O^{\cdot}_2^-$ species cannot be an initiator in the absence of iron ions.[323] Indeed, it has been shown[324] that the cell toxicity of the product of the adriamycin (an antibiotic used in tumour therapy) redox cycle in vivo is associated with the enhanced formation of oxygen radicals, which initiate the peroxide oxidation of lipids only in the presence of Fe^{3+} ions.

Redox cycle:

$$\text{Adriamycin} + \tfrac{1}{2}\text{NADP} + H^+ \xrightarrow{\text{NADPH–cytochrome P-450}} \text{adriamycin semiquinone} + \tfrac{1}{2}NADP^+$$
$$\text{Adriamycin semiquinone} + O_2 \longrightarrow \text{adriamycin} + O^{\cdot}_2^-$$

Stimulation:

$$Fe^{3+} + O^{\cdot}_2^- \longrightarrow Fe^{2+} + O_2$$

Peroxidation of lipids:

$$LipH + O_2 + Fe^{2+} + H^+ \longrightarrow Lip^{\cdot} + H_2O_2 + Fe^{3+}$$
$$Lip^{\cdot} + O_2 \longrightarrow LipO^{\cdot}_2$$
$$LipO^{\cdot}_2 + LipH \longrightarrow LipOOH + Lip^{\cdot}$$
$$Fe^{3+} + \tfrac{1}{2}NADPH + H^+ \xrightarrow{\text{NADPH–cytochrome P-450}} Fe^{2+} + NADP^+$$

Seemingly the $^{\cdot}OH$ radical should be the initiator of the peroxidation of lipids.[325] However, another point of view has been put forward nowadays, according to which the initiator of this process is tentatively identified as the ferryl species and not the $^{\cdot}OH$ radical, since the latter cannot be detected with the aid of usual trapping agents. It may be that the $^{\cdot}OH$ radical reacts with the hydrophilic lipid 'heads' and does not therefore reach the aliphatic acid side chains.[320] The formation of the ferryl species has also been postulated in the model microsomal and xanthine oxidase oxidation processes.[322]

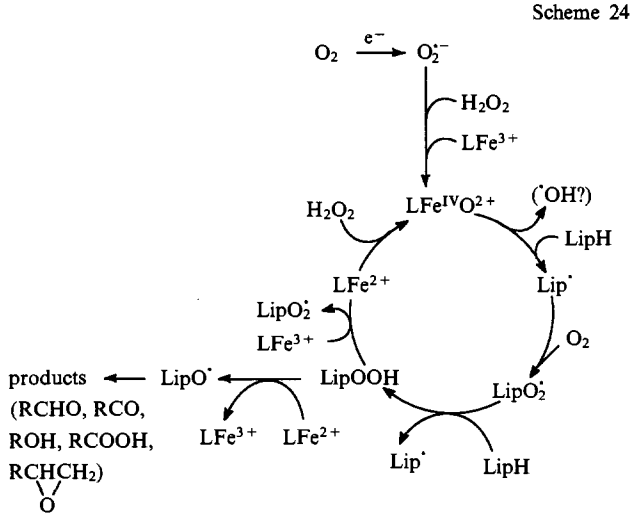
$$ADP{-}Fe^{2+}O_2 \xrightarrow[-2e^-]{2H^+} ADP{-}[FeO]^{2+} + H_2O$$

It has been assumed that this species may be the main product of the reaction of the adenosine diphosphate (ADP) complex of iron(II) with H_2O_2. This assumption was based on the fact that the addition of mannitol (which removes the $^{\cdot}OH$ radicals) to the $ADP{-}Fe^{2+} - H_2O_2 - LipH$ system did not alter the rate of peroxidation of lipids.

Similar claims concerning the formation of the ferryl species have been made in a communication[323] which dealt with the study of the model nonhaem system Fe^{2+} – diethylenetriaminepentaacetic acid – H_2O_2 – LipH. However, the idea that the oxoferryl species plays an initiating role requires further confirmation and elucidation.

Nevertheless, the peroxidation of lipids catalysed by the ferryl species $LFeO^{2+}$ (or 'OH?) may be illustrated by Scheme 24.

Scheme 24



Reductants such as ascorbate, NADH, NADPH, and others, which on interaction with H_2O_2 can also generate 'OH and can play an even more important role than $O_2^{\bullet-}$, are present in the cells in fairly large amounts.[326] Furthermore, H_2O_2 may oxidise ADP – Fe^{2+} to ADP – F^{3+} (L = ADP), generating 'OH, although the latter does not initiate the peroxidation of the lipid under these conditions, which is indicated by the finding that mannitol (an 'OH trapping agent) does not inhibit the reaction.[327] Thus the problem of the initiation of the peroxide oxidation of lipids is to a large extent controversial.

Together with the peroxide oxidation of lipids, there are a multiplicity of other processes, whose substrates are biological targets capable of being damaged by the products of the catalytic reduction of O_2 in the presence of iron compounds (degradation of deoxyribonucleic acid, phagocytosis, autoxidation of monosaccharides, and other reactions). In order to carry out in vivo reactions of the Haber – Weiss type, it is necessary to have not only sources of $O_2^{\bullet-}$ (discussed above), but also sufficient amounts of H_2O_2 and iron compounds.

Hydrogen peroxide is produced by bacteria of various types, it is generated in phagocytes, in spermatozoa, in mitochondria, and in many other formations. Thus H_2O_2 is produced by a series of enzymes (for example, by glycolate and urate oxidases).[320] the crystalline lens of the human eye also contains micromolar concentrations of hydrogen peroxide.[328] Its vapour is evolved even during human respiration [329] (although such vapour may be partly or fully the product of activity of dental bacteria [320]).

Iron compounds, not bound to a protein, at concentrations of several micromoles per litre, migrating between transferrin, cell cytoplasm, mitochondria, and ferritin and interacting with H_2O_2, can effect Fenton type reactions in which 'OH radicals are generated.[330] In aqueous solution, the $O_2^{\bullet-}$ species reduce iron(III) to iron(II), creating thereby conditions for the occurrence of the catalytic Haber – Weiss reaction accompanied by the formation of the 'OH radical. Under these conditions, different ligands affect differently the ability of $O_2^{\bullet-}$ to reduce iron(III). For example, the specific ligands desferrioxamine and bathophenanthroline inhibit this reaction [iron(III) is not reduced to iron(II)], while ethylenediaminetetraacetic acid, adenosine triphosphate, and picolinic acid promote it by the rapid reduction of the corresponding iron(III) complexes to iron(II) complexes.[320]

The use of specific complex forming agents, which bind iron(III) and thereby prevent its reduction, can promote the inhibition of the oxidative damage in the therapy of afflictions of the heart, the kidneys, the skin, and other tissues and can also weaken the post-traumatic degeneration of tissues in the brain and the spinal column.[193]

The 'OH radical formed in vivo by the Haber – Weiss reaction acts more disruptively and specifically than the same radical generated by radiolysis. In the former case, following its formation the radical interacts (by virtue of its high reactivity) with the nearest biological target separated from it by not more than 5 – 10 Å, while in the latter case the interaction takes place over a larger volume of the solution. On the other hand, if the $O_2^{\bullet-}$ radical-ion, with a low reactivity towards many biological molecules, is generated, then it is capable of diffusing over fairly long distances until it encounters an iron(III) complex of a biological target (for example, DNA).[193,196–198] The iron(III) in these complexes is reduced by the $O_2^{\bullet-}$ species to iron(II). By interacting with H_2O_2, the iron(II) compounds may generate 'OH in the vicinity of a biological target, which serves as the ligand for iron(III) and a substrate for 'OH. These 'OH radicals, generated by a locally specific mechanism, act more effectively and selectively than the same radicals obtained directly in the cell.[331]

The phagocytotic mechanism of the action of 'OH in the cell is described similarly.[332] The biological target may be protected by introducing into the system substances such as thiourea and mannitol, which are capable of binding iron and of extracting it from the biological targets.[196,197,333]

An alternative to the formation of 'OH radicals is the generation of iron(IV) or ferryl species, which, being less reactive than 'OH, exhibit also a different toxicity in relation to biological objects. Such compounds have been identified in the reactions of hydrogen peroxide with the water-soluble iron(III)-porphyrin.[188]

Protection against the toxicity of $O_2^{\bullet-}$ is known to be achievable with the aid of many iron(III) compounds, which catalyse the dismutation of $O_2^{\bullet-}$ via the action of superoxide dismutases in accordance with the 'ping-pong' mechanism.

$$Fe^{3+} + O_2^{\bullet-} \longrightarrow Fe^{2+} + O_2$$

$$\underline{Fe^{2+} + O_2^{\bullet-} + 2H^+ \longrightarrow Fe^{3+} + H_2O_2}$$

$$2O_2^{\bullet-} + 2H^+ \longrightarrow H_2O_2 + O_2$$

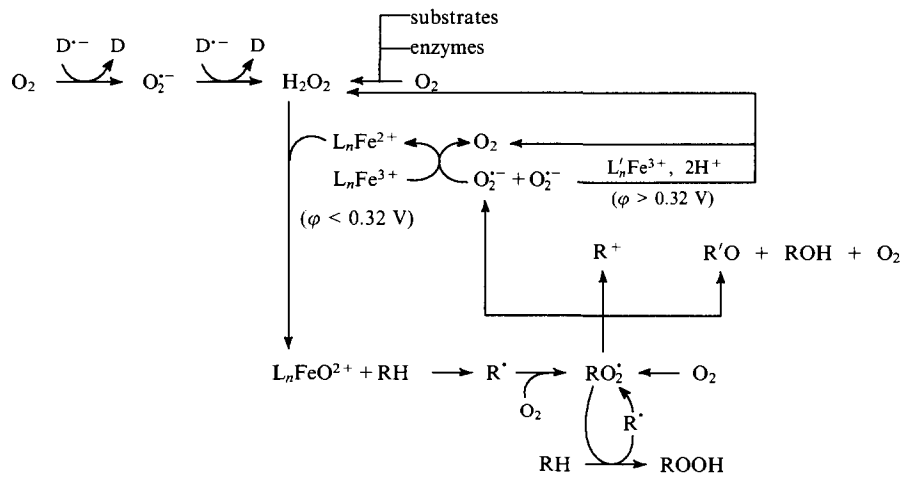
If the rate of the third stage exceeds significantly the rate of the second stage of the Haber – Weiss mechanism, then the iron compound will protect the biological system against the toxicity of $O_2^{\bullet-}$.[331]

A number of enzymes (catalase, glutathione peroxidase, cytochrome *c* peroxidase) protect the organism against oxidative damage.[334]

A thermodynamic condition for the occurrence of the Haber – Weiss reaction is a fairly low reduction potential of the iron complex ($\varphi = 0.32$ V under standard conditions).[335] For a higher potential ($\varphi = 0.32 - 0.94$ V), the iron complexes catalyse the dismutation reaction, but not the Haber – Weiss reaction. Thus, by employing different ligands, it is possible to vary the superoxide toxicity (this includes also a reduction of the toxicity). The inhibition or, conversely, the enhancement of the superoxide toxicity depend not so much on the stability of the iron(III) complexes formed with specific or nonspecific ligands as on the oxidation – reduction potential of iron, which varies under their influence. Depending on this factor, the process proceeds either via the dismutation path, whereupon the toxicity is suppressed, or via the path involving the Haber – Weiss reaction whereupon it is enhanced.

The overall mechanism of the manifestation of the oxygen toxicity has been described.[335,336] It can be supplemented slightly by taking into account the influence of specific (L') and nonspecific (L) ligands (Scheme 25).

Scheme 25



The electron donor $D^{\cdot -}$ reduces O_2 to $O_2^{\cdot -}$ and H_2O_2. By acting on L_nFe^{II}, the latter forms the ferryl species L_nFeO^{2+}, which, being an oxidant, interacts with the biological target, generating $R^{\cdot}$. On combining with O_2, the radical $R^{\cdot}$ gives rise to $RO_2^{\cdot}$, which is converted jointly with RH into the hydroperoxide ROOH and $R^{\cdot}$. Depending on the nature of the ligand (L or L') and the oxidation-reduction potentials φ, either the Haber–Weiss reaction or the dismutation reaction can take place. Lipids can also serve as the biological targets RH. Since the cell contains numerous reductants (for example, ascorbic acid), which may reduce iron(III) directly to iron(II) at a higher rate than that achieved by the superoxide radical-ion $O_2^{\cdot -}$, the decisive role of the latter in the manifestation of oxygen toxicity becomes doubtful, although it is not excluded.[187,337]

Oxygen toxicity is manifested in the autoxidation of monosaccharides (for example, glyceraldehyde). The monosaccharide enediols formed are oxidised catalytically by iron compounds, generating ketoaldehydes, $O_2^{\cdot -}$, H_2O_2, and $^{\cdot}OH$.[338] The oxidation of monosaccharides may be accompanied by the glycolysis of the proteins and a colour change (to brown). It promotes the appearance of hyperglycaemia (diabetes), i.e. the joint oxidation of tissues, which is frequently accompanied by secondary processes — atherosclerosis, kidney failure, cataracts, and pathological conditions in the eye retina. The autoxidation of monosaccharides may promote the appearance of diabetic complications. The concentration of monosaccharides increases greatly in hyperglycaemia, i.e. the content of hydrogen peroxide and other reactive species ($O_2^{\cdot -}$, $^{\cdot}OH$), participating in the autoxidation of monosaccharides, also rises. For example, the above species, toxic to cells, may be generated in erythrocytes and in the crystalline lens of the eye. The catalytic oxidation of the monosaccharide enediols by iron compounds may be accompanied by oxidative stress in hyperglycaemia and the atherosclerosis associated with it.[338]

VI. Conclusion

Comparative analysis of the experimental and theoretical data on the catalytic activation of dioxygen and hydrogen peroxide and the oxidation of organic substrates by these compounds made it possible to devise general mechanisms for these processes. In considering the mechanisms of catalytic reactions, the possible role of intermediates of the type of ferryl ions and complexes was emphasised, since their identification and vigorous investigation have begun comparatively recently. We attempted to consider from a single standpoint three main mechanisms of catalytic oxidation-reduction processes: radical, radical-chain, and ion-molecule. Since porphyrin and certain other iron complexes as well as ferryl species play an extremely important role in living organisms, the epoxidation and hydroxylation reactions with participation of these species have been examined in greatest detail. Using the general mechanisms of the catalytic oxidation-reduction reactions, we discussed in detail also the role of iron compounds in the manifestation of toxicity by the products of the reduction of dioxygen in vivo.

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Heterogeneous catalytic synthesis of alkanethiols and dialkyl sulfides from alcohols and hydrogen sulfide

A V Mashkina

Contents

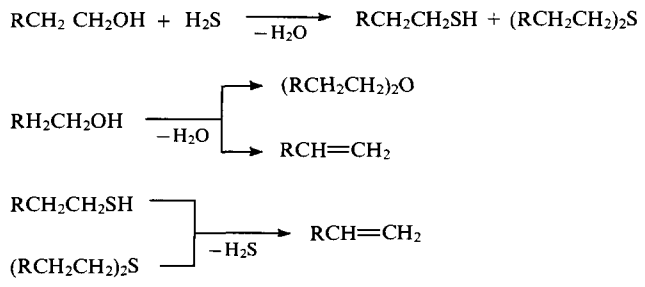
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Abstract. The results of studies of the heterogeneous acid-base catalysis of reactions of alcohols with hydrogen sulfides, which yield alkanethiols and dialkyl sulfides, are surveyed. Data concerning the activity and selectivity of the catalysts under the reaction conditions are considered. A relation is established between the catalytic and acid–base properties of the catalysts. The mechanism of the thiolation reaction is discussed and the criteria for the selection of the effective catalysts are formulated. The bibliography includes 97 references.

I. Introduction

Catalysis has played an important role in the development of the chemistry of organic compounds of sulfur.[1] This applies also to the synthesis of compounds with thiyl and sulfide groups, in particular of alkanethiols and dialkyl sulfides, which have valuable properties and have therefore found extensive applications.

Alkanethiols and dialkyl sulfides may be obtained also by noncatalytic methods, but these require the employment of expensive starting materials, which are in many cases difficult to obtain. It is more convenient to synthesise these substances from the industrially produced alcohols and hydrogen sulfides.



A V Mashkina Laboratory for the Catalytic Reactions of Sulfur Compounds, Boreskov Institute of Catalysis, Siberian Branch of the Russian Academy of Sciences, prosp. akad. Lavrent'eva 5, 630090 Novosibirsk, Russian Federation.
Fax (7-383) 235 57 56. Tel (7-383) 235 76 92

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The thermodynamic feasibility of reactions involving the formation of alkanethiols and dialkyl sulfides from alcohols and hydrogen sulfide, the dehydration of alcohols with formation of a dialkyl ether and an alkene, and the decomposition of alkanethiols and dialkyl sulfides with formation of hydrogen sulfides and alkenes is very high.[1–5]

The conversion of alcohols into thiols occurs only in the presence of catalysts. By regulating their composition and the reaction conditions, it is possible to direct the process towards the formation of the desired product. The heterogeneous-catalytic method of synthesis of alkanethiols and dialkyl sulfides is the most promising because it is highly productive and is susceptible to technological application, which makes it possible to simplify the isolation of the reaction products and the catalyst from the reaction medium and to reduce the amount of ecologically harmful waste.

The practical application of effective processes leading to the synthesis of alkanethiols and dialkyl sulfides requires active and selective solid catalysts. In 1910, Sabatier[6] was the first to use a solid catalyst (thorium dioxide) in the gas-phase reactions of alcohols with hydrogen sulfide, which lead to the formation of alkanethiols and dialkyl sulfides. In 1921, this reaction was achieved[7] in the presence of ThO_2 deposited in an amount of 25 mass% on pumice, at 260 – 380 °C, atmospheric pressure, and for the molar ratio H_2S : alcohol = 0.75 – 2.0. The main products of the reactions of hydrogen sulfide with methanol, ethanol, 1- and 2-butanols, and 2-pentanol were the corresponding thiols, with yields of 35% – 52%; aldehydes were also formed in yields up to 20% together with small amounts of alkenes and traces of dialkyl sulfides. During the first world war, this catalyst was used to produce butane-1-thiol from 1-butanol and hydrogen sulfide.[2,8,9] Further studies were directed to the search for more active and selective catalysts, which led to the creation abroad in the 1950s – 1970s of industrial processes in which unpromoted alumina was employed initially and then also other catalysts. However, neither the technology of the manufacturing process nor the catalysts employed are known.[8]

The available information about the catalysts and the conditions in the synthesis of alkanethiols and dialkyl sulfides from alcohols and hydrogen sulfide referring to the period up to 1970 – 1975 is contained mainly in patents and the reviews based on them.[2,8–10] It is claimed that catalysts active in the syntheses of methanethiol and dimethyl sulfide may be used in the synthesis of alkanethiols and dialkyl sulfides from hydrogen sulfide and various alcohols, but specific examples almost always refer to the reaction of methanol with hydrogen sulfide. Certain theoretical publications also appeared during this period, but the relevant

studies were not systematic and no attempts were made at a quantitative comparison of the properties of the catalysts in the thiol formation processes. Since the publication of the reviews mentioned above,[2,8-10] data have accumulated, but have not yet been arranged systematically, on the catalysts used in the gas-phase heterogeneous synthesis of alkanethiols and dialkyl sulfides from alcohols and hydrogen sulfide and on the mechanism of the thiolation reactions, which is important for the prediction of the catalytic action and the creation of new effective catalysts. These data are surveyed in the present review.

II. Catalysts for the conversion of alcohols into thiols by hydrogen sulfide

Alcohols are converted into thiols by treatment with hydrogen sulfide in the presence of both massive and supported catalysts. The rate of reaction (w) and the selectivity (S) in the formation of the thiol and the sulfide, which is equal to the ratio of the yield of the corresponding product to the degree of conversion of the alcohol (x), depend on the reaction conditions: temperature, molar ratio of hydrogen sulfide to the alcohol (M), the pressure (P)†, and the contact time (τ)‡.

1. Metal oxides and sulfides

The reaction of alcohols with hydrogen sulfides is accelerated, albeit to different extents, by massive metal oxides and sulfides. Silicon dioxide is relatively ineffective in the conversion of alcohols into thiols.[11-13] Thus, in the interaction of methanol with hydrogen sulfide in the presence of SiO_2, the yields of methanethiol and dimethyl sulfide were 5 mol% and 1.2 mol% respectively (360 °C, M = 0.6–1.6, τ = 42 s, $x \leqslant 20\%$).[11,12] The activity of magnesium oxide is also low in this reaction: the yield of methanethiol was 2 mol%–3 mol% (350 °C, M = 0.5–2.0, $\tau \approx 2$ s).[14] The reaction of 1-butanol with hydrogen sulfide on MgO leads to the formation of butane-1-thiol and butene in 32 mol% and 50 mol% yields respectively (300 °C, M = 10, τ = 21 s, x = 62%).[15] High yields of sulfur-containing products have been attained in the conversion of alcohols into thiols on a series of massive oxides. It has been found[14] that, in the interaction of methanol with hydrogen sulfide on TiO_2 (anatase), the selectivity with respect to methanethiol is 31% and 57% and that with respect to dimethyl sulfide is 52% and 41% respectively for M = 0.5 and 2.0 (350 °C, $\tau \approx 5$ s, and x = 32%–91%). On TiO_2 (rutile), the degree of conversion under these conditions is lower (15%–45%), but a high selectivity with respect to methanethiol and a reduced selectivity with respect to dimethyl sulfide are observed (85%–95% and 3% respectively). Methanol decomposes with formation of methane on both modifications of TiO_2. The conversion of ethanol into the thiol takes place less selectively on TiO_2: dimethyl ether (15%) and ethene (19%) are formed in addition to ethanethiol and diethyl sulfide [yields 56 mol% and 9 mol% respectively (320 °C, M = 2.5, x = 97%)].[2] Tungsten and vanadium oxides exhibit a high activity in the conversion of alcohols into thiols. Thus, on WO_3 at 360 °C and for M = 1.6, the yield of methanethiol corresponding to the complete conversion of methanol was 81 mol% (τ = 0.5 s), whilst the yield of dimethyl sulfide was 31 mol% (τ = 4.2 s).[11]

The activities of the Mg, Ti, Zr, Ce, and Al oxides in the reaction of methanol with hydrogen sulfide for M = 0.5–2.0, 350 °C, and τ = 2–6 s have been compared.[14] It was found that the degree of conversion of the alcohol diminishes on all the catalysts with decrease in the H_2S:CH_3OH molar ratio and the selectivity with respect to methanethiol falls, but the selectivity with respect to dimethyl sulfide increases. The oxides investigated differ in their catalytic properties. Thus the activities of the oxides in the conversion of methanol into the thiol (for M = 1) vary in the following sequence:

$$Al_2O_3\,(99) > CeO_2\,(59) \geqslant TiO_2\ \text{(anatase)}\,(52) > > ZrO_2\,(34) > MgO\,(3)\ .$$

The degree of conversion of methanol [x(%)] is indicated in brackets. The catalysts can be arranged in approximately the same sequence in terms of the selectivity in the formation of dimethyl sulfide (the selectivity expressed in % is given in brackets):

$$Al_2O_3\,(84) > TiO_2\ \text{(anatase)}\,(57) > ZrO_2\,(9) \geqslant \geqslant CeO_2\,(7) > MgO\,(0)\ .$$

On the other hand, the virtually opposite sequence is observed for the variation of the selectivity of the catalysts with respect to methanethiol:

$$MgO\,(100) > ZrO_2\,(90) > CeO_2\,(50) > > TiO_2\ \text{(anatase)}\,(36) > Al_2O_3\,(15)\ .$$

The authors[14] attribute the observed variations to the different acid–base characteristics of the above oxides. The strong basic centres in magnesium oxide and the higher electronegative charge on the oxygen atom promote a low degree of conversion of methanol and a high selectivity with respect to methanethiol.

The low rate of the reaction of methanol with hydrogen sulfide on certain oxides can be explained also by their low specific surfaces (for example, the specific surface of ZrO_2 is 18 $m^2\ g^{-1}$ and that of ZrO is 5.4 $m^2\ g^{-1}$). Mashkina et al.[11] inferred the relative activities of the oxides from the rate of reaction per unit surface for a constant degree of conversion achieved by varying the contact time. The highest rate of conversion of methanol and a high selectivity with respect to methanethiol are observed on tungsten and vanadium oxides; aluminium and titanium oxides are approximately an order of magnitude less active, while Zr, Be, Mg, Zn, and Si oxides are less active by 2–3 orders of magnitude (Table 1). The specific activities of the majority of the oxides investigated increase with increase in the ionisation potentials of the cations (Table 1), which may indicate a dependence of the activity on the electron-accepting capacity of the cation.

Table 1. The specific activities and selectivities of metal oxides in the reaction of methanol with hydrogen sulfide (360 °C, M = 1.6, x = 50%–60%).[11]

Catalyst (ionisation potential/eV)	w/ mmol $m^{-2}\ h^{-1}$	S (%)	
		CH_3SH	$(CH_3)_2S$
SiO_2 (45.13)[a]	0.006	22	7
BeO_2 (18.21)[a]	0.04	47	0
MgO (15.03)[a]	0.05	65	0
ZrO_2 (33.97)	0.06	85	4
ZnO (17.96)	0.10	0	12
TiO_2 (43.24)	1.2	56	27
γ-Al_2O_3 (28.44)	1.9	37	35
η-Al_2O_3 (28.44)	3.2	35	38
WO_3 (56)	32	73	13
V_2O_5 (65.2)	44	85	0.4

[a] $x \leqslant 40\%$.

† In most cases, the experiments are carried out at P = 0.1 MPa, so that henceforth the pressure will be indicated only when it is higher than atmospheric.

‡ The contact time τ is equal to the ratio of the volume of the catalyst (in ml) to the gas flow rate (in ml s^{-1}) at 20 °C and P = 0.1 MPa. In certain cases the values of τ calculated from the volume flow rates quoted in the relevant communications have been used in the review; such quantities are designated by the symbol $\approx$.

Although the activity of aluminium oxide calculated per m^2 of the surface area is low, it has an advantage over other massive oxides, since it can have a large surface area thus ensuring a high activity per unit weight of catalyst. Furthermore, Al_2O_3 is fairly thermostable, is relatively readily available, and is cheap. For this reason, it was initially preferred to use Al_2O_3 as the catalyst for the conversion of alcohols into thiols.[2,8] In the interaction of methanol with hydrogen sulfide in the presence of γ-Al_2O_3, a high rate of reaction per unit weight of the catalyst is attained. The principal reaction products are methanethiol, dimethyl ether, and dimethyl sulfide, whilst under severe conditions carbon oxides and methane are also formed. In the presence of a deficit of hydrogen sulfide relative to methanol and at a high temperature, dimethyl sulfide is formed preferentially. In order to obtain methanethiol with a high selectivity, it is necessary that the hydrogen sulfide : methanol ratio should be greater than 5.[3] The phase composition of the catalyst is also improtant — γ- and η-Al_2O_3 are the most active.[11,12,16] The inadequate stability of Al_2O_3 during a prolonged thiolation reaction, caused by the saturation of the surface by coke, has been noted.[13] The high activity of aluminium oxide in the reaction involving the conversion of methanol into the thiol has been explained[11] by the presence in the oxide of paired acid–base centres promoting the activation of the reactants.

The reactions of higher alcohols with hydrogen sulfide on Al_2O_3 take place at a lower temperature than the reaction of methanol. The conversion of the alcohol into the thiol is accompanied by its dehydration with formation of an ether and an alkene, which entails a decrease in selectivity in the formation of sulfur-containing products. Table 2 presents some examples of the conversion of alcohols into thiols in the presence of Al_2O_3.

The massive Cd, Sb, Ni, W, Mo, Re, K, and Na sulfides also accelerate the interaction of alcohols with hydrogen sulfide,[2,3,11,13,20,21] although it has been noted[2] that they sometimes exhibit a reduced activity in the thiolation reaction compared with the corresponding metal oxides. Thus Sb_2S_3 has a low activity in the reaction of methanol with hydrogen sulfide: $x = 14\%$ and methanethiol is not formed, the yield of dimethyl sulfide amounting to 5 mol% (360 °C, $M = 1.6$, $\tau = 50$ s).[11] In the reaction of ethanol with hydrogen sulfide[2] on the NiW sulfide catalyst, ethanethiol is formed in 6 mol% yield (220–280 °C, $M = 3.5$, $\tau = 3.5$–4.0 s, $x = 21\%$), while on WS_2 the yield of ethanethiol is 27% (280 °C, $M = 3.3$, $\tau = 3.3$–4.0 s, $x = 99\%$). On Re_2O_7, the yield of dodecane-1-thiol, obtained from 1-dodecanol and hydrogen sulfide, is 55 mol%. The reaction is accompanied by the formation of a large amount of dodecene (240 °C, 10 MPa, duration of the experiment in an autoclave 3 h, $M = 0.7$; the reaction takes place in the presence of hydrogen).[22]

2. Aluminosilicates and zeolites

Silicon dioxide, which hardly exhibits any activity in the conversion of alcohols into thiols, acquires such an activity when some of the $(SiO_4)^{4-}$ ions are replaced by $(AlO_4)^{3-}$ ions with formation of aluminosilicates — amorphous (AlSi) and crystalline (zeolites). Thus, in the reaction of methanol with hydrogen sulfide on AlSi, the rate of conversion of methanol is 14 mmol g^{-1} h^{-1}, which is seven times higher than on SiO_2: under these conditions, the selectivity is 6% with respect to methanethiol and 62% with respect to dimethyl sulfide; dimethyl ether is formed (360 °C, $M = 1.6$, $\tau = 6.3$ s, $x = 87\%$).[11] In the presence of a reduced content of hydrogen sulfide in the reaction mixture, the selectivities with respect to methanethiol and dimethyl sulfide are 5% and 68% respectively (450 °C, $M = 0.6$, $\tau \approx 9$ s, $x = 76\%$).[23] The higher activity of AlSi compared with SiO_2 is due to the difference between their acid–base properties: SiO_2 contains only very weak proton and basic centres, while AlSi contains strong proton and Lewis acid centres as well as moderately strong basic centres, which participate in the activation of the reactants.[11] On the amorphous AlSi, 2-propanol reacts with hydrogen sulfide to form propane-2-thiol in 29%–47% yield (275–300 °C, $P = 0.9$ MPa, $M = 5$–6, $\tau \approx 0.14$–0.50 s).[19]

The conversion of alcohols into thiols is also accelerated by decationated zeolites. On HNaX, the selectivities in the formation of methanethiol and dimethyl sulfide from methanol and hydrogen sulfide are 2%–5% and 8%–19% respectively (350 °C, $M = 1$–2, $\tau \approx 6$ s, $x = 90\%$–95%),[24] whilst on HNaY (under the same conditions, for the total conversion of methanol) the selectivities are $\leqslant 10\%$ and $\leqslant 20\%$.[25,26] Best results have been obtained by employing the decationated high-silica HZSM-5 zeolite, on which the selectivity reached 5%–40% with respect to methanethiol and 50%–93% with respect to dimethyl sulfide for $\tau \approx 4.5$ s. The authors[25,26] attribute the activity of the decationated zeolites to the presence in the latter of the acid OH groups, which play the role of catalytically active centres. In the conversion of ethanol and 1-propanol into the thiols on HNaY and HZSM-5 (350 °C, $M = 1$–4, $\tau \approx 6.7$ s, $x = 70\%$–85%), the yields of the thiols did not reach 1 mol%; ethanethiol and diethyl sulfide were detected qualitatively in the ethanol conversion products, while propane-1-thiol, dipropyl sulfide, and traces of propane-2-thiol, ethanethiol, and dimethyl sulfide were detected in the 1-propanol conversion products.[27] The low selectivity is due to the dehydration of the alcohols with formation of alkenes at a high rate. In the presence of HZSM-5, 1-butanol is also only dehydrated with formation of but-1-ene and but-2-ene in the presence of a large excess ($M = 10$) of hydrogen sulfide (300 °C, $M = 10$, $\tau = 0.003$–0.025 s, $x = 26\%$–90%).[1,5]

In order to compare the catalytic properties of zeolites, a kinetic study of the reaction of methanol with hydrogen sulfide was carried out.[28,29] It was found that the rate and selectivity of

Table 2. The interaction of alcohols with hydrogen sulfide on Al_2O_3.

Alcohol	T/°C	M	τ/s	x (%)	S (%)				Ref.
					thiol	sulfide	ether	alkene	
Methanol	370	1	3	100	37	63	0	0	17
	370	10.8	3	100	88	12	0	0	17
	350	2	~6	97	50	50	0	0	14
	360	1.6	0.06	86	40	35	24	0	11
	360	0.6	0.2	85	6	81	12	0	12
Ethanol	317	2.9	5.6	93	46	2	13	39	3
	350	4.5	~7.3	99	78	–	–	–	18
1-Propanol	290	2	0.1	< 10	15	0	32	20	5
1-Butanol	300	10	0.12	100	36	0	0	64	15
1-Octanol	317	7.7	7.2	100	34	0	–	7	4
2-Propanol	300	5	0.14	–	< 5	–	–	–	19

the process depend on the degree of conversion of methanol ($x = 20\%-90\%$) and the concentrations of the reactants in the range 38 vol%–62 vol%. The activity and selectivity series for the zeolites investigated were established. For example, at 360 °C, $x = 50\%$, and $M = 0.6$ and 1.6, the rate of conversion of methanol (w/mmol g^{-1} h^{-1}; the first figure in brackets corresponds to $M = 0.6$ and the second corresponds to $M = 1.6$) varies in the sequence:

$$\text{HZSM-5}\,(175;\ 280) > \text{HNaY}\,(61;\ 92) > \\ > \text{NaX}\,(27;\ 52) > \text{NaY}\,(3;\ 7)\ .$$

The selectivities of these catalysts are presented below.

Catalyst	NaX	NaY	HNaY	HZSM-5
S_{MeSH} (%)	60–88	69–76	8–16	5–20
S_{Me_2S} (%)	36–24	38–12	32–36	86–80

The authors[28,29] explained the characteristic features of the variation of the catalytic properties as a function of the composition of the zeolites by the difference between the acid–base characteristics of the catalyst surfaces. The strength and concentration of the active centres of zeolites and other catalysts (Table 3) have been determined[11,12,29–32] by analysing the IR spectra of adsorbed probe molecules. Ammonia and pyridine were used in testing the proton centres, carbon monoxide was used in testing the Lewis acid centres, and deuteriochloroform was used in testing the basic centres.[33] On the basis of the data presented in Table 3, the authors[28,29] explained the high activity of the decationated zeolites and their selectivity with respect to dimethyl sulfide by the high content of strong acid centres on the surface. The reduced activity of NaX compared with the decationated forms of the zeolites (by a factor of 2–10 under the given conditions) is attributed to the difficulty of activating methanol on a surface lacking strong acid centres. The high selectivity with respect to methanethiol is due to the occurrence on paired centres (sodium cations–lattice oxygen atoms adjoining the cation) of the dissociative chemisorption of hydrogen sulfide with formation of reactive thiyl groups. The reduced activity of NaY compared with NaX is explained by the lower content in NaY of the nonlocalised Na^+ cations, which play an important role in the activation of hydrogen sulfide. However, the reaction mechanisms on NaX and NaY are the same, so that the selectivities in the formation of methanethiol and dimethyl sulfide are similar on both catalysts.

The activity of alkaline forms of zeolites has also been investigated.[25,26] An increased selectivity with respect to methanethiol (70%–90%) and a low selectivity with respect to dimethyl sulfide (5%–15%) have been observed not only on NaX (350 °C, $M = 1-4$, $\tau \approx 6$ s, $x = 30\%-80\%$) but also when a proportion of the sodium in the zeolite has been replaced by Li, K, or Cs. Under the conditions indicated, the same zeolites accelerate the reaction of hydrogen sulfide with ethanol: for $x = 47\%-82\%$, the selectivity is 17%–70% with respect to ethanethiol and 0%–6% with respect to diethyl sulfide; ethene is also formed, the selectivity with respect to this substance amounting to 24%–83%.[24,27,34] It has been found[35] that the interaction of ethanol with hydrogen sulfide on the NaX, NaY, CaX, HY, and Ln/Y (a type Y zeolite containing lanthanide elements), zeolites leads to the formation of only ethanethiol (350 °C, $P = 0.6-3.0$ MPa, $x \leqslant 5\%$). The rate of reaction (w/mmol g^{-1} s^{-1}) varies in the following sequence:

$$\text{HY}\,(1.12) > \text{Ln/Y}\,(0.89) > \text{CaX}\,(0.31) > \\ > \text{NaY}\,(0.24) > \text{NaX}\,(0.15)\ .$$

Since the activity increases on passing from cation-containing to decationated forms of zeolites, it was concluded[35] that the reaction proceeds via an ionic mechanism and is facilitated in the presence of proton centres on the surface.

In terms of the activity in the reaction involving the formation of ethanethiol from methanol and hydrogen sulfide, the zeolites can be arranged in the sequence

$$\text{LiNaX} < \text{NaX} < \text{CsNaX} < \text{KNaX}\ ,$$

Table 3. The acid–base properties of catalysts.[11,12,29–32]

Catalyst[a]	Strength of centres/kJ mol^{-1}[b] (concentration of centres/μmol m^{-2})		
	proton centres	Lewis acid centres	basic centres
HNaY	⩽ 1200 (0.2)	45–55 (0.1)	800–900 (1.0)
HZSM-5	1180 (0.4)	41–55 (0.1)	800–900 (1.1)
NaX	–	20 (3)[c]	800–900 (0.3)
MgO	1560	16 (3.9)[c]	930 (0.7)
SiO_2	1390 (2.8)	–	< 800
30% H_3PO_4/SiO_2	1300 (1.2)	–	< 800
7.5% $H_4SiW_{12}O_{40}/SiO_2$	⩽ 1180 (1.0)	–	< 800
2.3% Cr_2O_3/SiO_2	< 1300 (0.25)	28 (0.4)[c]	800 (2.0)
7% WO_3/AlSi	< 1300 (0.74)	56 (0.62)	–
γ-Al_2O_3	1420	34 (2.3); 41 (0.2)	800–900 (4.0)
η-Al_2O_3	–	34 (1.6); 56 (0.1)	800–900
2.3% Cr_2O_3/Al_2O_3	< 1300 (0.15)	36 (2.4)	900 (2.8)
8.5% WO_3/Al_2O_3	< 1300 (0.1)	36 (1.4)	800–900 (1.3)
3% HF/Al_2O_3	1310 (0.25)	42 (2.0)	< 800 (2.4)
20% K_2CO_3/SiO_2	–	< 20[c]	830–930 (2.4)
20% K_2WO_4/SiO_2	–	< 20[c]	830–900 (1.83); 950 (1.2)
5.2% KOH/Al_2O_3	–	29 (1.3)	850 (2.2); 930–950 (1.4)
6.4% K_2CO_3/Al_2O_3	–	29 (1.6)	860 (2.4); 925–950 (1.4)
3.7% $NaOH/Al_2O_3$	–	28 (1.1)	860 (1.8); 930–950 (1.2)
15% K_2WO_4/Al_2O_3	–	31 (0.5)	800–900 (2.9); 925 (0.71)
5% $NaOH/Al_2O_3$	–	20 (1.4)	850–915 (2.3); 920–960 (1.5)

[a] The content of promoting agents is indicated in mass%.
[b] A dash indicates the absence of centres.
[c] The presence of the Lewis acid centre is due to the presence of sodium, magnesium, chromium, and potassium cations (Al^{3+} in the remaining cases).

which reflects the increase in the electronegativity of the cations on passing from lithium to potassium. It has been suggested that the cations play the role of active centres activating hydrogen sulfide and participating in the formation of acid hydroxy-groups, which are necessary for the activation of the alcohols.[24]

The reaction of ethanol with hydrogen sulfide is accelerated by the $M^{2+}NaX$ (M = Cd, Zn, Ni, Co, Mn) zeolites.[36,37] The yield of the sulfur-containing product depends on temperature and the ratio $H_2S : C_2H_5OH$. Thus on ZnNaX at 300 °C, $M = 2$, $\tau \approx 6$ s, and $x = 100\%$, the selectivity is 20% in the formation of ethanethiol and 80% in the formation of diethyl sulfide, whilst at 350 °C and $M = 1$ the selectivities are 7% and 40% respectively. The reaction is complicated by the dehydration of ethanol with formation of ethene. It is believed[36,37] that the active centres in the $M^{2+}NaX$ system in the conversion of ethanol into the thiol are the acid OH groups arising from dissociative chemisorption of hydrogen sulfide on the cations and the basic centres coupled with them. The selectivity in the formation of diethyl sulfide increases with increase in the strength of the proton centres:

$$CdNaX > ZnNaX > CoNaX \gg NiNaX \gg MnNaX .$$

The ethanol dehydration side reaction occurs with participation of the acid–base centres of the $M^{2+}NaX$ zeolite.

The interaction of 1-propanol with hydrogen sulfide on NaX leads to the formation of propane-1-thiol in 10%–20% yield with a small amount of ethanethiol and dimethyl sulfide (350 °C, $\tau \approx 6$ s, $M = 1-4$). On NaY, the yield of propane-1-thiol under these conditions is less than 2 mol%. The thiolation reaction is accompanied by the decomposition of 1-propanol with formation of propene.[27] In the interaction of 1- and 2-propanols with hydrogen sulfide on the $M^{2+}NaX$ (M = Cd, Zn, Ni, Co, Mn) zeolites, the dehydration of the alcohol with formation of propene predominates. The overall selectivity with respect to the thiol and the sulfide (with the former predominating) is 2%–36% (350 °C, $M = 1-4$, $x = 10\%-90\%$).[27,38] It is suggested that the acid OH groups and the cationic centres of the zeolites participate in the thiolation process. At a high concentration of strong proton centres on the zeolite surface, the contribution of the alcohol dehydration side reaction increases.

The interaction of 1-butanol with hydrogen sulfide has been investigated[15] in the presence of the NaX zeolite. The reaction products are butane-1-thiol and butenes, which are formed with selectivities of 40% and 60% respectively (300 °C, $M = 10$, $\tau = 0.4-2.1$ s, $x = 27\%-83\%$).

Table 4. Synthesis of alkanethiols from alcohols and hydrogen sulfide in the presence of cationic forms of zeolites.

Alcohol	Zeolite	T/°C	M	τ/s	x (%)	Yield of alkanethiol (mol%)	Ref.
Methanol	NaX	350	4	~6	85	65	24, 25
	NaX	360	1.6	4.2	80	66	29
	KNaX	350	2	~6	80	71	25
	NaY	350	4	~6	50	30	25, 26
	NaY	360	1.6	8.4	64	40	29
Ethanol	NaX	350	4	~6	95	74	34
	KNaX	350	2	~6	82	52	24
	CdNaX	250	2	~6	85	21	36
	NiNaX	300	2	~6	76	28	36
1-Propanol	NaX	350	4	~6	70	20	27
	CdNaX	250	4	~6	80	23	38
2-Propanol	CdNaX	250	4	~6	80	10	38
1-Butanol	NaX	300	10	21	83	35	15

Thus dialkyl sulfides are formed under the influence of various forms of zeolites, their cationic forms being more suitable for the synthesis of alkanethiols. The highest attained experimental yields of alkanethiols are indicated in Table 4.

3. Supported catalysts

From the practical point of view, it is preferable to use catalysts obtained by depositing the active components on a carrier, since this involves a smaller consumption of the active substance, a high degree of its dispersion is attained, and thermal stability of the catalyst is ensured. This was already noted in an early study,[7] the authors of which established that ThO_2 deposited on pumice is preferable to the massive oxide. Catalysts consisting of the oxides, sulfides, and salts of Group 1–6 and 8 elements deposited on aluminium oxide, silicon dioxide, aluminosilicate, pumice, and carbon have been mentioned in patents (see the relevant reviews[2–8]). In the later studies considered in the present review, the supported catalysts for the conversion of alcohols into thiols were compared quantitatively, in many instances on the basis of kinetic investigations, and the relations between the catalytic and acid–base properties of the catalysts were deduced.

a. Acid catalysts

The catalysts obtained by modifying SiO_2 with phosphoric and sulfuric acids as well as the carrier itself exhibit a low activity in the reaction of methanol with hydrogen sulfide. Thus, on the H_3PO_4/SiO_2 specimens, the degree of conversion of methanol was less than 1% and sulfur-containing products were not formed (350 °C, $M = 0.5-2.0$, $\tau \approx 10$ s).[14] On the 30% H_3PO_4/SiO_2 catalyst at 360 °C, $M = 1$, and $\tau \approx 25$ s, the selectivities with respect to methanethiol and dimethyl sulfide were 1% and 10% respectively for a rate of consumption of methanol of 5 mmol g^{-1} h^{-1}, whilst after the increase in τ to 42 s and for $M = 0.6$, the degree of conversion x reached 100% and the selectivity with respect to dimethyl sulfide was 25%.[11,12] According to the authors[11,12] the activity of catalysts of this type is determined by the presence on the surface of proton centres, but the low acidity of H_3PO_4/SiO_2 as well as the low acidity of SiO_2 (Table 3) made the thiolation reaction ineffective.

It has been established[19] that hydrogen sulfide reacts with an alcohol at an elevated pressure on the H_3PO_4 (50 mass%–85 mass%)/kieselguhr catalyst, but the isomeric thiol is then formed preferentially. For example, instead of propane-1-thiol, propane-2-thiol is formed from 1-propanol is 41% yield (276 °C, $P = 0.9-1.0$ MPa, $M = 6$, $\tau = 0.14$ s); in the interaction of hydrogen sulfide with 1-dodecanol, only dodecane-2-thiol was obtained (350 °C, $P = 1.2$ MPa, $M = 4$); on interaction with hydrogen sulfide, 2-propanol, 2-butanol, and 2-pentanol are converted into the corresponding alkane-2-thiols in 37%–63% yields (175–300 °C, $P = 0.9-1.0$ MPa, $M = 4-5$, $\tau \approx 0.14$ s).[19]

Heteropolyacids with a Keggin type anion, such as silicotungstic acid $H_4SiW_{12}O_{40}$ (HSiW) and phosphotungstic acid $H_3PW_{12}O_{40}$ (HPW), deposited on silicon dioxide and containing very strong proton centres on the surface, were found to be more effective in the reaction of methanol with hydrogen sulfide[11,13] (Table 3). Thus the selectivities with respect to methanethiol and dimethyl sulfide on the 7.5% $HSiW/SiO_2$ catalyst at 360 °C, $M = 1.6$, and $x = 80\%$ were 49% and 51% respectively. The increase in the HSiW concentration to 25 mass% leads to an increase in the selectivity with respect to dimethyl sulfide to 80%. On the 30% HPW/SiO_2 catalyst, the selectivities under the conditions indicated were 70% with respect to methanethiol and 24% with respect to dimethyl sulfide, which differs from the results obtained on massive HPW, where the selectivities with respect to methanethiol and dimethyl sulfide were 16% and 64% respectively. The increase almost by an order of magnitude in the activity of the deposited heteropolyacid compared with SiO_2 and H_3PO_4/SiO_2 can be explained by the increased proton acidity. The different selectivities in the formation of thiolation products on the deposited and massive

Table 5. The activities and selectivities of supported acid catalysts in the reaction of methanol with hydrogen sulfide at 360 °C, $x = 80\%$, and a methanol concentration of 38–62 vol%.[11,12,30]

Catalyst	$M = 0.6$			$M = 1.6$		
	w/mmol $g^{-1}h^{-1}$	S (%)		w/mmol $g^{-1}h^{-1}$	S (%)	
		methanethiol	dimethyl sulfide		methanethiol	dimethyl sulfide
$HSiW/SiO_2$	–	–	–	21	49	51
Cr_2O_3/SiO_2	5	40	60	–	–	–
WO_3/SiO_2	12	23	74	21	46	43
WO_3/AlSi	–	–	–	102	43	49
γ-Al_2O_3	340	15	54	637	37	35
Cr_2O_3/Al_2O_3	460	10	80	832	22	50
MoO_3/Al_2O_3	330	20	70	767	53	47
V_2O_5/Al_2O_3	400	40	40	661	54	31
WO_3/Al_2O_3	214	2	70	547	51	37
HF/Al_2O_3	307	4	20	1338	34	51
B_2O_3/Al_2O_3	–	–	–	554	41	47
H_2SO_4/Al_2O_3	–	–	–	612	37	38

HPW are due to the decrease in the strength of the proton centres of the heteropolyacid on the carrier. However, in the reactions of hydrogen sulfide with higher alcohols, the heteropolyacids are relatively ineffective catalysts. Thus the HPW/SiO_2 catalyst as well as massive HPW are almost inactive in the reaction of 2-propanol with hydrogen sulfide:[38] at 250 °C, $M = 4$, $\tau \approx 6$ s, the degree of conversion of the alcohol being less than 1%. Only the dehydration of the alcohol with formation of but-1-ene and but-2-ene takes place in the reaction of hydrogen sulfide with 1-butanol on the 25% $HSiW/SiO_2$ specimen (300 °C, $M = 10$, $\tau = 0.04-5.40$ s, $x = 38\%-100\%$).[15]

The reaction of methanol with hydrogen sulfide is accelerated by transition metal oxides deposited on SiO_2 or AlSi and having on their surfaces strong proton centres, weak Lewis acid centres, and moderately strong basic centres (Table 3). The catalytic properties of these specimens differ little from that of the proton-donor $HSiW/SiO_2$ catalyst (Table 5).

By varying the reaction conditions (360 °C, $M = 0.6-1.6$, $\tau = 4-7$ s, $x = 80\%-95\%$) in the presence of chromium, molybdenum, and tungsten oxides deposited on SiO_2, it was not possible to obtain methanethiol and dimethyl sulfide in yields exceeding 40 mol% and 60 mol% respectively.[11,12] Higher alcohols react with hydrogen sulfide with difficulty. Thus, even in the presence of an excess of hydrogen sulfide, 1-butanol is converted on Cr_2O_3/SiO_2 into butane-1-thiol and butenes, the selectivities in the formation of which amount to 20% and 80% respectively (300 °C, $M = 10$, $\tau = 0.36-7.90$ s, $s = 20\%-92\%$).[15]

The reaction of methanol with hydrogen sulfide has been investigated[11,12] on catalysts obtained by introducing acid additives (boric, sulfuric, and hydrofluoric acids and the Cr, V, Mo, and W acid oxides) into Al_2O_3. The selectivities of the above catalysts were close to that of the $HSiW/SiO_2$ acid catalyst, but their activities were 25–50 times higher than that of the latter. In terms of their catalytic properties, the acid aluminium oxide catalysts do not differ greatly from pure aluminium oxide. Certain data on this point are presented in Table 5. According to the authors,[11,12] this is due to the similarity of the acid–base characteristics of their surfaces. It follows from Table 3 that the Al_2O_3 surface contains strong Lewis acid centres and moderately strong basic centres, weak proton centres also being present. The modification of Al_2O_3 by acid additives leads to an increase in the strength of the Lewis acid centres, arising due to the presence of Al^{3+}, a decrease in the basicity of the specimen, and also the appearance of strong proton centres; it may be that weak Lewis acid centres (cations) may also function as active centres on the surfaces of specimens containing chromium, molybdenum, and tungsten oxides on Al_2O_3.

An increase in the acidity of aluminium oxide catalysts leads to an increase in the rate of conversion of methanol per gram of the catalyst.[11,12] The rate of reaction, referred to a single Lewis acid centre, increases with increasing strength of these centres. A decrease in the basicity of the catalyst, for example as a result of the introduction of hydrofluoric acid into Al_2O_3, reduces the selectivity for the formation of the products of the reaction involving the conversion of methanol into the thiol and promotes the formation of dimethyl ether (360 °C, $M = 0.6$, $x = 80\%$).

With increase in the content of transition metal oxides on Al_2O_3, the activity of the catalyst also increases, whilst the selectivity changes little. It follows from the results of the above studies[11,12] that acid aluminium oxide catalysts are insufficiently selective with respect to methanethiol: in the presence of chromium, molybdenum, and tungsten oxides as well as sulfuric, hydrofluoric, and boric acids deposited on Al_2O_3, the yield of methanethiol obtained from methanol and hydrogen sulfide does not exceed 50 mol% (360 °C, $M = 1.6$, $\tau = 0.12-1.10$ s, $x = 80\%-100\%$). On the other hand, dimethyl sulfide is formed selectively on these catalysts, the yield amounting to 80 mol% – 95 mol% (360 °C, $M = 0.6$, $\tau = 0.5-3.0$ s, $x = 80\%-100\%$).

It has been found[39] that, among the catalysts containing Cu, Cr, Co, Ni, Th, and Mg oxides on Al_2O_3, the specimens modified with 0.11 mass% of chromium or 0.22 mass% of copper are the most effective as regards the formation of dimethyl sulfide from methanol and hydrogen sulfide; in their presence, the yield of dimethyl sulfide is 90 mol%–97 mol% and that of methanethiol is 2 mol%–3 mol% (400 °C, $M = 0.6$, $\tau = 6.2$ s).

The reactions of hydrogen sulfide with methanol homologues on acid aluminium oxide catalysts have been investigated to a lesser extent. The reaction involving the conversion of 1-propanol into the thiol on the 3.7% WO_3/Al_2O_3 catalyst results in the formation of propane-1-thiol, propene, and dipropyl ether with selectivities of 24%–29%, 13%–17.5%, and 26.7%–31.5% respectively (250–270 °C, $M = 4.7$, $\tau = 0.1-2.0$ s, $x \leqslant 10\%$).[40] In the presence of Al_2O_3 modified by titanium and zirconium oxides, the yield of dodecane-1-thiol, obtained from 1-dodecanol and hydrogen sulfide at 200–400 °C, did not exceed 12 mol%.[22] Massive HPW, which is inactive in the conversion of 1-propanol into the thiol, became active after its deposition in an amount of 16 mass%–44 mass% on δ-Al_2O_3: the yields of propane-1-thiol and propane-2-thiol from 1- and 2-propanols reached 20 mol% (250 °C, $M = 4$, $\tau \approx 6$ s, $x = 35\%-75\%$).[38] However, it may be that the activity of this catalyst is only partly associated with the presence of the heteropolyacid, since the latter decomposes on contact with the carrier.[30]

b. Basic catalysts

The modification of the carrier by alkali metal compounds leads to the formation of catalysts with a reduced activity, a low selectivity with respect to the dialkyl sulfide, but with a high selectivity in the formation of the alkanethiol. This was already noted in early studies devoted to the conversion of methanol into the thiol.[2-4,8] Under identical conditions (400 °C, $M = 2$, $\tau = 5.5$ s, $x = 70\%-80\%$), the selectivity in the formation of methanethiol on the alkali-modified aluminium oxide is 1.2 times higher than on the unpromoted Al_2O_3, while the selectivity with respect to dimethyl sulfide is lower by a factor of 2.4. Similar changes occur in the reactions of hydrogen sulfide with ethanol (400 °C, $M = 2$, $\tau = 5.6$ s, $x = 70\%-90\%$) and with 1-octanol (317 °C, $M = 2.9$, $\tau = 5.6$ s, $x = 83\%-91\%$): the selectivity with respect to the alkanethiol on the alumina–potassium tungstate specimen is higher by a factor of 1.4–2.3 than on pure Al_2O_3, while the selectivity with respect to the dialkyl sulfide is significantly lower.[4] In the reaction of 1-propanol with hydrogen sulfide, aluminium oxide with added potassium or sodium oxide is an order of magnitude less active than pure Al_2O_3; the selectivities for the formation of propane-1-thiol are 15% and 34%–80% respectively on pure Al_2O_3 and on the oxide modified by various amounts of alkalies (290 °C, $M = 2$, $x \leqslant 10\%$).[40]

The interaction of methanol with hydrogen sulfide on carriers modified by potassium or sodium hydroxide, carbonate, and tungstate has been studied in detail.[31,41-45] The rate of conversion of methanol and the selectivity with respect to dimethyl sulfide on these catalysts are low, while the selectivity with respect to methanethiol is high. The activity of the catalysts may be due to the presence on their surfaces of definite numbers of acid–base centres. In contrast to SiO_2, which contains mainly weak proton centres, in the SiO_2 with added potassium compounds there are no proton centres—weak Lewis acid centres (apparently alkali metal cations) and strong basic centres are present (Table 3). Compared with pure silicon dioxide, the activity of the alkaline specimen at 360 °C is higher by a factor of 1.5–4.0, the selectivity with respect to methanethiol has increased from 25% to 70%–98%, while the selectivity with respect to dimethyl sulfide remains low (2%–15%). The promoting effect of the alkaline additive to SiO_2 is higher, the higher the potassium or sodium content of the silicon dioxide. For the same atomic content of potassium, the activity of, for example, K_2CO_3/SiO_2 is twice as high as that of K_2WO_4/SiO_2, but methanethiol is formed somewhat more selectively on the tungstate specimen.

The acid–base characteristics of aluminium oxide also change after the introduction of an alkaline additive (Table 3): the number of the weak proton centres present in the Al_2O_3 diminishes or they vanish altogether, the concentration and strength of the Lewis acid centres (Al^{3+}) decrease, and weak Lewis acid centres (alkali metal cations) probably also appear. Furthermore, together with the moderately strong basic centres present in the Al_2O_3, a large number of strongly basic centres are generated.

The introduction of alkaline additives into Al_2O_3 increases the activity of the catalyst in the conversion of methanol into the thiol to a greater extent than their introduction into the SiO_2. This is due to the presence on the surfaces of the aluminium oxide specimens of Al^{3+} ions, which are stronger Lewis acid centres than alkali metal cations.

The change in the acid–base properties of Al_2O_3 when the latter is modified by alkali leads, in its turn, to a change in the catalytic properties. Thus the introduction of an alkaline additive into Al_2O_3 lowers the activity with respect to methanethiol by 1–1.5 orders of magnitude and that with respect to dimethyl sulfide by 2–4 orders of magnitude compared with pure Al_2O_3. The selectivity with respect to methanethiol increases accordingly from 35%–50% on Al_2O_3 to 98% on the modified catalyst, whilst that with respect to dimethyl sulfide falls sharply. The content of the alkaline additive also affects the catalytic properties: with increase in the concentration of the promoting agent, the activity and selectivity of Al_2O_3 with respect to dimethyl sulfide diminish, whilst the activity with respect to methanethiol increases.

The similarity of the acid–base properties of specimens with identical atomic contents of the alkali metal on Al_2O_3 also ensures their virtual identical activity at 360–500 °C.[31,42,45] The nature of the anion exerts a stronger influence: among the specimens containing potassium on Al_2O_3, the carbonate and tungstate specimens exhibit the highest and lowest activities respectively, but the latter are more selective with respect to methanethiol. The carbonate and hydroxide specimens exhibit an increased activity for the formation of decomposition products—methane and carbon oxides. These differences are associated with the acid–base properties of the surface. It follows from Table 3 that the KOH/Al_2O_3, $NaOH/Al_2O_3$, and K_2CO_3/Al_2O_3 specimens differ little as regards the concentration and strength of the Lewis acid centres. Very strong basic centres are also present in the carbonate and hydroxide specimens. On the other hand, the tungstate catalyst, which is most selective with respect to methanethiol,[44] contains stronger basic centres than in the above specimens. The catalytic properties are independent of the nature of the tungstate promoting agent. Thus the catalysts obtained by introducing sodium heptatungstate, dodecatungstate, metatungstate, and the normal tungstate into Al_2O_3 exhibit approximately the same activities in the reaction of methanol with hydrogen sulfide.[43] The specimen in which the alkali metal : tungsten atomic ratio is 2 : 1 exhibits the greatest selectivity with respect to methanethiol. The similarity of the catalytic properties of the specimens obtained by impregnating Al_2O_3 with solutions of the monomeric normal tungstate and by different polynuclear oxo-complexes of tungsten is a consequence of the formation of similar surface compounds.

The conversion of methanol homologues into thiols in the presence of Al_2O_3 modified by alkaline additives takes place at a lower temperature. The selectivity in the formation of alkanethiols from primary alcohols is fairly high (80%–90%) even for a high degree of conversion of the alcohol, but diminishes when secondary alcohols are converted into thiols, since this is accompanied by side reactions involving the formation of alkenes, ethers, etc. Thus in the interaction of ethanol with hydrogen sulfide on 10% K_2WO_4/Al_2O_3, the selectivities with respect to ethanethiol and diethyl sulfide are 93%–78% and 2.5%–3.6% respectively (290–382 °C, $M = 2$, $x = 60\%-83\%$).[4] In the interaction of 1-octanol with hydrogen sulfide on the same catalyst, the selectivity for the formation of octane-1-thiol is 99%–74% (235–318 °C, $M = 7.7$, $x = 48\%-100\%$); the reaction is accompanied by the formation of an alkene.[4] In the reaction of 1-butanol with hydrogen sulfide on potassium-modified Al_2O_3, the selectivity with respect to butane-1-thiol was 92%–98%, but-1-ene being formed as a side product (300 °C, $M = 10$, $\tau = 1.2-12.1$ s, $x = 30\%-95\%$).[15] The reaction of 1-dodecanol with hydrogen sulfide on the K/Al_2O_3 catalyst afforded dodecane-1-thiol with a selectivity of 47%–82%, a selectivity of 7%–42% with respect to dodecene, and a selectivity of 2%–33% with respect to the sum of dodecyl ether and dodecyl sulfide [(300–350) °C, $M = 2.6-24.0$, $\tau = 0.04-2.50$ s, $x = 15\%-100\%$].[46] 2-Butanol, a secondary alcohol, is largely dehydrated in hydrogen sulfide on the catalysts indicated above with formation of butene; among the sulfur-containing substances, only butane-2-thiol is formed with a selectivity of 11%–26% (275–300 °C, $P = 0.1-0.3$ MPa, $M = 4$, $\tau = 0.3-0.9$ s, $x = 59\%-71\%$).[47]

Thus the composition of the catalysts exerts a considerable influence on the rate of the interaction of alcohols with hydrogen sulfide and on the mode of the reaction. By varying the type of the acid–base centres and their numbers on the surface, it is possible to obtain an active and selective catalyst for the formation of the thiol. Deliberate search for such catalysts is facilitated when the reaction mechanism is known.

III. The mechanism of conversion of alcohols into thiols by hydrogen sulfide

1. Routes to the formation of the reaction products

Knowledge of reaction paths is important for the regulation of the process selectivity. This problem has been elucidated in greatest detail for the interaction of methanol with hydrogen sulfide.

It has been postulated[25,26,28,29] that the products of the thiolation of methanol and dimethyl ether are formed from methanol by independent paths on the NaX, NaY, HNaY, and HZSM-5 zeolites. In a number of instances, for example on AlSi and γ-Al_2O_3 (both pure and modified by HF and B_2O_3), the selectivity in the formation of dimethyl ether for low degrees of conversion of methanol was much higher than the overall selectivity with respect to methanethiol and dimethyl sulfide.[11,12,17] This justified the conclusion that the latter are formed as a result of the interaction of hydrogen sulfide with dimethyl ether produced on dehydration of methanol.

The routes to the formation of methanethiol and dimethyl sulfide may differ. It has been suggested[25,26,29] that they are obtained via independent paths on zeolites. However, the view that dimethyl sulfide is a secondary product arising from methanethiol predominates.

The most reliable conclusions concerning the routes to the formation of the products from methanol and hydrogen sulfide on different catalysts have been reached on the basis of kinetic studies.[11,12,30,31,45,48,49] The primary oxygen-containing product arising from methanol is its dehydration product—dimethyl ether:

$$2\,CH_3OH \rightleftharpoons (CH_3)_2O + H_2O\,.$$

Dimethyl ether as well as the initial methanol can decompose with formation of carbon oxides and methane.[50] The increase in selectivity with respect to methanethiol with decrease in the degree of conversion of methanol permitted the conclusion that methanethiol is the primary sulfur-containing product of the interaction of methanol with hydrogen sulfide:

$$CH_3OH + H_2S = CH_3SH + H_2O\,.$$

However, the reaction of hydrogen sulfide with dimethyl ether is also possible:

$$(CH_3)_2O + H_2S = CH_3SH + CH_3OH\,.$$

For example, it may occur on Al, K, W, and Mo oxides and sulfides.[2,4,45,48,49,51,52] The rates of reaction of methanethiol and dimethyl ether and also the selectivities in the formation of methanethiol with hydrogen sulfide under similar conditions are comparable.[45,48,49] Hydrogen sulfide is consumed in the reaction with methanol on different catalysts only in the formation of methanethiol and dimethyl sulfide and the degree of its conversion is therefore equal to the overall yield of these products.

Methanethiol, formed from hydrogen sulfide and methanol, can undergo various reactions, in particular reactions involving the formation of dimethyl sulfide. The formation of the latter from methanethiol is indicated by a series of experimental facts.[45,49,53] Thus the selectivity with respect to methanethiol decreases and that with respect to dimethyl sulfide increases with increase in the degree of conversion of the reactants (methanol, dimethyl ether, hydrogen sulfide). When methanethiol is added to the initial reaction mixture, the rate of formation of dimethyl sulfide increases. Indirect evidence is provided also by the occurrence on the catalysts accelerating the interaction of methanol with hydrogen sulfide of the selective reaction involving the synthesis of dimethyl sulfide by the decomposition of methanethiol in helium or of the reactions of methanethiol with methanol or dimethyl ether. However, although the selectivity with respect to dimethyl sulfide in the above reactions increases with increasing degree of conversion of the reactants, it does not reach 100% even for the total conversion of the latter, which is associated with the occurrence of a reversible reaction of dimethyl sulfide with hydrogen sulfide. The catalysts active in the reaction of methanol with hydrogen sulfide or methanethiol accelerate the above interaction as well.[54,55] The experimental data presented demonstrate that the following reactions take place involving methanethiol:

$$CH_3SH + CH_3OH = (CH_3)_2S + H_2O\,,$$

$$CH_3SH + (CH_3)_2O = (CH_3)_2S + CH_3OH\,,$$

$$2\,CH_3SH \rightleftharpoons (CH_3)_2S + H_2S\,.$$

For a long contact time and at an elevated temperature, methanethiol and dimethyl sulfide are partly decomposed with formation of methane and the deposition of coke on the surface.[54]

Thus the products of the interaction of methanol with hydrogen sulfide may be formed as a result of the occurrence of the reactions listed below on various catalysts, the composition of which influences only the rates of individual stages. The dehydration of methanol leads to the formation of dimethyl ether. The reaction of methanol with hydrogen sulfide or possibly with dimethyl ether affords methanethiol, which is converted into dimethyl sulfide either by reacting with a second molecule of methanol or dimethyl ether or by disproportionating. The partial decomposition of dimethyl ether and methanol leads to the formation of carbon monoxide and methane. The latter is also a product of the degradation of methanethiol and dimethyl sulfide.

In the conversion of higher alcohols into thiols, additional reaction paths appear—the decomposition of the initial alcohol and of the sulfur-containing products formed from it. In the interaction of hydrogen sulfide with ethanol and 1- and 2-propanols on zeolites, both decationated and in the sodium-form, the principal reaction products are the corresponding thiols and an alkene. The occurrence of the consecutive reactions,

$$RCH_2CH_2OH \xrightarrow[-H_2O]{} RCH{=}CH_2 \xrightarrow{H_2S} RCH_2CH_2SH\,,$$

has been suggested.[27,36] The alcohol is dehydrated with formation of an alkene, which then reacts with hydrogen sulfide to produce the thiol. However, the authors do not rule out also the possibility of the parallel formation of the thiol and the alkene.

$$RCH_2CH_2OH \begin{cases} \xrightarrow{H_2S} RCH_2CH_2SH \\ \xrightarrow[-H_2O]{} RCH{=}CH_2 \end{cases}$$

According to the authors,[27,36] a small amount of ethanethiol and dimethyl sulfide is formed in this reaction when hydrogen sulfide interacts with the propanol decomposition products.

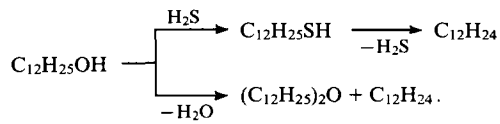
Kinetic study[5] led to the conclusion that, in the presence of Al_2O_3, 1-propanol reacts via three independent paths in hydrogen sulfide:

$$C_3H_7OH \begin{cases} \xrightarrow{-H_2O} C_3H_8\,, \\ \xrightarrow{-H_2O} (C_3H_7)_2O\,, \\ \xrightarrow{H_2S} C_3H_7SH\,. \end{cases}$$

The reaction of hydrogen sulfide with 1-butanol on the NaX, MgO, Al_2O_3, and Cr_2O_3/SiO_2 catalysts does not lead to the formation of dibutyl ether and dibutyl sulfide, only butane-1-thiol and butenes (mainly but-1-ene) being produced. The selectivity with respect to the latter compounds is independent of the degree

of conversion of butanol.[15] On the grounds of these findings, it is suggested that the 1-butanol conversion products, like those obtained from 1-propanol,[5] are obtained via independent routes from the initial alcohol. However, bearing in mind the high rate of the decomposition of alkanethiols and dialkyl sulfides compared with alcohols[27,46,56] and its increase with increasing molecular mass,[57-59] one cannot rule out the possibility that butenes appear on decomposition not only of the alcohol but also of the products of its thiolation.

The routes to the formation of the products of the reaction of 1-dodecanol with hydrogen sulfide on the alkali-modified aluminium oxide have been investigated.[56] The main products are dodecane-1-thiol and dodecene, the overall yield of dodecyl ether and dodecyl sulfide not exceeding 5 mol%. The selectivity with respect to dodecane-1-thiol remains approximately constant at $x \leqslant 60\%$, decreasing at higher degrees of conversion. This is owing to the fact that mainly the dodecanethiol and not the initial alcohol decomposes, which is indicated by the form of the variation of the selectivity in the formation of the 1-dodecanol conversion product, by the increased yield of dodecene when dodecane-1-thiol is added to the initial mixture, and also by data on the decomposition of 1-dodecanol under a helium atmosphere and of dodecane-1-thiol in hydrogen sulfide. Mainly the consecutive process involving the formation and decomposition of dodecane-1-thiol takes place, the contribution of the parallel alcohol dehydration reaction being small:



2. Relation between the catalytic and acid–base properties

The acid–base properties of the surfaces of the catalysts influence not only their activity in the reaction of an alcohol with hydrogen sulfide to form an alkanethiol and a dialkyl sulfide (see above), but also the rates of the individual stages of the process. This has been established as a result of detailed studies of the synthesis of methanethiol or dimethyl sulfide from methanol and hydrogen sulfide and of the reactions involving the formation of dimethyl sulfide by the disproportionation of methanethiol and its interaction with methanol.[11,12,28-31,53,54,60] The results permitted the conclusion that all these reactions are accelerated by catalysts having both proton and Lewis acid centres. The activity of the catalyst per centre increases with increase in the strength of the acid centre.[11,12,60] Identical features of the variation of the activity as a function of the nature and strength of the centres are characteristic of different reactions. This is illustrated by the results, presented in Table 6, of the determinations of the activities of the catalysts in various reactions involving the synthesis of methanethiol and dimethyl sulfide. Taking into account the available data concerning the acid–base properties of the catalyst (Table 3), one may conclude that the reactions proceed under the influence of both proton and Lewis acid centres. A catalyst with weak proton centres (H_3PO_4/SiO_2) exhibits a low activity in the formation of methanethiol and dimethyl sulfide. Catalysts with strong proton centres ($HSiW/SiO_2$) have the best parameters. The activity of catalysts having weak Lewis acid centres (NaX, MgO, Cr_2O_3/SiO_2) is approximately at the same level as that of the catalysts with strong proton centres. The activity of aluminium oxide catalysts containing strong Lewis acid centres is appreciably higher than that of the catalysts with strong proton centres. For this reason, the activity of the proton-donating specimens containing even a small number of strong Lewis acid centres (decationated zeolites) is higher than the activity of a 'purely' proton-donating specimen.

The effectiveness of catalysts with strong Lewis acid surface centres is due to the presence of the basic centres associated with them, which participate in the activation of both the alcohol and hydrogen sulfide. The suppression of the basic centres, even when it is accompanied by some increase in the strength of the acid centres (for example, as a result of the introduction of hydrofluoric acid into Al_2O_3), lowers the overall activity and selectivity of the catalyst as regards the formation of the products of the thiolation reaction.[12] It has been established[11,12,28-31,53,54,60] that both the overall activity of the catalysts in all the reactions indicated and their activity in relation to the formation of dimethyl sulfide decrease with increase in the strength of the basic centres and with decrease in the strength of the acid centres (for example, when the carrier is modified by alkali). The selectivity with respect to methanethiol increases under these conditions in the reaction of hydrogen sulfide with methanol. A catalyst containing strong Lewis acid centres and moderately strong basic centres (for example Al_2O_3 modified by acid additives or a decationated high-silica zeolite) is an active and selective catalyst in the synthesis of dimethyl sulfide from methanol and hydrogen sulfide or methanethiol.

Since the type, concentration, and strength of the active centres influence the activity of the catalyst equally in all the reactions indicated above, the conclusions concerning the routes to the formation of the products of the thiolation of methanol, reached on the basis of kinetic studies, must be regarded as valid (see Section III).

The acid–base properties of the catalyst surfaces influence the rate of the reaction of hydrogen sulfide with methanol homologues and the mode of the reaction. Thus it has been established[15] that the rate of conversion of 1-butanol in an excess of hydrogen sulfide is very high on catalysts with very strong proton centres (decationated zeolite, heteropolyacid), whilst on catalysts with weakened Lewis acid centres (NaX, MgO, Cr_2O_3/SiO_2) it is much lower. Butanol is converted fastest on Al_2O_3, having strong Lewis acid centres and moderately strong basic centres. The rate of reaction increases with increase in the concentration and strength of the acid centres on the surface. Thus the rate of conversion of 1-butanol, referred to one acid centre, is higher the greater the strength of these centres. However, 1-butanol decomposes rapidly with formation of butenes on highly active acid catalysts, the rate of the process increasing with increase in the acidity of the surface. An additional amount

Table 6. The rates of formation of methanethiol and dimethyl sulfide on catalysts with different acid–base properties.

Catalyst	Rate of formation/μmol m^{-2} h^{-1}			
	of methanethiol[a]	of dimethyl sulfide		
		b	c	d
H_3PO_4/SiO_2	0.22	18	–	3
$HSiW/SiO_2$	28	30	17	34
NaX	46	10	5	10
MgO	33	–	–	20
Cr_2O_3/SiO_2	37	8	12	12
γ-Al_2O_3	715	4066	800	3200
η-Al_2O_3	1137	869	–	2000
Cr_2O_3/Al_2O_3	1126	1269	1000	2720
H_2SO_4/Al_2O_3	863	–	270	1900
$NaOH/Al_2O_3$	44	3	6	10
HNaY	8.4	24	91	8
HZSM-5	112	300	200	600

[a] Methanethiol is formed by the $CH_3OH + H_2S$ reaction: $T = 360$ °C, $[CH_3OH] = 17$ mM, $[H_2S] = 28$ mM, $x = 80\%$, $M = 1.6$.[11,29]
[b] $CH_3OH + H_2S$: $T = 360$ °C, $M = 0.6$, $[CH_3OH] = 28$ mM, $[H_2S = 17$ mM, $x = 80\%$.[11,12,29]
[c] $CH_3OH + CH_3SH$: $T = 350$ °C, $[CH_3SH] = 3.2$ mM, $[CH_3OH] = 1.7$ mM, $x = 50\%$.[53]
[d] $2CH_3SH \rightleftharpoons (CH_3)_2S + H_2S$: $T = 350$ °C, $[CH_3SH] = 2$ mM, $x = 20\%$.[60]

of butenes probably appears as a consequence of the decomposition of the sulfur-containing substances produced. The formation of the products of the thiolation reaction between 1-butanol and hydrogen sulfide is therefore hindered on acid catalysts: dibutyl sulfide was not detected at all and the selectivity with respect to butane-1-thiol was low. In the presence of catalysts with strong basic centres and weakened Lewis acid centres (for example, K/Al_2O_3), butane-1-thiol is mainly formed. The decrease in the selectivity in the formation of the products of the thiolation reaction in the presence of acid catalysts and the increase in the selectivity in the formation of an alkanethiol on basic catalysts have been observed also in the reactions of hydrogen sulfide with ethanol, 1- and 2-propanols, and 1-dodecanol.[2,3,5,24,27,36–38,46]

3. Adsorption

In considering the mechanism of the conversion of alcohols into thiols by hydrogen sulfide, it is necessary to take into account the available information about the structure and reactivity of the intermediate surface compounds arising when the reactants and their reaction products are adsorbed on the catalyst. These data have been obtained mainly by IR spectroscopic, NMR, and thermoprogrammed desorption (TPD) methods.

Alcohols may be adsorbed on the surfaces of acid–base catalysts[61,62] in the molecular form as a result of the interaction of the oxygen atom of the alcohol with a proton or Lewis acid centre of the catalyst and of the hydrogen atom of the alcoholic hydroxy-group with a basic surface centre. The decomposition of the alcohol in the molecularly adsorbed form leads to the formation of hydroxide and alkoxide groups on the surface. The latter may in addition form a hydrogen bond with the basic centres of the catalyst.

The adsorption of a dialkyl ether[63,64] on proton-donating catalysts at a low temperature leads to the appearance of a hydrogen-bonded form involving a proton catalyst centre and the oxygen atom of the ether. On catalysts with paired acid–base centres, a coordinate bond is formed between the oxygen atom of the ether and the Lewis acid centre together with an additional bond between a hydrogen atom of the alkyl group and a basic centre. At an elevated temperature, these forms decompose with formation of alkoxide groups on the surface.

In the adsorption of an alkanethiol on the surface of an acid–base catalyst, there is a possibility of the formation of an associatively bound form as a result of the interaction of the sulfur atom of the alkanethiol with an acid catalyst centre and of the hydrogen atom of the thiyl or alkyl group with a basic centre. The decomposition of the molecular form of the adsorbed thiol leads to the appearance of OH and RS groups on the surface and also to the formation of hydrogen sulfide and the alkoxylation of the surface.[1,58,65–69]

The dialkyl sulfide is adsorbed on the surface[1,65,67] with participation of different centres. At a low temperature, the sulfide is protonated at the sulfur atom by the acid OH groups on the surface; a donor–acceptor complex with participation of the sulfur atom in the sulfide is formed on Lewis acid centres; there is also a possibility of an additional bond between a hydrogen atom of the alkyl group and a basic centre. At an elevated temperature, and also at a low surface coverage, the surface complex decomposes at the C–S bond to form RS and RO groups.

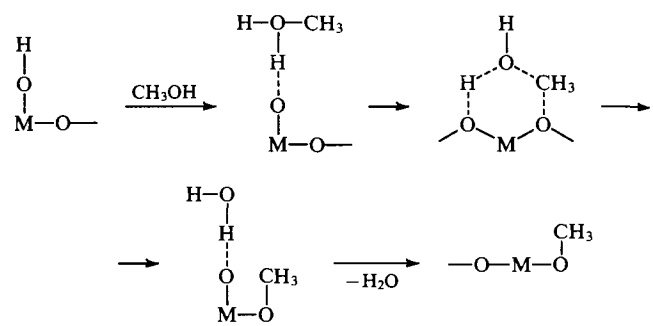
Hydrogen sulfide is adsorbed on proton-donor catalysts only via an associative mechanism:[70–74] a hydrogen-bonded form arises as a consequence of the interaction of the sulfur atom with a proton centre. On catalysts with paired Lewis acidic–basic centres, hydrogen sulfide is chemisorbed. At a reduced temperature and a high surface coverage, a donor–acceptor bond is formed between the sulfur atom and a Lewis acid centre and between a hydrogen atom of hydrogen sulfide and a basic surface centre. With increase in temperature and with decrease in surface coverage, the initial structure decomposes and acid OH groups and HS fragments are formed on the surface. There is a possibility of the dissociation of both H–S bonds in hydrogen sulfide with formation of S^{2-} groups, whereupon the concentration of the acid OH groups on the surface increases.

4. Elementary stages of the thiolation reaction

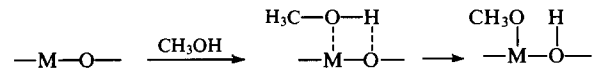
In view of the ease of the dissociative chemisorption of alcohols, the majority of investigators assumed that the thiolation reaction begins with the formation of alkoxide groups on the catalyst surface. This applies to the reactions of hydrogen sulfide with methanol on massive metal oxides and sulfides, deposited acid and alkaline catalysts, heteropolyacids, and zeolites,[11,12,25,26,28–31,75] with ethanol on the M^{2+} NaX zeolites,[36] with 1- and 2-propanols on NaX, NaY, HNaY, HZSM-5,[27] and Al_2O_3,[5] with 1-butanol on MgO, NaX, Cr_2O_3/SiO_2, K/Al_2O_3, and γ-Al_2O_3,[15] and with 1-dodecanol on K/Al_2O_3.[56]

It has been suggested[25,26,28,29] that the acid OH groups, present in the initial decationated zeolite or produced as a consequence of the dissociative chemisorption of hydrogen sulfide on the cationic forms of the zeolites, participate in the interaction of methanol with hydrogen sulfide on zeolites. However, it has been established[69,76] that methanol may be adsorbed on the sodium-forms of the NaX and NaY zeolites with participation of the sodium cation. On other catalysts, without strong proton centres on the surface (for example, the massive Al, Ti, Mg, Zr, and Ce oxides and deposited catalysts of the basic type), the coordination of methanol to the paired centres is most probable:[14,45,61] the oxygen atom of the alcohol is coordinated to a Lewis acid centre, while the hydrogen atom of the alcoholic OH group is coordinated to a basic centre. The subsequent decomposition of the associatively bound methanol leads to the methoxylation of the surface. The surface methoxide groups may react. Thus their interaction with a second alcohol molecule leads to the formation of dimethyl ether. The processes occurring on the proton and paired acid–base surface centres may be described by the following schemes (Schemes 1–3):

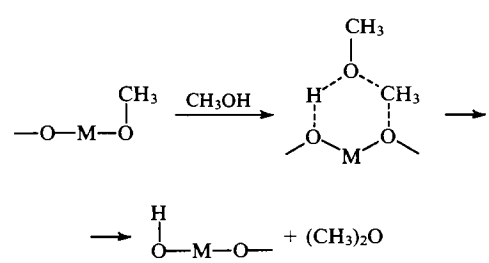
Scheme 1



Scheme 2

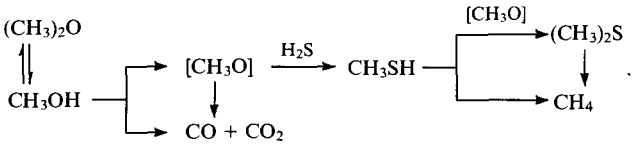


Scheme 3



As already mentioned above, dimethyl ether may react with hydrogen sulfide, affording methanethiol and dimethyl sulfide. Since the ether is readily dissociatively chemisorbed on different catalysts with formation of surface RO groups, there are no grounds for the hypothesis that methanethiol and dimethyl sulfide are formed directly from dimethyl ether. Its involvement in the formation of the thiolation products is usually accounted for by the decrease in the selectivity with respect to the ether as the degree of conversion of the alcohol increases. However, this may be a consequence not of the consumption of the ether in the formation of sulfur-containing compounds, but of the decrease in the surface concentration of the CH_3O groups interacting with hydrogen sulfide and methanethiol, which leads to a decrease in the rate of interaction of the RO groups with the alcohol.[29] The increase in the rate of conversion of methanol into the thiol, sometimes observed[77-79] in the presence of dimethyl ether, may be due to the additional methoxylation of the surface.

The following sequence of catalytic reactions with participation of methanol and hydrogen sulfide has been postulated:[45]



Both associatively[25,26,29] and dissociatively adsorbed hydrogen sulfide[45,49,80,81] may participate in the formation of methanethiol and dimethyl sulfide.

The conclusion that the thiolation reaction takes place with participation of surface methoxide groups and activated hydrogen sulfide has been confirmed by studies on the process by NMR and IR spectroscopic methods. Thus it has been found[14] that the addition of hydrogen sulfide to a SiO_2 specimen on which methanol has been adsorbed previously with subsequent heating to 350 °C leads to the disappearance of the absorption bands due to the methoxy-groups (1152 and 1044 cm^{-1}) from the IR spectrum, and to the appearance of the absorption bands of methanethiol (960 and 2845 cm^{-1}) and dimethyl sulfide (980, 1032, 1435, and 2980 cm^{-1}). The absorption bands due to methane (3017 and 1306 cm^{-1}) and the bands due to the formate structures produced on decomposition of methanol (1372, 1386, and 1583 cm^{-1}) appear under certain conditions. Similar results have been obtained on the decationated HNaY zeolite,[25,26] TiO_2, and Al_2O_3.[14] The exposure of the weakly active PO_4^{3-}/SiO_2 catalyst to hydrogen sulfide leads to some decrease in the intensity of the absorption bands due to the methoxide groups, but the high strength of the bond with the surface virtually precludes their reaction and the IR spectrum contains no absorption bands due to sulfur-containing compounds.[14]

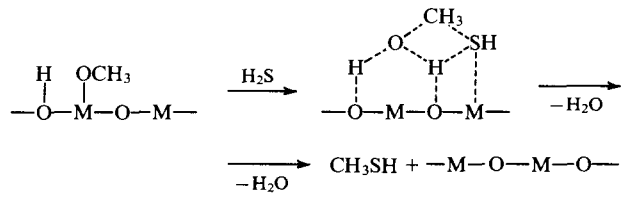
After the exposure to hydrogen sulfide of Al_2O_3 modified by potassium or sodium compounds and containing preadsorbed methanol and after heating to 200 °C, there is a decrease in the intensity of the IR absorption bands not only of the CH_3O group but also of the thiyl groups bound to Al^{3+} (in the range 2560–2580 cm^{-1}); the absorption bands due to adsorbed methanethiol and dimethyl sulfide appear simultaneously.[45]

Similar conclusions have been reached on the basis of studies of the reaction of methanol with hydrogen sulfide by the high-resolution ^1H and ^{13}C NMR methods in the solid state.[49,82] For example, when an Al_2O_3 specimen containing adsorbed methanol was exposed to hydrogen sulfide, the anisotropic line due to CH_3O ($\delta = 50$ ppm) disappeared from the ^{13}C NMR spectrum after heating above 150 °C and new lines due to dimethyl ether ($\delta = 61.9$ ppm), methanethiol ($\delta = 6.7$ ppm), and dimethyl sulfide ($\delta = 19.8$ ppm) appeared. After heating the specimen to 400 °C, the line due to methane ($\delta = -8.4$ ppm) appeared in the spectrum. On the NaX specimen, a decrease in the intensity of the signal due to the adsorbed hydrogen sulfide—molecular hydrogen sulfide ($\delta = 1.0$ ppm) and the dissociatively chemisorbed hydrogen sulfide ($\delta = -3.6$ ppm) in equilibrium with the molecular form ($H_2S \rightleftharpoons HS^- + H^+$)—was also observed.

On interaction of hydrogen sulfide with NaX on which dimethyl ether had previously been adsorbed, signals due to the methanol, methanethiol, and dimethyl sulfide formed were observed in the ^{13}C NMR spectrum and there was a simultaneous decrease in the intensity of the signal due to dimethyl ether.

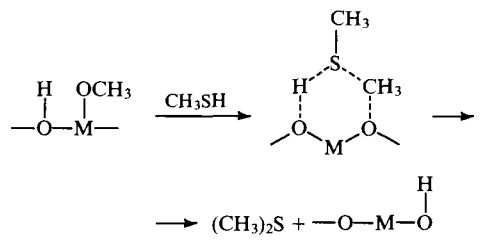
The results of the study of the conversion of methanol into the thiol on aluminium oxide catalysts made it possible to postulate the following mechanism.[45,49,80,81] When methanol interacts with a catalyst, it undergoes dissociative chemisorption, as a result of which the surface is methoxylated (Schemes 1 and 2). The interaction of the chemisorbed hydrogen sulfide with the methoxide groups leads to the formation of methanethiol (Scheme 4).

Scheme 4



The methoxide groups interact with methanethiol, activated with participation of the basic surface centres, affording dimethyl sulfide (Scheme 5).

Scheme 5

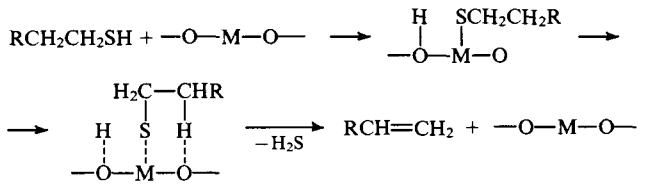


The differences between the activities and selectivites of the catalysts with respect to the formation of methanethiol depend mainly on the form in which hydrogen sulfide reacts. On proton-donor catalysts, molecular hydrogen sulfide (from the gas phase or associatively adsorbed on the surface) participates in the reaction with the CH_3O groups.[25,26,29] On catalysts with paired acid–base centres, the HS groups produced by the dissociative chemisorption of hydrogen sulfide interact with the methoxide groups, which increases the rate of formation of methanethiol. Dimethyl sulfide is formed as a result of the interaction of the CH_3O groups with the methanethiol associatively adsorbed on a basic centre, the attainment of a high rate of reaction requiring that the strength of the bond between methanethiol and the surface is optimal.[80]

The detailed mechanism of the conversion of higher alcohols into thiols has been investigated. It is believed[27,36] that in the initial stage of the reaction of hydrogen sulfide with ethanol and 1-propanol on a fresh zeolite specimen, the alcohol is dehydrated with formation of an alkene, which then reacts with the surface HS groups and is converted into the thiol; propane-2-thiol is then formed from 1-propanol. On the catalyst modified by the influence of the reaction medium, the reaction proceeds via the stage involving the interaction of hydrogen sulfide with the surface alkoxide groups, in which ethanethiol and propane-1-thiol are formed, i.e. it is postulated that the thiolation mechanism is analogous to the mechanism of the formation of methanethiol from methanol (see Scheme 4). Mashkina and coworkers[15,56] took into account the high probability of the occurrence of side reactions in the conversion of higher alcohols into thiols. In particular, the alkanethiols and dialkyl sulfides appearing on interaction of the alkoxide groups with hydrogen sulfide may be

adsorbed preferentially on the active centres, being stronger bases than the initial reactants, decomposing under these conditions with formation of alkylthio-groups (RS). An additional bond between the β-hydrogen atom of the RS group and a basic surface oxygen atom is formed on catalysts containing basic centres on the surface. As a result of the decomposition of this two-point surface complex, the alkene is eliminated. For example, the elimination of the alkene from alkanethiol is described by Scheme 6.

Scheme 6



On proton-donor catalysts without sufficiently strong basic centres, the alkene may be formed on decomposition of the hydrogen-bonded associative complex. As a result of the occurrence of similar processes, the alkene is also eliminated from the surface alkoxide groups.[77]

5. Kinetics

The validity of the postulated mechanism of the conversion of alcohols into thiols has been confirmed by the study of the kinetics of the reactions of methanol with hydrogen sulfide, of methanethiol with methanol, and of hydrogen sulfide with 1-dodecanol. A simplified mechanism, in which the formation of small amounts of CO and CH_4 is neglected and the rapid occurrence of the stages involving the chemisorption of hydrogen sulfide, the methoxylation of the surface, and the desorption of methanethiol is assumed, has been postulated for the reaction of methanol with hydrogen sulfide on acid aluminium oxide catalysts.[45,48,49,79,81] Account is also taken of the possibility that water blocks the surface (Scheme 7).

Scheme 7

$$CH_3OH + [X_1] \overset{(1)}{\rightleftharpoons} [X_2] + H_2O$$

$$H_2S + [X_2] \overset{(2)}{\rightleftharpoons} [X_1] + CH_3SH$$

$$CH_3SH + [X_2] \overset{(3)}{\rightleftharpoons} [X_1] + (CH_3)_2S$$

$$CH_3OH + [X_2] \overset{(4)}{\rightleftharpoons} [X_1] + (CH_3)_2O$$

$$H_2O + [X_1] \overset{(5)}{\rightleftharpoons} [X_3]$$

$[X_1]$, $[X_2]$, and $[X_3]$ are the initial active surface centre, the methoxylated centre, and the centre covered by water respectively.

Because of the wide distribution of the acid and basic centres on the catalyst surfaces with respect to their strength, the theoretical procedure developed by Temkin[83] for the description of the kinetics of heterogeneous-catalytic reactions occurring on a uniformly inhomogeneous surface, where the heat of adsorption varies linearly with the surface coverage by the reactants, was employed in devising the kinetic model. By assuming a high coverage of the active surface sites by water and that the rate of the process is limited by stages *2–4*, the following simplified kinetic equations were obtained:

$$w_{H_2S} = k_2^0 k P_{H_2S} P_{MeOH}^{1/2} P_{H_2O}^{-1} ,$$

$$w_{Me_2S} = k_3^0 k P_{MeSH} P_{MeOH}^{1/2} P_{H_2O}^{-1} ,$$

$$w_{Me_2O} = k_4^0 k P_{MeOH}^{3/2} P_{H_2O}^{-1} ,$$

$$w_{MeSH} = w_{H_2S} - w_{Me_2S} ,$$

where

$$k = \left(\frac{k_1^0 k_{-5}}{k_{-1}^0 k_5}\right)^{1/2} .$$

When alkali metal ions are introduced into the acid aluminium oxide catalyst, the Lewis acid centres are weakened. This hinders the activation of methanol and methanethiol involved in the formation of dimethyl ether and dimethyl sulfide. As a result, the third and fourth stages (Scheme 7) are suppressed and may be neglected, whereupon the kinetic equation assumes the form

$$w_{MeSH} = \frac{k' P_{H_2S} P_{MeOH}^{1/2}}{[P_{H_2O}(P_{H_2S} + \lambda P_{H_2O})]^{1/2}} ,$$

where

$$k' = \left(\frac{k_1^0 k_2^0 k_{-5}}{k_5}\right)^{1/2} ; \qquad \lambda = k_{-1}^0 k_2^0 .$$

Subject to certain assumptions, this equation is identical with the equation for the kinetics of the conversion of methanol into the thiol on an acid aluminium oxide catalyst. A kinetic equation of the same form has been obtained for the reaction of methanethiol with methanol.[53,81,84,85]

Formally the mechanism of the reversible reaction in which methanethiol decomposes to dimethyl sulfide and hydrogen sulfide is represented by a two-stage scheme:[30,81,85–88] The dissociative chemisorption of methanethiol leads to the formation of hydrogen sulfide and the methoxylation of the surface, after which the methoxide groups interact with a second methanethiol molecule with formation of dimethyl sulfide:

$$CH_3SH + [X_1] \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} [X_2] + H_2S ,$$

$$CH_3SH + [X_2] \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} [X_1] + (CH_3)_2S .$$

The simplified kinetic equation for the reaction on an inhomogeneous surface assumes the form

$$w = \frac{k P_{MeSH}^{3/2} (1 - P_{H_2S} P_{Me_2S} / P_{MeSH}^2 K)}{P_{Me_2S}^{1/2}} ,$$

where

$$k = k_1 \left(\frac{k_2}{k_{-2}}\right)^{1/2} .$$

The kinetic equations for the reaction of 1-dodecanol with hydrogen sulfide were derived[56] on the basis of the mechanism:

$$C_{12}H_{25}SH + [X_1] \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} [X_2] + H_2O ,$$

$$H_2S + [X_2] \xrightarrow{k_2} [X_1] + C_{12}H_{25}SH ,$$

$$C_{12}H_{25}SH + [Y_1] \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} [Y_2] ,$$

$$[Y_2] \xrightarrow{k_4} [Y_1] + C_{12}H_{24} + H_2S ,$$

$$H_2O + [X_1] \underset{k_{-5}}{\overset{k_5}{\rightleftharpoons}} [X_3] ,$$

where $[X_1]$ and $[Y_1]$ are the active centres on the initial catalyst surface and $[X_2]$, $[Y_2]$, and $[X_3]$ are the active centres on the surface covered by alkoxide groups, the chemisorbed dodecanethiol, and water respectively. The simplified equation

describing the dependence of the rate of formation of dodecane-1-thiol (w_1) and dodecene (w_2) on the partial pressures of 1-dodecanol (P_1), hydrogen sulfide (P_2), dodecane-1-thiol (P_3), and water (P_4) are

$$w_1 = k_1' P_1^{1/2} P_2 P_4^{-1} ,$$

$$w_2 = k_2' P_3 ,$$

where

$$k_1' = k_2 \left(\frac{k_1 k_{-5}}{k_{-1} k_5}\right)^{1/2} ; \quad k_2' = \frac{k_4 k_5}{k_{-5}} .$$

The reaction rates calculated by these equations agree satisfactorily with the experimental values, which confirms the validity of the postulated reaction mechanism.

It follows from the results of a study of the mechanism of the conversion of alcohols into thiols that an active catalyst should ensure in the first place the dissociative chemisorption of the alcohol with formation of reactive alkoxide groups on the surface. This is possible on both acid and basic catalysts. Furthermore, dissociative chemisorption of hydrogen sulfide with formation of thiyl groups reacting with the alkoxide groups should take place on an effective catalyst for the synthesis of an alkanethiol. Such conditions are satisfied by catalysts with paired acid – base centres. In order to reduce the probability of the further reaction of the alkanethiol — its interaction with alkoxy-groups involving the formation of a dialkyl sulfide or decomposition accompanied by the elimination of an alkene, the acid centres must be weakened and the basic centres must be strong. In contrast to the above, an active catalyst for the synthesis of a dialkyl sulfide must contain strong acid centres and moderately strong basic centres. The presence of weakened basic centres promotes the activation of the alkanethiol, which is necessary for its interaction with alkoxide groups and the formation of a dialkyl sulfide, but does not induce the decomposition of the alkanethiol to the alkylthio-groups which readily react further with formation of an alkene.

IV. Selection of catalysts and conditions for the conversion of alcohols into thiols

1. Synthesis of alkanethiols

The results of studies on the synthesis of alkanethiols under various conditions have been published.[3,4,11,14,23,25,29,30,42,48,56] A survey of these data permits the conclusion that, overall, the degree of conversion of the alcohol increases with increase in temperature, contact time, and the hydrogen sulfide : alcohol ratio. Bearing in mind the difficulty of separating an alcohol and an alkanethiol, it is recommended[47] that industrial processes be carried out under the conditions of extensive, best of all total, conversion of the alcohol. With increase in contact time, the yield of the alkanethiol increases only up to a certain value, after which it falls. With increase in temperature, the yield of the alkanethiol also rises, but the selectivity then diminishes. The temperature for conversion of higher alcohols into thiols is lower than for methanol. An increase in selectivity with respect to the alkanethiol is promoted by an increase in the hydrogen sulfide : alcohol ratio, especially in the conversion of higher alcohols into thiols. However, even in the presence of a large excess of hydrogen sulfide in the system, the selectivity with respect to the formation of alkane-2-thiols is low. It rises when carbonyl compounds are added to the reaction mixture. Thus the addition of 5 mass% of acetone to 2-propanol on a 4% K_2O/Al_2O_3 catalyst increases the overall rate of reaction by a factor of 4, while the selectivity with respect to propane-2-thiol increases from 50% to 80%. A much smaller effect is observed in the case of primary alcohols.[40]

The rate of formation of the alkanethiol increases in proportion to the partial pressure of hydrogen sulfide and the partial pressure of the alcohol (in the conversion of 1-propanol into the thiol)[5] or its square root (in the conversion of methanol and 1-dodecanol into the thiols).[56] In practice, the thiols are synthesised in the following ranges of parameters: synthesis temperatures of 350–420 °C for methanethiol and 300–350 °C for its homologues; contact time 5–35 s depending on the temperature; molar ratio hydrogen sulfide: alcohol = 1.5–7.5; overall pressure in the system as a rule not above 1 MPa.[47]

Table 7. Optimum conditions in the synthesis of alkanethiols on basic catalysts at $P = 0.1$ MPa.

Alcohol	Catalyst	Reaction conditions			Degree of conversion of alcohol (%)	Yield of alkanethiol (%)	Ref.
		T/°C	M	τ/s			
Methanol	10% K_2WO_4/Al_2O_3	400	2	5.6	92.7	90.9	4
	10% K_2WO_4/Al_2O_3	320	1.8	39[a]	98.5	90	89, 90
	K_2WO_4/Al_2O_3	400	1.5	10.5[b]	100	80	47
	25% K_2WO_4/SiO_2	360	1.6	25	84	77	31
	20% K_2CO_3/SiO_2	360	1.6	25	84	75	31
	2.9% Na_2O/Al_2O_3	360	1.6	4.2	80	75	31
	6.4% K_2CO_3/AlO	360	1.6	8.4	74	72	31
	10% K_2WO_4/Al_2O_3	360	1.6	4.2	95	62	31
Ethanol	10% K_2WO_4/Al_2O_3	318	2.86	5.6	83.4	68.7	2, 4
1-Propanol	K_2WO_4/Al_2O_3	330	3	10	95	80	47
1-Butanol	4.3% K_2O/Al_2O_3	300	10	10.4	93	91	15
2-Butanol	K_2WO_4/Al_2O_3	275	4	0.9[b]	59	15	47
	K_2WO_4/Al_2O_3	300	4	0.3	71	8	47
1-Hexanol	K_2WO_4/Al_2O_3	310	7.5	10.7[c]	100	80	47
1-Octanol	10% K_2WO_4/Al_2O_3	287	7.73	7.4	100	91	2, 4
1-Dodecanol	K/Al_2O_3	300	15	2.5	100	70	46, 92

[a] $P = 0.8$ MPa; [b] $P = 0.3$ MPa; [c] $P = 0.2$ MPa.

High yields of alkanethiols may be obtained under certain conditions on a series of supported acid catalysts and on zeolites in the cationic form. However, the process is insufficiently selective, particularly in the syntheses of methanethiol homologues and the selectivity of the above catalysts cannot be increased by varying the reaction conditions. Supported basic catalysts, in particular alkali-modified Al_2O_3, exhibit a high selectivity with respect to alkanethiols: in their presence, the selectivity is close to 100%. Table 7 presents the optimum conditions for the syntheses of alkanethiols on such catalysts.

The quality of the alkaline aluminium oxide catalyst for the synthesis of alkanethiols is influenced not only by the nature of the active component but also by its content on the surface, as well as by the characteristics of the carrier—specific surface, porous structure, phase composition, and purity. Although the use of various alkaline additives is usually mentioned, in practice potassium tungstate deposited on Al_2O_3 is apparently employed, its content being $\geqslant$10 mass%.[3,4,89–91] The active component must be present on the surface in a highly disperse state, so that the Al_2O_3 used as the carrier must have a specific surface not less than 200 $m^2\ g^{-1}$.[89–91] The presence of an considerable number of transport pores in the catalyst is necessary in order to rule out diffusional complications. γ-Al_2O_3 is usually employed, but the use of other phases is also permissible.[93] The method used to prepare the catalyst is also important, but the relevant data have scarcely been published or it has been stated[2–4] that the catalyst was prepared by impregnation or mixing methods.

The active and selective IKT-31-1 catalyst for the synthesis of methanethiol from methanol and hydrogen sulfide has been developed by the Institute of Catalysis of the Siberian Division of the Russian Academy of Sciences jointly with the Special Technical Design Bureau for Catalysts. It is prepared in two ways.[93] In the first procedure, an aqueous solution of the alkali metal compound is deposited in the form of an aerosol on an aluminium oxide carrier incorporating γ-Al_2O_3 and 20%–30% of χ-Al_2O_3 with a large macropore volume (radius exceeding 100 nm). The second procedure consists in mixing an aqueous solution of the active substance with aluminium hydroxide and subsequent granulation. The specimens obtained are heat-treated. The IKT-31-1 catalyst is employed in the industrial manufacture of methionine (the stage involving the synthesis of methanethiol) by the 'Orgsintez' Volga Industrial Conglomerate.

Alkaline aluminium oxide catalysts are more stable in the reaction involving the conversion of alcohols into thiols than the unpromoted Al_2O_3.[3,4] The activity of the catalyst does not change when the starting material contains carbon disulfide or dimethylamine[4] and also carbon monoxide[47] as impurities. Although water in fact inhibits the process, its presence in an amount of 0.5 mass%–1 mass% has a positive effect on the stability of the catalyst.[3,4] Preliminary sulfiding of the catalyst by treatment with hydrogen sulfide before use has a stabilising effect on it.[5,91] The stability of the catalyst is reduced if the process is carried out at a temperature exceeding 420 °C, since the surface becomes saturated with coke.[3] For the stable operation of the alumino–potassium tungstate catalyst, it is important to provide for the effective removal of heat from the system. The simultaneous passage of methanol and hydrogen sulfide through the K_2WO_4/Al_2O_3 catalyst at an initial temperature of 320 °C leads to the heating of the catalyst, which decreases its surface area and the yield of methanethiol. This deficiency is eliminated by dividing the catalyst into consecutively arranged layers, all the hydrogen sulfide being introduced into the first layer, whilst methanol is added in portions to each catalyst layer. This ensures the stable operation of the catalyst for three years.[89–91]

2. Synthesis of dialkyl sulfides

It has been stated in patent specifications (see the relevant reviews[2,8]) that various dialkyl sulfides R_2S ($R = C_1–C_{12}$) may be obtained under certain conditions by the reactions of alcohols with hydrogen sulfide, but real results have been published only for the synthesis of dimethyl sulfide.

The parameters of the synthesis of dimethyl sulfide are influenced by the reaction conditions. Thus an increase in the yield of dimethyl sulfide is promoted by an increase in temperature and contact time and by a decrease in the hydrogen sulfide : alcohol ratio.[2,11,12,14,17,23,25,28,30,94] The rate of formation of dimethyl sulfide increases with increase in the partial pressure of methanol and of the methanethiol formed from it. On acid aluminium oxide catalysts, the rate of reaction increases with the square root of the partial pressure of methanol and with the partial pressure of methanethiol; water inhibits the process.[49,79,81]

It follows from the analysis of the kinetic equations obtained that, in order to increase the selectivity with respect to dimethyl sulfide, it is necessary to carry out the process at a reduced partial pressure of methanol, while the hydrogen sulfide concentration should be below that required for the establishment of the stoichiometric component ratio (0.5 : 1).

In the presence of alkaline catalysts, high yields of dimethyl sulfide cannot be attained by varying the conditions in the reactions of methanol with hydrogen sulfide. This can be achieved only by employing acid catalysts and also cationic forms of zeolites on the surfaces of which strong Brønsted acid centres arise under the reaction conditions. Table 8 indicates the optimum conditions for the synthesis of dialkyl sulfides on acid catalysts. Evidently dimethyl sulfide may be obtained in an almost quantitative yield (up to 97 mol%). However, the synthesis of its homologues is difficult. Thus a relatively high yield of diethyl sulfide (up to 67 mol%) is reached in the reaction of ethanol with hydrogen sulfide only on cationic forms of zeolites. On other catalysts, active in the synthesis of dimethyl sulfide, dialkyl sulfides are not formed in the interaction of higher alcohols with hydrogen sulfide even when the reaction conditions are varied.

The achievement of the second stage in the reaction of an alcohol with hydrogen sulfide, namely its interaction with the alkanethiol, gives rise to considerable possibilities for the synthesis of dialkyl sulfides from higher alcohols in a preparative yield.

The interaction of methanol with methanethiol has been investigated[9,10,53,75,95] in the presence of various acid catalysts (see, for example, Table 6). The reaction conditions influence the rate and mode of this process.[53,81,84,85] With increase in temperature, the degree of conversion of the reactants and the yield of dimethyl sulfide also increase. At a constant temperature, the degree of conversion of the reactants and the yield of dimethyl sulfide increase with contact time; dimethyl ether is formed as a side product, its yield diminishing with increasing degree of conversion of the alcohol. Dimethyl ether and dimethyl sulfide are formed via independent paths. The rate of formation of dimethyl sulfide increases in proportion to the square root of the partial pressure of methanol and to the partial pressure of methanethiol, water inhibiting the process. An equation taking into account the degree of utilisation of the catalyst surface when the reaction takes place under conditions of internal diffusion has been obtained.[96] It follows from the analysis of the kinetic data that the influence of the side reaction involving the formation of dimethyl ether diminishes, while the selectivity with respect to dimethyl sulfide increases with decrease in the methanol : methanethiol ratio and with increase in the degree of conversion of methanol.

Unfortunately, only isolated examples of the synthesis of higher dialkyl sulfides by this procedure have been described. Thus the interaction of ethanethiol with aliphatic $C_1–C_4$ alcohols on Al_2O_3 and AlSi results in the formation of alkyl ethyl sulfides.[95]

Table 8. Optimum conditions for the synthesis of dialkyl sulfides by the reactions of alcohols with hydrogen sulfide on catalysts having different compositions.

Alcohol	Catalyst	Reaction conditions			Degree of conversion of alcohol (%)	Yield of dialkyl sulfide (mol%)	Ref.
		T/°C	M	τ/s			
Methanol	WO_3	360	1.6	4.2	99	34	11
	TiO_2	350	2	~5	91	37	14
	γ-Al_2O_3	300	0.5	12	100	94	94
	γ-Al_2O_3	350	1.0	~6	99	83	14
	γ-Al_2O_3	450	0.6	7.5	100	94	23
	η-Al_2O_3	400	0.6	0.84	100	96	16
	HPW	360	1.6	1.2	80	64	30
	AlSi	360	1.6	6.3	87	54	11
	HNaY	300	1.0	~6.5	98	92	25, 26
	HZSM-5	350	1.0	~4.5	98	93	25, 26
	HZSM-5	400	0.6	1.2	100	88	29
	NaX	350	0.5	~6	65	40	25, 26
	25% $HSiW/SiO_2$	360	1.6	1.1	100	80	30
	7% WO_3/SiO_2	360	0.6	4.2	80	59	11
	2.3% Cr_2O_3/SiO_2	360	0.6	3.7	85	52	12
	15% MoO_3/SiO_2	360	1.6	4.2	92	42	12
	0.3% Cr_2O_3/Al_2O_3	400	0.6	7.5	100	96.8	23
	0.3% CuO/Al_2O_3	400	0.6	7.5	100	90	23
	7% WO_3/Al_2O_3	360	0.6	1.1	80	56	12
	10% V_2O_5/Al_2O_3	360	0.6	0.6	80	32	12
Ethanol	WS_2	280	3.3	4	99	27	2
	TiO_2	320	2.5	3.1	97	9	2
	γ-Al_2O_3	317	2.86	5.6	93	1.6	3
	NaX	350	2	~6	–	5	24
	CdNaX	250	2	~6	85	67	36, 37
	ZnNaX	250	2	~6	76	60	36, 37
	CoNaX	250	2	~6	73	54	36, 37
	NiNaX	300	2	~6	76	25	37
1-Propanol	CdNaX	350	4	~6	80	< 10	36
1-Dodecanol	K/Al_2O_3	300	15	2.5	100	~6	46, 56, 92

V. Conclusion

Thus the studies initiated previously on the gas-phase heterogeneous-catalytic synthesis of alkanethiols and dialkyl sulfides from alcohols and hydrogen sulfide have developed further in our time. During the last 20–25 years, the main efforts in this field have been directed to the determination of the relation between the catalytic and acid–base properties of catalysts of various composition and to the elucidation of the mechanism of the thiolation reactions by means of a set of physicochemical methods (kinetic, adsorption, IR spectroscopic, and NMR methods). This made it possible to create active and selective catalysts for the synthesis of methanethiol and dimethyl sulfide, which are widely used in the manufacture of methionine (a food additive) and dimethyl sulfoxide (extractant, solvent, medicinal preparation). Higher alkanethiols (C_2–C_{12}) can be obtained in fairly satisfactory yields by the interaction of hydrogen sulfide with 1- and 2-alkanols on the catalysts proposed. The alkanethiols are employed as odorants for fuel gases, as starting materials for the synthesis of agrochemicals, as domestic chemicals, as surfactants, and as regulators of the polymerisation processes in the manufacture of raw rubbers and plastics.[97] The parameters of the processes involving the synthesis of higher alkanethiols which have been achieved may be improved by a more precise regulation of the acid–base characteristics of the catalyst surfaces.

The problem of the creation of effective catalysts for the synthesis of dimethyl sulfide homologues is still by no means fully solved. Active catalytic systems have been found only for the synthesis of diethyl sulfide. It has so far been impossible to obtain dialkyl sulfides in preparative yield by the interaction of higher alcohols with hydrogen sulfide, because the thiolation process is complicated by the occurrence of competing reactions. There are good prospects for the practical utilisation of dialkyl sulfides, since they can serve as extractants for noble metals, as flotation agents, and as additives to oils. They can also be used as the starting compounds for the synthesis of biologically active substances.[97] Bearing in mind the practical importance of dialkyl sulfides and the availability of the starting material, it may be expected that studies in the field of their catalytic synthesis will be continued, primarily with the aim of elucidating the detailed reaction mechanism, since this will help in the deliberate regulation of the properties of the catalyst and in controlling the thiolation process.

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