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Reactions involving the heterolytic cleavage of carbon–element σ-bonds by Grignard reagents

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ABSTRACT. The reactions involving the heterolysis of the C–O, C–C, C–N, C–S, C–Cl, etc. bonds by organomagnesium compounds are examined and the nature of this interesting phenomenon is analysed. On the basis of the analysis of the characteristic features of the cleavage under discussion, it is shown that the heterolysis of the carbon–element bond is, firstly, a general reaction for all classes of organic compounds (provided that two conditions are observed: the substrate molecule must fragment into two stable species—a carbonium ion and an anion—and the strength of the Lewis acid properties should be adequate for the occurrence of the above reaction) and, secondly, the heterolysis of the carbon–element bond is one of the independent pathways in the reactions of the Grignard reagents.

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I. Introduction

For more than 85 years investigators have been studying extensively Grignard reagents in organic synthesis, especially in nucleophilic addition and substitution reactions. This is apparently why, for historical reasons, chemists concentrated attention on the nucleophilic properties of organomagnesium compounds and regarded these reagents as typical nucleophiles. The Lewis acid properties of Grignard reagents were hardly taken into account in assessing their reactivity. Nevertheless, the initial coordination of the RMgX (R_2Mg, MgX_2, $R_2Mg.MgX_2$) molecules via the free electron pair of the most nucleophilic heteroatom of the substrate has been frequently included in the mechanisms of the reactions of Grignard reagents with various compounds.

It has been shown that, on the one hand, this intensifies the deficiency of the electron density on the reactive carbon (element) atom, which is as a rule linked to the heteroatom via a σ- and π-bond. On the other hand, the coordination considered increases the nucleophilicity of the reagent cryptobase.

Thus the coordination (i.e. Lewis acid) properties of the reagent merely assist in a more striking manifestation of the nucleophilic properties. The reactions proceeding via this mechanism (and this happens in most cases) have been referred to as "normal". Those which do not fit into the framework of the above mechanism have been called the "anomalous" (including reduction and enolisation reactions).

The segregation of processes in which the Lewis acid properties of RMgX merely supplement the nucleophilic properties greatly simplifies the understanding of the nature of this reagent but does not therefore provide a complete and correct idea about its reactivity.

The dual nature of the Grignard reagent consists in the fact that, in reactions with molecules whose skeleton is extremely sensitive to the action of weak Lewis acids, the initial coordination of RMgX (R_2Mg, $MgX_2.R_2Mg$, etc.) already leads to pronounced and irreversible changes in the molecular skeleton and to the appearance of new reaction centres not provided for by the mechanism of the "normal" nucleophilic addition. In such cases, the Lewis acid properties of organomagnesium compounds determine the structure and yield of the reaction products. The application of the term "anomalous" to these reactions is illegitimate.

This review deals with reactions in which the structure of the products is determined precisely by the Lewis acid properties of RMgX.

II. The structure and reactivity of Grignard reagents

1. The structure of RMgX

In a review published in 1980, Ashby[1] traced the development of ideas about the structure of organomagnesium compounds in solutions in organic solvents. He proposed a model described by the following scheme:

$$\ldots \rightleftarrows \text{trimer} \rightleftarrows \text{dimer} \rightleftarrows 2RMgX \rightleftarrows R_2Mg + MgX_2 \rightleftarrows \text{dimer} \rightleftarrows \text{trimer} \rightleftarrows \ldots \quad (1)$$

The above scheme takes into account the possibility of the establishment in solution of the Schlenk equilibrium and the formation of dimers, trimers, and more complex associated species. In view of their insignificant amount, ionic species have not been included in this scheme.

The Schlenk equilibrium for isobutylmagnesium bromide[2] and t-butylmagnesium bromide[3] in solution in tetrahydrofuran (THF) was investigated by ^1H NMR spectroscopy and that of dicyclopentadienylmagnesium was studied by ^{25}Mg NMR spectroscopy.[4] It was shown that the equilibrium depends greatly on the reagent concentration and to a lesser extent on temperature.

In a later study[5] the existence of the Schlenk equilibrium in solution was questioned. According to the authors,[5] the following equilibria occur in solution in THF:

$$4[RMgX(THF)_n] \rightleftarrows 2[MgR_2(THF)_2] + [MgCl_4]^{-2} + [Mg(THF)_6]^{+2}, \quad (2)$$

$$4[RMgX(THF)_n] \rightleftarrows [(THF)_nMg(\mu\text{-}Cl)_2MgR_2] + [RMg(\mu\text{-}Cl)_2MgR(THF)_3]. \quad (3)$$

The above scheme, extended also to other solvents and other halogen atoms, was proposed on the basis of indirect data. Thus $[NBu_4]_2MgCl_4$ and $[(THF)_4Mg(\mu\text{-}Cl)_2FeCl_2]$ have been isolated from a solution of a Grignard reagent. According to Sobota and Duda,[5] $MgCl_2$ is too reactive to exist in solution in a free state. On this basis, the existence of the Schlenk equilibrium is in fact rejected.

The evidence presented by Sobota and Duda[5] is apparently inadequate and too controversial to question the existence of the Schlenk equilibrium, but it is necessary to take into account Eqns. (2) and (3) in considering the structure of RMgX in solution.

In the study of equilibria involved in Scheme (1), it has been noted[6,7] that the equilibrium depends on many factors — the nature of the organic group, the halogen, the temperature, the concentration of the organomagnesium compound investigated, and the solvent. The influence of the solvent, or more precisely of its solvating capacity, on the equilibrium plays a decisive role under these conditions.

The solvating capacity of the solvent is a complex function of the coordination properties of the heteroatom involving the lone electron pairs of the solvent and the steric hindrance of the coordination of its molecules to the substrates.[8] For this reason, the solvating capacities of solvents can be compared only when their basic properties are referred to the Lewis acid properties of a specific substrate.

The quantity serving as a measure of the solvating capacity of the solvent relative to a given Lewis acid can be estimated from ^1H NMR spectra.[9,10] The strength of strong Lewis acids relative to a given base can be estimated similarly.[11]

Another approach to the quantitative allowance for the effect of steric and basic properties of the solvent on its solvating capacity has been proposed by Tuulmets and co-workers.[12–14] They introduced the function B^* — the effective basicity characterising the solvating capacity of the solvent relative to a given Lewis acid (organomagnesium compound):

$$B^* = B(B_0/B + \varphi^* + E_s^{0'}).$$

The quantities B and $E_s^{0'}$ — characteristics of the basic and steric properties of solvent molecules — have been tabulated. The values of the effective acidity index φ^* of the reference substrate can be calculated from the following correlation equation:

$$\varphi^* = 10.1 + 2.4\,E_s^{0'} + 0.6\,\Sigma\sigma^*. \quad (4)$$

where $E_s^{0'}$ are the isosteric constants of the substrate molecules and $\Sigma\sigma^*$ is the sum of the inductive constants of the cryptobase and the halogen of RMgX. These have been tabulated. B_0 is a constant.

Thus the quantity B^* characterises the effectiveness of the interaction of the selected reference substrate with the solvent, the decisive role being attributed, according to the author,[12] to steric hindrance of coordination.

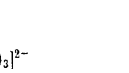
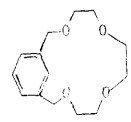
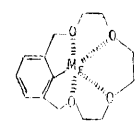
It follows from Eqn. (4) that the quantity φ^* serves as an estimate of the effectiveness of the interaction of the Lewis acid with the molecules of the given solvent and the effective acidity indices were therefore used by the author[12] to determine the position of the Schlenk equilibrium:

$$K_{Schl} = -\gamma(2\varphi^*_{RMgX} - \varphi^*_{R_2Mg} - \varphi^*_{MgX_2}), \quad (5)$$

where γ is a characteristic of the base, entering as a proportionality coefficient between the left- and right-hand sides of Eqn. (5).

The structural transitions defined by Eqn. (1) and occurring in solvents can be understood more readily by determining the driving force of the processes described — the coordinative unsaturation of the RMgX molecule. This is manifested primarily by the formation of complexes by organomagnesium compounds (Table 1).

Table 1. Composition of the complexes formed by RMgX.

Ligand (L)	Composition of the complex RMgX : L	Refs.
Ph^-	$[Li(TMEDA)^*]_2Mg_2Ph_6$	[15]
Ph^-	$LiMgPh_3$	[16]
Ph^-, H^-	$KMgPh_2H$	[17]
$(CH_3)_2N(CH_2)_2NHCH_3$	$(CH_3)_2Mg \cdot L$	[18]
$N[CH(CH_3)CH(CH_3)OCH{-}CH{-}OCH_3]_3$ (CH$_3$ CH$_3$)	$CH_3MgI \cdot L$	[19]
$(CH_3)_2N{-}(CH_2)_2O(CH_2)_2OCH_3$	$PhMgBr \cdot L$	[20]
$[(CH_2)_3{-}O{-}(CH_2)_3]^{2-}$		[21]
		[22]

* TMED = tetramethylethylenediamine.

The magnesium in Grignard reagents can have different coordination numbers in crystals and in solution but in a solvent a coordination number of four is most characteristic of these compounds.[23]

In the absence of the solvent (either at high concentrations or in the case of weak interactions with the solvent molecules), the hypothetical RMgX molecule is then coordinatively unsaturated. The coordination saturation of asymmetric organomagnesium compounds is attained in this instance as a result of the creation of halogen bridges[24] or alkyl(aryl) bridges.[25] Symmetrical organomagnesium compounds form polymer chains in the solid state[26] while in solution they give rise to self-association species formed via alkyl(aryl) groups.[2,27]

The solvent molecules competing with the halogen atoms and the atoms of the organic group for coordination sites at the magnesium atom hinder the formation of self-associated species, and the greater the solvating capacity of the solvent the more intense is this competition. This is why highly basic solvents not only decompose

the conglomerates RMgX (X = Br, I) at low reagent concentrations as far as monomeric species but they also solvate effectively the symmetrical molecules of organometallic compounds, displacing the Schlenk equilibrium to the right. This claim is confirmed by the weaker effect of solvation on the rate of exchange of organic groups in symmetrical Grignard reagents compared with the asymmetric reagents.[9]

Certain halogen bridges (X = F, Cl) are so strong that a highly solvating solvent cannot disrupt them and the molecules of the organomagnesium are associated even at high dilution.[1] On the other hand, in the presence of a highly electron-accepting substituent in the skeleton of the cryptobase, for example, fluorine atoms (R = C_6F_5), certain Grignard reagents behave even in weakly basic solvents as if they were placed in highly basic solvents. This is reflected not only by the absence of association but also by a rightward shift of the Schlenk equilibrium.[28]

Since the substrates used in reactions with Grignard reagents have lone electron pairs in the heteroatoms, they are all Lewis bases. When these substrates are introduced into a RMgX solution, they begin to compete with solvent molecules for coordination sites at the magnesium atom. The ability of Lewis bases to complete with solvent molecules and the strength of the Lewis acid properties of RMgX determine in many respects the reactivity of the organomagnesium compound.

2. The reactivity of RMgX

The reactions of organomagnesium compounds with various substrates are difficult to study because even in the simplest case (at high dilution and for X = Cl, Br, or I) there exist in solution at least three, in conformity with the Schlenk equilibrium, species with different reactivities.

It has been found that in many instances symmetrical organomagnesium compounds are more reactive than asymmetric compounds,[29,30] while the opposite behaviour was noted in other cases.[31]

The reactivities of monomeric and polymeric forms are in its turn also different, as shown by a number of workers.[32,33]

When the amount of Grignard reagent is equivalent or deficient, the primary products of the addition reagent—magnesium enolates or alkoxides—can themselves function as competing reactants.[34,35] The competitive reactions are suppressed by a large excess of the Grignard reagent.

Thus the reactivity of organomagnesium compounds is equal to the sum of the reactivities of all the magnesium-containing species present in solution.

(a) Nucleophilic, basic, and reducing properties of RMgX. It has been suggested[36] that the entire wide variety of reactions of organomagnesium compounds proceeding via the polar mechanism be divided arbitrarily into two main types in terms of the effect of solvation on their course, for example:

$$R_2C{=}O + R'MgX \rightarrow R_2R'C{-}OH \text{ addition—first type;}$$

$$RMgX + R'X \rightarrow R{-}R' + MgX_2 \text{ substitution—second type.}$$

The reactions of the first type are inhibited and those of the second type are promoted with increase in the solvating capacity of the solvent.[37] Intense solvation polarises the Mg—C bond, enhancing the electron-donating properties of the α-carbon atom of the cryptobase of the organomagnesium compound, on the one hand, and blocks the coordination sites at the magnesium atom, on the other.[37]

In the reactions of the first type, the nucleophilic attack on the cryptobase R^- is preceded by the coordination of the Grignard reagent to the carbonyl compound with formation of a complex. The existence of such complexes has been confirmed spectroscopically.[38,39] It is believed that this stage enhances the electrophilic properties of the attacked carbon atom.[40]

Weakly basic substrates, for exzmple $C_2F_5CH{=}O$, cannot displace solvent molecules and give rise to reactions of an intermediate type occurring without preliminary coordination.[41]

In reactions of the second type, the coordination of RMgX to the substrate does not play a decisive role and Grignard reagents behave like typical nucleophiles.[42]

We believe that there exists a further type of reactions of organomagnesium compounds proceeding via a polar mechanism. The substrate cleavage (isomerisation) reactions under the influence of RMgX belong to this type. These reactions proceed as a rule in weakly basic solvents, highly basic solvent retarding or fully inhibiting them. Not only the primary coordination of RMgX but also the Lewis acid strength of the reagent are important for reactions of the third type.

In our view, highly solvating solvents weaken the acid properties of organomagnesium compounds. This fact is important because, whilst causing an overall retardation of addition reactions, intense solvation makes their occurrence possible. Under the conditions of intense solvation, cleavage (isomerisation) reactions are as a rule inhibited.

Since reactions of the third type take place via a carbonium-like state (or via the intermediate formation of a carbonium ion, the solvation (stabilisation) of these states plays an important role in the above reactions. Therefore, if the solvating capacities of the solvents do not differ greatly, cleavage (isomerisation) reactions can take place in solvents with a higher solvating capacity as a result of the solvation stabilisation of carbonium-like transition states.

In order to understand the structures and yields of the products of the reactions of RMgX with various substrates, we shall now turn to conclusions reached for reactions of ketones with RMgX.[42–44] In the first place, in the presence of a large excess of RMgX magnesium alkoxides and enolates compete weakly with the Grignard reagent in addition, enolisation, and reduction reactions. Consequently, ketones react with RMgX via three main pathways.

The influence of structural differences in these three reactions is susceptible to quantitative interpretation. The partial rate constants for the reactions of ketones having the general formula $RCOCH_3$ with RMgX can be calculated from the following equations:

$$\lg(K_{add}/K_0) = \rho^*\sigma^* + \delta E_s^0 + h\Delta n, \quad \text{(Ref.42)}$$

$$\lg(K_{red}/K_0) = \rho^*\sigma^* + \delta E_s^0, \quad \text{(Ref.43)}$$

$$\lg(K_{enol}/K_0) = \delta\Sigma E_s^0. \quad \text{(Ref.44)}$$

The influence of the inductive effect of the group R on the addition constant (K_{add}) and the reductive constant (K_{red}) is taken into account by the first term in the equations (σ^* are the Taft inductive constants of the substituents). The steric hindrance in the addition and reduction reactions is described by the term δE_s^0 (the steric constant of the substrate group R) and enolisation (the enolisation constant K_{enol}) is described by the term $\delta\Sigma E^0$ (the steric constants of the substituents at the α-carbon atom of the ketone).

The third term ($h\Delta n$) in the equation describing the kinetics of the addition reaction takes into account the influence of the C–H and C–C σ-bonds in the α-positions. Among the wide variety of factors influencing the rates of parallel reactions, steric factors are believed to play a decisive role.[42–44]

The study of the kinetics of the reactions of ketones with RMgX enabled the authors[42–44] to conclude that, for the three reactions analysed, the transition state has a structure close to that of the initial compounds, i.e. the ketone and RMgX, and in this sense they can be regarded as related. One cannot therefore differentiate one of them (addition) as the only "correct" or "normal" reaction of RMgX with carbonyl compounds.

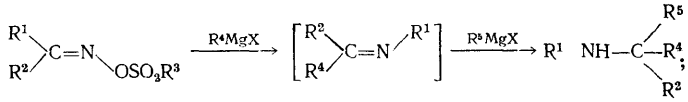
The partial rate constants for parallel reactions are greatly influenced by the basicity of the solvent, whose increase as a rule entails a decrease in the above quantities.[45]

Later studies[46,47] of the interaction of ketones with Grignard reagents confirmed the validity of the conclusions reached by Khyrak et al.[45]

Thus the reactions of organomagnesium compounds with ketones (and other carbonyl compounds) proceed via at least three independent pathways examined above. The yield of the products in each pathway is not related to the structures of the ketone and the Grignard reagent. This feature is reflected in the partial rate constants.

Many reactions of organomagnesium compounds involving major internal rearrangements of the substrate have now been discovered. These reactions are not characteristic of organolithium compounds and cannot be understood from the standpoint of reactions of the second type (nucleophilic substitution). These reactions are determined by the Lewis acid properties of RMgX.

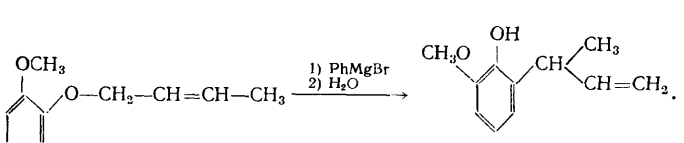
(b) The Lewis acid properties of organomagnesium compounds. Before discussing specific reactions involving the heterolysis of C–element σ-bonds, we should like to quote a number of examples of the behaviour of the Grignard reagent as a typical electrophile. The Beckmann rearrangement of oxime sulphonates has been discovered.[48] It takes place on treatment with organomagnesium compounds:



$R^4MgX = CH_3MgI$, n-$C_4H_9C{\equiv}CMgBr$.

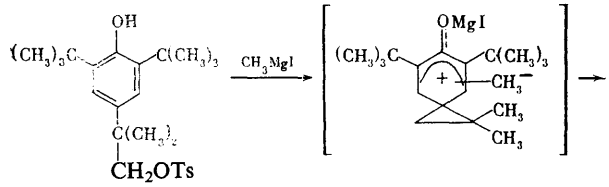
The imines formed are converted under the influence of the excess R_5MgX into secondary amines. Neither the nature of the organic group nor that of the halogen influences significantly the rearrangement.

Another example illustrating strikingly the Lewis acid properties of a Grignard reagent may be the Claisen rearrangement of the ether shown below under the influence of phenylmagnesium bromide:[49]

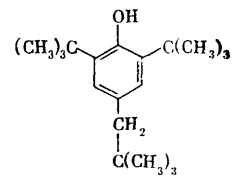


23%

It is believed that phenyl tosylate also undergoes a rearrangement on treatment with a Grignard reagent and it is assumed that the latter proceeds via a pyrocyclic complex:



Ts = *n*–$CH_3C_6H_4SO_2$–



The question of the existence of the complex is apparently controversial but presumably a carbonium-like transition state may be formed on treatment with RMgX.

Thus organomagnesium compounds, acting on certain substrates as Lewis acids, can induce profound changes in their molecular skeleton.

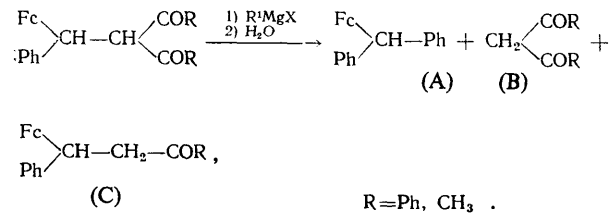
The data described below are devoted to the analysis of the characteristics of the structures of the substrate and the reagent necessary for the fragmentation of σ-bonds under the influence of the Grignard reagent.

III. Reactions involving the heterolysis of carbon–element α-bonds by Grignard reagents

1. C–C heterolysis

σ-C–C heterolysis on treatment with RMgX is not by itself a very interesting reaction, since in the given instance a very strong bond is usually readily fragmented. The authors of the present review studied this reaction in detail in relation to β-dicarbonyl compounds and discovered its principal characteristic features which made it possible to regard σ-C–C heterolysis as a special case of the more general fragmentation of the C–element σ-bond by organomagnesium compounds and other Lewis acids. We therefore decided to begin the consideration of the problem indicated in the heading of this Section with the cleavage of a C–C σ-bond.

The interesting reaction involving the fragmentation of a C–C σ-bond in ferrocene-containing β-diketones by Grignard reagents was discovered in 1980 (Table 2):[51,52]



R = Ph, CH_3 .

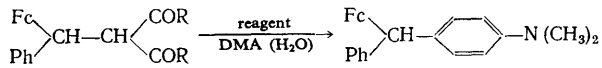
Together with the C–C cleavage products, traces of the ketone cleavage products were detected. The difference between the yields of the σ-C–C fragmentation products has been explained[51,52] by the difference between the nucleophilic properties of the Grignard reagents.

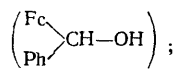
Table 2. The yields of the products of the reactions of RMgX with β-diketones.

R	Reagent	Yield of products, %			Refs.
		(A)	(B)	(C)	
CH_3	PhMgBr	35	см.*	см.*	[51]
CH_3	CH_3MgI	17	см.*	см.*	[52]
Ph	PhMgBr	60	74	insignificant	[53]

*Not isolated.

In another study,[53] the same workers showed that ferrocene-containing β-diketones are cleaved at a C–C σ-bond by strong Lewis acids: $MgBr_2$, $ZnCl_2$, $SnCl_4$, as well as trifluoroacetic acid:

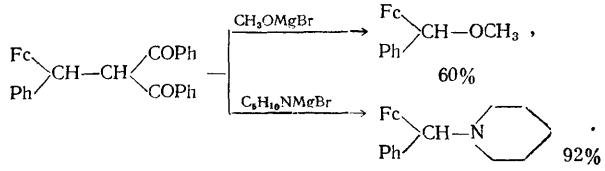




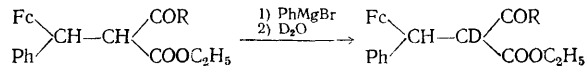
DMA = dimethylaniline.

According to the authors[52,53] the nature of the cleavage by RMgX and by strong Lewis acids is different.

The nature of the interaction of α-monosubstituted β-dicarbonyl compounds with Grignard reagents was studied in detail by the present authors.[54] In the first place, we established that the Lewis acid properties of RMgX are in fact responsible for the σ–C–C fragmentation. This conclusion follows from the following observations: firstly, an increase in the solvating capacity of the solvent led to a sharp increase in the yield of the product of the fragmentation considered, as far as its complete disappearance from the reaction mixture in the presence of crown-ethers, and, secondly, in contrast to lithium piperidide and alcoholic alkali, dibenzoyl-(ferrocenylphenylmethyl)methane is cleaved by piperidylmagnesium bromide and methoxymagnesium bromide:[55]



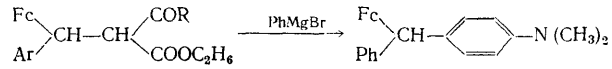
It has also been established that this reaction depends on the structure of the β-dicarbonyl component of the substrate. In contrast to β-diketones, a β-ketoester and diester are not cleaved by phenylmagnesium bromide at a C–C σ-bond. In this case, the enolisation of the β-dicarbonyl compound takes place quantitatively:



100%

R = CH_3, OC_2H_5.

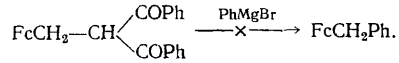
The σ-C–C fragmentation depends in many respects on the stability of the carbonium ion, which can be formed by the α-substituent. *p*-Dimethylaminophenylferrocyenylmethylmalonic and acetoacetic esters are cleaved at a C–C σ-bond:[56]



Ar = *n*-$(CH_3)_2NC_6H_4$

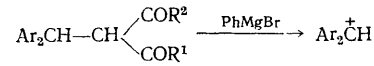
R = CH_3 (83%),
R = OC_2H_5 (7%).

On the other hand, as a result of a decrease in the stability of the carbonium ion formed by the α-substituent, dibenzoyl-(ferrocenylmethyl)methane is not fragmented by phenylmagnesium bromide:[57]



Thus we reached the following conclusions: the course of the σ-C–C cleavage reaction is determined by the stability of the carbonium ion formed by the α-substituent of the substrate and also by the stability of the carbanion formed by the unsubstituted β-dicarbonyl compound, the role of the Lewis acid properties of the organomagnesium compound being decisive.[57,59] The σ-C–C fragmentation reaction should therefore be characteristic also of compounds without the ferrocenyl fragment and also not only of β-dicarbonyl compounds.

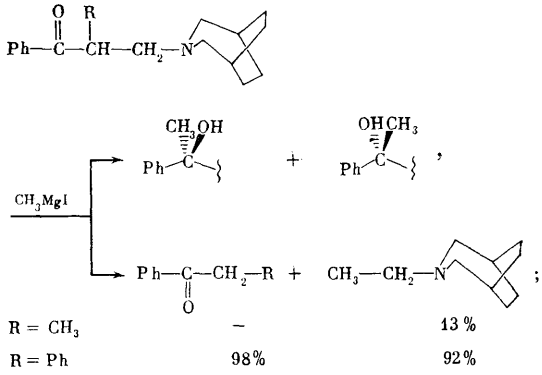
The reaction under discussion has been observed, for example, with derivatives of bis(*p*-dimethylaminophenyl)methyl series:[60]



$R^1 = R^2 = CH_3$, Ph, OC_2H_5;
$R^1 = CH_3$, $R^2 = OC_2H_5$.

The occurrence of fragmentation was inferred from the appearance of the λ_{max} = 611 nm band characteristic of bis(*p*-dimethylaminophenyl)methyl carbonium ion.[61]

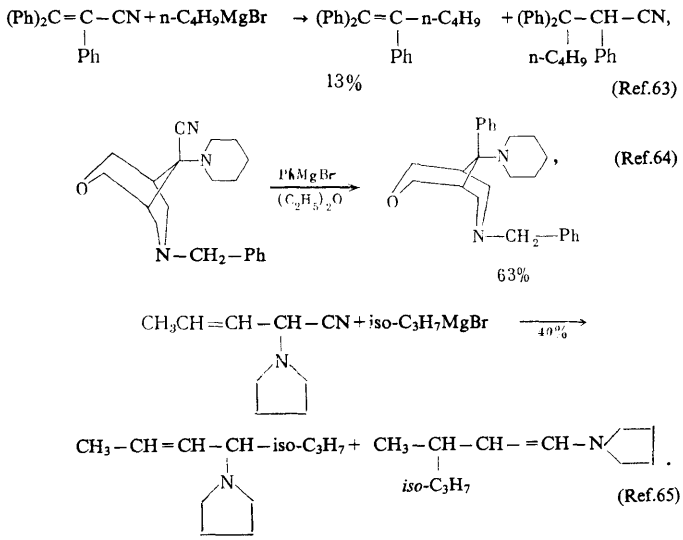
It has been established[62] that the σ-C−C fragmentation reaction also takes place with certain monocarbonyl compounds:



R = CH_3	–	13 %
R = Ph	98%	92%

This "anomalous" reaction, in the view of Angiolini et al.,[62] is accompanied by the "normal" nucleophilic addition reaction.

The σ-C−C cleavage reaction has been observed[63–65] for nitrile derivatives:



(Ref.63)

(Ref.64)

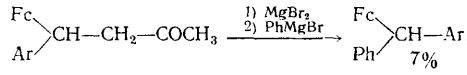
(Ref.65)

In all the studies examined above, the σ-C−C cleavage reaction is accompanied by addition to the nitrile group[64,65] (1,2-addition) and to alkene double bond (1,4-addition).[63]

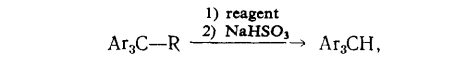
Thus the σ-C−C fragmentation of organic compounds by Grignard reagents is one of the possible reaction pathways, provided that (1) the substrate molecules can be imagined to be cleaved into a stable carbonium ion and a carbanion (the stability of the fragment is correlated with the values of pK_{R^+} and pK_a for the carbonium ion formed by the α-substituent and the carbanion derived from the unsubstituted β-dicarbonyl compound respectively) and (2) the strength of the Lewis acids RMgX must be sufficient for the fragmentation of the substrate molecule.

The σ-C−C dissociation reactions are obscured by parallel reactions involving addition to the carbonyl group and enolisation. This apparently leads to a complex dependence of the yield of the σ-C−C cleavage products on the Lewis acidity of the organomagnesium compounds expressed in terms of φ*.[12]

This obstacle can be avoided using strong Lewis acids or protic acids. Thus, although monocarbonyl compounds are not fragmented by a Grignard reagent, they are cleaved at a C−C σ-bond by magnesium bromide etherate:[54]

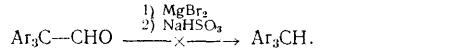


Aldehydes, nitro-compounds, and the nitrile oxides of the tris(*p*-dimethylaminophenyl)methyl series undergo σ-C−C fragmentation:[66–68]

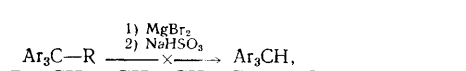


reagent = $MgBr_2$, CH_3COOH; R = CH_2CHO, CH_2NO_2, $CH_2CH=CH-CHO$, $C\equiv N^+-O^-$.

Although the authors[66–68] do not explain the observed phenomenon, it can be understood in terms of the values of pK_{R^+} and pK_a. The relation between these quantities, estimated in terms of pK_a and pK_{R^+}, can be demonstrated by the following example. Despite the high thermodynamic stability of $Ar_3\overset{+}{C}H$, compounds forming unstable carbanions are not cleaved:[66]

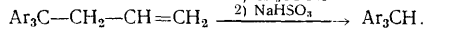


The primary coordination of the reagent and the substrate is extremely important for the σ-C−C fragmentation reaction. This postulate is well illustrated by the following example:[68]

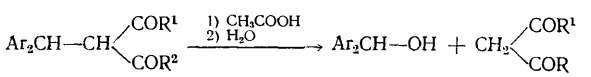


R = $CH_2-CH=CH_2$, CH_3, n-C_3H_7.

On formation of two stable ions, the possibility of the protonation of the olefinic double bond by acetic acid appears, which leads to the σ-C−C fragmentation of tris(*p*-dimethylaminophenyl)methylallyl:[68]



The ready fragmentation of β-dicarbonyl compounds of the bis(*p*-dimethylaminophenyl)methyl series at a C−C σ-bond by acetic acid, discovered in 1909 by Fosse,[698] also becomes entirely explicable:

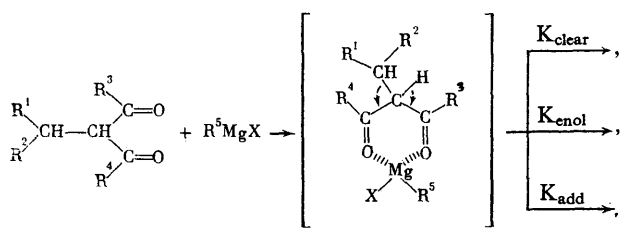


$R^1=R^2=OC_2H_5$, CH_3; $R^1=OC_2H_5$, $R^2=CH_3$.

Table 3. The yields of the products of the cleavage of ethers.

No.	Substrate	Reagent	Yield of products, %		Refs.
			(D), (D′)	(E), (E′)	
1	Ph–CH=CH–CH_2–O–$(CH_2)_2$Ph	n-C_6H_{13}MgBr	Ph(n-C_6H_{13})CH–CH=CH_2 15	$Ph(CH_2)_2OH$ 23	[76]
2	PhCH=CH–CH_2–O–C_4H_9	n-C_7H_{15}MgBr	Ph(n-C_7H_{15})CH–CH=CH_2 52	n-C_4H_9OH 76	[77]
3	CH_2=CH–CH_2–O–Ph	PhMgBr	Ph–CH_2–CH=CH_2 30	PhOH 60	[77]
4	CH_3–CH=CH–CH(t-C_4H_9)–O–$C(CH_3)_3$	n-C_8H_{17}MgBr	CH_3–CH(n-C_8H_{17})–CH=CH–$C(CH_3)_3$ 62	$(CH_3)_3COH$ 88	[78]

The following mechanism has been proposed for the σ-C–C fragmentation of β-dicarbonyl compounds (different classes of organic compounds) by Grignard reagents (and other Lewis acids):[54]



In the first stage of the reaction, the β-dicarbonyl compounds is coordinated to the Grignard reagent (chelate formation).[70] It is well known that the coordination of Lewis acids, especially of the Mg^{2+} ion,[71] labilises the proton in the α-position relative to the carbonyl group.[72] When the molecule contains an α-substituent capable of giving rise to a stable carbonium ion, the α-substituent begins to compete with the proton as regards lability, i.e. the σ-C–C cleavage and enolisation reactions complete, whereupon the coordination of the reagent enhances also the electrophilic properties of the carbonyl groups.

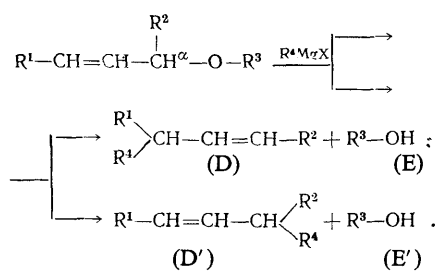
Thus coordination (chelate formation[73,74]) of the Grignard reagent leads to polarisation (in extreme cases to ionisation) of the C–C, C–H, and C=O bonds, which are in any case already polarised.[75] In the second stage, the three cryptobasic centres formed are attacked with different effectiveness. The ratio of the products via the three pathways — σ-C–C cleavage, enolisation, and addition of the carbonyl group — depends on the ratio of the partial constants K_{cleav} (cleavage) K_{enol}, and K_{add}.

The characteristics noted for the σ-C–C fragmentation of β-dicarbonyl and monocarbonyl compounds hold also for other classes of organic compounds.

2. C–O Heterolysis

(a) The cleavage of ethers. A number of ethers undergo heterolysis at a C–O σ-bond on treatment with Grignard reagents. This reaction is observed only for a particular structure of organic compounds of this class.

Vinyl and allyl ethers undergo cleavage at a C–O σ-bond. The observed reaction can be represented schematically in the following manner in relation to αβ-unsaturated ethers:



Data on the σ-C–C heterolysis of unsaturated ethers are compiled in Table 3.

By analogy with ketones, it is believed,[77,78] that a complex of the Grignard reagent with the ether is formed initially and then rearranges with formation of the products of the given reaction. Hill et al.[77] believe that the coordination of the RMgX molecule to that of the ether increases the electron density deficiency on the α-carbon atom with subsequent attack on the latter by the cryptobase (1,2-addition). The 1,4-adducts are consistent with the mechanism involving a six-membered transition state.[77]

On the other hand, the authors themselves[76,78] noted that the model with the six-membered state is not universally applicable to the given reaction, since it does not explain the composition of the products of the reaction of RMgX with ethers having bulky substituents in the 2- or 4-position (Table 3, example 4).

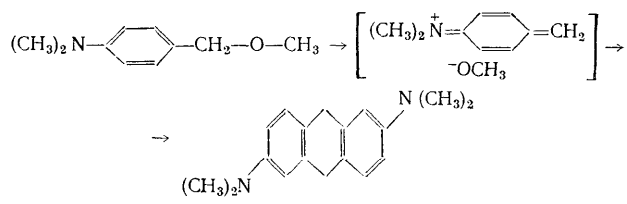
We may note that the molecules of unsaturated ethers, presented in Table 3, can be cleaved into two fragments: the stable allylcarbonium ion and the alkoxide (enolate) anion.

The presence of the carbonium ion in the transition state explains satsifactorily the presence in the reaction mixture of the products of the Claisen isomerisation of the enol ether. The presence in the molecule of a group which can be readily eliminated makes possible the cleavage at a C–O σ-bond of the tosylate derived from a sterically hindered enol (see above).

As in σ-C–C heterolysis, the coordination of RMgX to the oxygen atom of the ether leads to intense polarisation (ionisation) of a C–C σ-bond and attack by the nucleophilic completes the heterolysis.

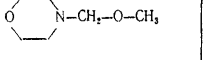
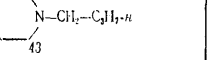
The data presented in Table 4 may serve as evidence in support of the occurrence of the reaction investigated via an ionic mechanism.

The existence of immonium structures in the transition state has been postulated.[79] According to these workers, this explains the presence of condensed systems in the reaction mixture:



The immonium ion was formed not under the influence of RMgX, but, as follows from the mechanism proposed by the authors,[79] resulted from σ–σ conjugation.

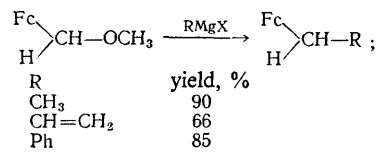
Table 4. Yields of the products of the cleavage of ethers.

No.	Substrate	Reagent	Yield of product, %	Refs.
1	Ar–CH_2–O–CH_3	PhMgBr	Ar–CH_2–Ph 84	[79]
2		**n-C_3H_7MgBr**	 43	[80]
3	$(CH_3O)_2CH$–$N(CH_3)_2$	PhMgBr	$(Ph)_2CH$–$N(CH_3)_2$ 89	[81]
4	PhO–$CH(OC_2H_5)_2$	**n-C_4H_9MgBr**	**n-$C_4H_9CH(OC_2H_5)_2$** 90	[82]
5	CH_3O–CH_2NR_2	$(CH_3)_3SiCH_2MgCl$	$(CH_3)_3SiCH_2$–CH_2NR_2 70	[83]
6	PhOCH$(OC_2H_5)_2$	CH_2=CH–CH_2MgBr	CH_2=CH–CH_2–$CH(OC_2H_5)_2$ 70	[84]
7	$(PhO)_2CHOC_2H_5$	**n-C_4H_9MgBr**	$(C_4H_9)_2CHOC_2H_5$ 74	[85]
8	(PhO)$CH(OC_2H_5)_2$	**n-C_4H_9MgBr**	**n-$C_4H_9CH(OC_2H_5)_2$** 80	[86]
9	$CH_3OCH_2N[Si(CH_3)_3]_2$	CH_3MgBr	$CH_3CH_2N[Si(CH_3)_3]_2$ 89	[87]

The C–O σ-bond in the ethers listed in Table 4 is so labile that, in contrast to the compounds listed in Table 3, the σ-C–O heterolysis by organomagnesium compounds in THF of ethers, which are cleaved in diethyl ether or diethyl ether–benzene mixtures, takes place with high yields.

In all the examples listed in Table 4, the C–O σ-bond is cleaved selectively — on the side of the most stable immonium cation. On the other hand, when the molecule contains carbonium ions of comparable stability, cleavage takes place on the side of the more stable anion (Table 4, examples 4 and 6–8).

There is nothing surprising about the fact that the ethers containing the ferrocenyl group — a powerful stabiliser of the α-carbonium ion — undergo σ-C–O heterolysis by organomagnesium compounds:[88]

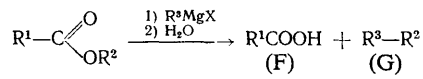


R	yield, %
CH_3	90
$CH=CH_2$	66
Ph	85

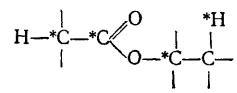
In this case, the σ-bond under consideration is highly polarised (ionised) and coordination of RMgX leads to σ-C–O fragmentation in the presence of a leaving group which is effectively eliminated.

Thus ethers are selectively cleaved at a C–O σ-bond, the latter being fragmented on the side where stable carbonium ions and alkoxides are formed.

(b) The cleavage of esters. A number of esters undergo σ-C–O fragmentation on treatment with RMgX:



At least three parallel reactions take place simultaneously due to the existence of the following four reaction centres:[89]

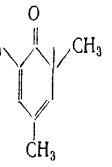
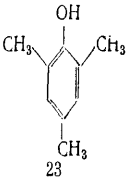
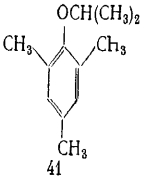


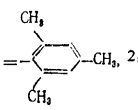
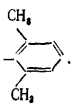
All the possible reaction pathways operate after the formation of the coordination complex of RMgX and the substrates as a result of its rearrangement.[90] The reaction with a six-membered transition state has been postulated[91,92] as anomalous for σ-C–O heterolysis. In a later study,[93] the mechanism with a six-membered transition state was questioned and an ionic reaction mechanism was put forward for the reaction with the following characteristic features: (1) the alkyl substituent linked to the oxygen atom is capable of giving rise to a stable carbonium ion; (2) among the ethoxycarbonyl groups, the "normal" addition to the carbonyl group is hindered and is therefore retarded.

Table 5 presents a compilation of data on the σ-C–O heterolysis of esters.

The postulates of Arnold and Searles[93] are applicable in cases 2, 3, 6, and 7 (Table 5), while in other instances they fail to account for the occurrence of σ-C–O heterolysis. Indeed, in examples 1, 4, 5, 8, and 9, the ethoxycarbonyl group is not blocked to nucleophilic attack by the cryptobase, but the cleavage under consideration does not occur.

Table 5. The yields of the products of the cleavage of esters.

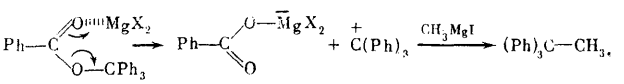
No.	R^1	R^2	Reagent	Yields of products, % (F)	Yields of products, % (G)	Refs.
1	Ph	$CH_2-CH=CH_2$	Mes*MgBr	Mes–CH_2–CH=CH_2 57	PhCOOH 26	[90]
2	$PhCH_2$, CH_3, C_2H_5–C	$CH_2-CH=CH_2$	PhMgBr	Ph–CH_2–CH=CH_2 70	$PhCH(CH_3)(C_2H_5)-C(=O)-OH$ 87	[92]
3	Mes	$C(CH_3)_3$	PhMgBr	Ph–$C(CH_3)_3$ 24	MesCOOH 9	[93]
4	CH_3	$C(Ph)_3$	$(CH_3)_3CMgCl$	$(Ph)_3C-C(CH_3)_3$ 20 + $(Ph)_3C-H$ 10	2*	[94]
5	Ph	$CH(Mes)_2$	C_2H_5MgBr	$(Mes)_2CH-C_2H_5$ 32 + $(Mes)_2CH_2$ 12	PhCOOH 9	[95]
6	Dur[3*]	$CH_2CH=CH_2$	PhMgBr	Ph–CH_2–CH=CH_2 70	DurCOOH 35	[96]
7	Mes	$CH_2-CH=C(CH_3)$	PhMgBr	$Ph(CH_3)CH-CH=CH_2$ 58 + Ph–CH_2–CH=CH–CH_3 12	2*	[97]
8	CH_3	$C(Ph)_3$	CH_3MgBr	$(Ph)_3C-CH_3$ 68	2*	[98]
9	CH_2		$(CH_3)_3CMgBr$	 23 +  41	2*	[99]

* Mes = , [2]* Not isolated. [3]* Dur = .

The occurrence of cleavage in case 5 is inexplicable from the standpoint of these two postulates. Firstly, the carbonyl group of the ester is fairly active in nucleophilic addition reactions and, secondly, the dimesityl carbonium ion is apparently unstable.[98] It is sufficient to note that, according to the data of Fieser and Heymann,[98] neither diphenylmethyl acetate nor fluorenyl acetate are cleaved by phenylmagnesium bromide at the C–O σ-bond.

In the given instance, the stability of the leaving group assumes an important role in our view: $K_a = 1.75 \times 10^{-5}$ for CH_3COOH and $K_a = 6.5 \times 10^{-5}$ for PhCOOH. Incidentally, one cannot rule out also an important contribution by the *I* effect of the methyl group to the stability of the dimesityl carbonium ion.

It is important to note that both in the original studies[89–99] and in the monographs referring to these investigations, in the interpretation of the σ-C–O cleavage of esters by RMgX the authors invoke the Lewis acid properties of magnesium bromide etherate:[100]



The examination of the structure of RMgX in the earlier part of the review showed that even at high dilutions the content of MgX_2, formed in accordance with the Schlenk equilibrium in ethereal solutions and in other weakly solvating solvents, where the heterolysis under consideration takes place, is extremely insignificant. The formation of magnesium halides as a result of the reaction analogous to the Wurtz reaction, occurring simultaneously with the formation of asymmetric and symmetrical organomagnesium compounds, is unlikely.[101]

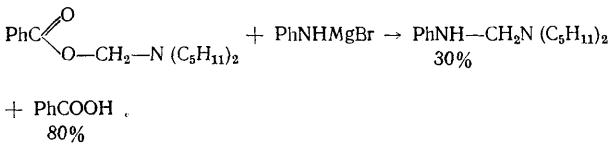
Under the experimental conditions (ethereal solution, $c > 0.01$ M), polyassociated species always exist and the MgX_2 formed therefore forms part of the composition of these macromolecular formations, its acid properties being weakened under these conditions.

In the case of organomagnesium compounds with branched alkyl groups (Table 4, example 4), a reduction reaction is observed together with the nucleophilic substitution reaction. In our view this is associated with the fact that, on coordination to the ester molecule via the C—O σ-bond, RMgX is highly polarised to such an extent that attack on the new electrophilic centre becomes possible not only by R^- but also by the hydride ion.

The presence of 1,2- and 1,4-adducts derived from allyl esters can be readily accounted for from the standpoint of a carbonium-like transition state, while the mechanism with a six-membered transition state and a synchronous redistribution of electrons does not explain it—for example in case 7 in Table 5.

Thus the σ-C—O cleavage reaction can be observed or not observed for esters with a bulky substituent R^1, i.e. the steric hindrance to nucleophilic addition via the carbonyl group generated by this substituent is not obligatory or of decisive importance for the reaction considered. On the other hand, the σ-C—O heterolysis may be expected if the substituent R^2 is capable of forming stable carbonium ions. The influence of the structure of R^3 on the cleavage considered is expressed by the fact that, together with the cleavage products (G) (in the scheme above), one may expect also the reduction products (H-R_2) in the case of branches groups R_3, and is also reflected by the contribution resulting from the Lewis acidity, expressed, for example, in terms of φ * (see above).

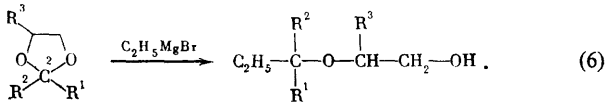
The nucleophilicity of the Grignard reagent is apparently unimportant for the heterolysis reaction, since esters are cleaved by various organomagnesium compounds. The cleavage of esters by RNHMgX has been described:[102,103]



The C—O fragmentation involving ethers and R_2NMgX takes place similarly.[104]

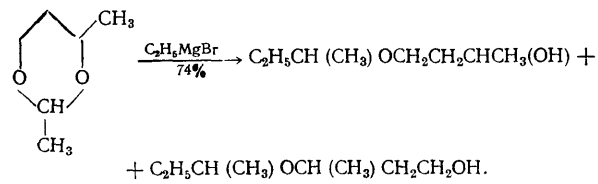
Thus the heterolysis examined above is analogous to the reaction involving ethers and is determined by the stability of the carboxylate ions and carbonium ions which can be formed by the substituent R^2. The role of the Lewis acid properties of RMgX is then decisive.

(c) The cleavage of 1,3-dioxolans. Cyclic ketals and acetals undergo the σ-C—O heterolysis on treatment with organomagnesium compounds. This reaction proceeds as a rule under more severe conditions than those examined above—in boiling benzene or toluene:[105]



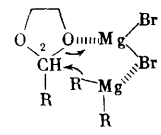
(6)

Dioxolans forming six-membered rings are cleaved under still more severe conditions than the five-membered compounds. This is believed[105] to be associated with the smaller strain in six-membered rings:



Data on the σ-C—O heterolysis of 1,3-dioxolans are compiled in Table 6.

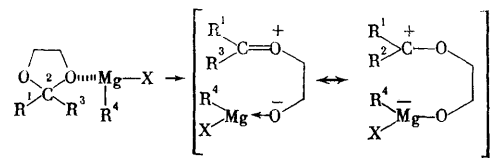
The mechanism of σ-C—O heterolysis involving a six-membered transition state was postulated in almost all the studied presented in Table 6:



It has been suggested[106–110] that the driving force of the σ-C—O heterolytic process is the polarisation of the cleaved C—O bond by magnesium bromide etherate. The cleavage process is regarded as a concerted circular electron transfer. According to the authors,[106–110] this mechanism is confirmed by the isolation of the complexes of 1,3-dioxolans with MgX_2 (2,4-dimethyl-1,3-dioxolan : MgX_2 = 1.65 : 1).

In their assessment of the influence of substituents in the 2-position on the ease of opening of the dioxolan ring, Trofimov et al.[108] noted the parallel variation of the yield of the products of σ-C—O heterolysis and the electron-donating capacity of the substituents (for example, the unsubstituted dioxolan is not cleaved by RMgX). However, the observed variation has not been explained.[106–110]

Blomberg et al.[111] explained the influence of the substituents in the 2-position in the dioxolan molecule by the fact that the mesomeric form of the transition state includes the C(2)-carbonium ions, which is stabilised by electron-donating substituents.



In a later study,[114] it was suggested that the interaction of a series of dioxolans with Grignard reagents results in the formation of an oxocarbonium transition state and that the driving force of the process is the Lewis acid properties of all the organomagnesium conglomerates present in solution: the RMgX monomers at a low concentration and the $(RMgX)_n$ polymers at a high concentration:

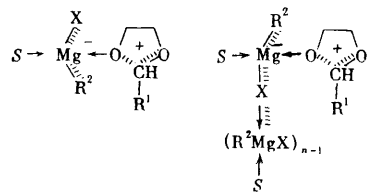
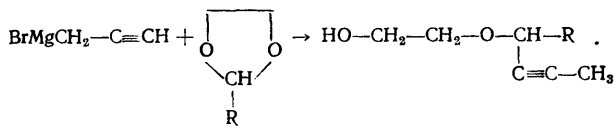


Table 6. The yields of the products of the cleavage of dioxolans via reaction (6).

No.	R^1	R^2	R^3	Reagent	Yield of product, %	Refs.
1	CH_3	H	H	$CH_2=CH-C\equiv CMgBr$	$CH_2=CH-C\equiv C-CH(CH_3)-O-(CH_2)_2OH$ 58	[106]
2	CH_3	H	CH_3	C_2H_5MgBr	$(C_2H_5)(CH_3)CH-O-CH(CH_3)CH_2OH$ 54	[107]
3	CH_3	C_2H_5	H	$CH_3CH_2-C\equiv CMgBr$	$CH_3-CH_2-C\equiv C-C(CH_3)(C_2H_5)-O-(CH_2)_2OH$ 80	[108]
4	CH_3	H	H	$PhC\equiv CMgBr$	$PhC\equiv C-CH(CH_3)-O-(CH_2)_2OH$ 67	[109]
5	CH_3	C_2H_5	CH_3	$BrMgOCH_2C\equiv CMgBr$	$HO-CH_2-C\equiv C-C(CH_3)(C_2H_5)-O-CH(CH_3)-CH_2-OH$ 75	[110]
6	$n\text{-}C_3H_7$	H	H	C_2H_5MgBr	$(n\text{-}C_3H_7)(C_2H_5)CH-O-CH_2-CH_2OH$ 78	[111]
7	CH_3	$-CH(SCH_3)-CH_2-CH_3$	H	$CH_2=CH-C\equiv CMgBr$	$CH_2=CH-C\equiv C-C(CH_3)(CH(CH_3)SCH_3)-CH_2-CH_2-OH$ 53	[112]
8	H	CH_3	CH_3	$(CH_3)_2CHMgBr$	$(CH_3)_2CH-CH(CH_3)-O-CH(CH_3)-CH_2OH$ 71	[113]

In a study[115] of the σ-C–O cleavage of a dioxolan by a Grignard reagent, the formation of the final reaction product was attributed to the nucleophilic properties of RMgX and its structure was attributed to the migration of the triple bond under the influence of the base and temperature:



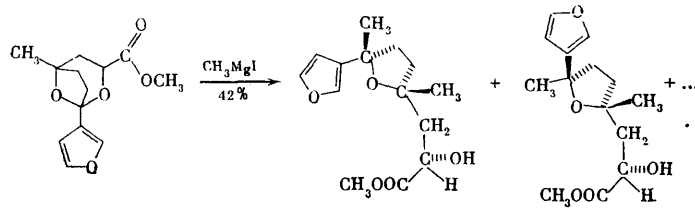
We believe that, firstly, in the given case σ-C–O heterolysis takes place and, secondly, that the above workers[115] indicate an erroneous structure of the reagent.

In view of the greater basicity of a carbanion with an sp^3-hybridised carbon atom than that of a carbanion with an *sp*-hybridised carbon atom,[116] the structure of the reagent can be represented by the formula $CH_3-C\equiv CMgBr$.

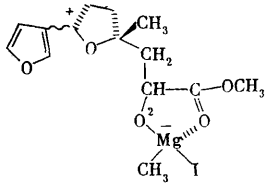
The following equilibrium may be established in solution:

$$CH_3C\equiv CMgBr \rightleftarrows BrMgCH_2-C\equiv CH.$$

Abell and Mass-Westropp[117] observed the heterolytic cleavage of the C–O σ-bond in dioxolan:

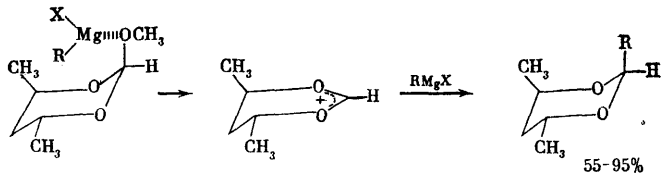


The selectivity of the reaction, reflected in the products, can be explained according to the authors[117] by the chelation reaction of the methoxycarbonyl group, via the O(2) atom, with methylmagnesium iodide and the subsequent formation of an oxocarbonium ion:

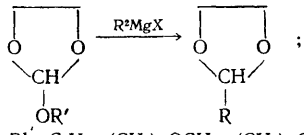


A competing reaction involving nucleophilic addition to the carbonyl group takes place simultaneously. The relation between the stabilities of the two fragments produced as a result of the breakup of the dioxolan molecule after coordination was not investigated in the above study.

The stereospecific synthesis of 1,3-dioxolans with an axial substituent at the C(2) atom has been described:[118]



This character of the reaction is determined, according to the authors,[118] by the need for a stereoelectronic factor in the formation and subsequent reaction of the oxocarbonium ion. It has been shown[119] that at high temperatures cyclic ortho-esters are cleaved by Grignard reagents also in a highly basic solvent—tetrahydrofuran



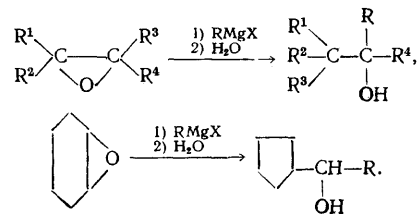
$R^1 = C_2H_5$, $(CH_2)_2OCH_3$, $(CH_2)_2O(CH_2)_2OCH_3$.

The driving force of the above process is believed[119] to be the coordination of MgX_2 to the oxygen atom linked directly to the C(2) atom. An increase in the number of oxygen atoms in the substituent R leads to a fall in the yield of the product of σ-C—O heterolysis owing to the saturation of the coordination sites of magnesium by the oxygen atoms of the substituent R^1 remote from the C(2) atom (i.e. owing to the weakening of the Lewis acid properties of the Grignard reagent).

Thus the σ-C—O heterolysis of 1,3-dioxolans by RMgX is one of the examples of the fragmentation of substrates by a Lewis acid. This reaction proceeds if a stable carbonium ion can be generated in the dioxolan molecule under the influence of RMgX. An alkoxide ion is invariably the leaving group. The acceleration of the heterolysis by the introduction of electron-donating substituents in the 2-position occurs, in our view, as a result of the stabilisation of the carbonium ion in the transition state. The introduction of alkoxy-substituents, i.e. effective leaving groups, into the 2-position in cyclic ortho-esters leads to the formation of 1,3-dioxolans.

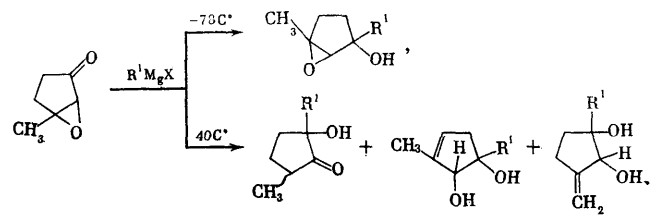
The marked dependence on the solvating capacity of the solvent and the uncharacteristic course of the σ-C—O heterolysis of organolithium compounds show that the Lewis acid properties of RMgX in the reaction under discussion are responsible for the possibility of the occurrence of the σ-C—O heterolysis of dioxolans.

(d) Isomerisation of epoxides. Organomagnesium compounds induce the isomerisation of epoxides similarly to the Lewis acids MgX_2:[120–125]



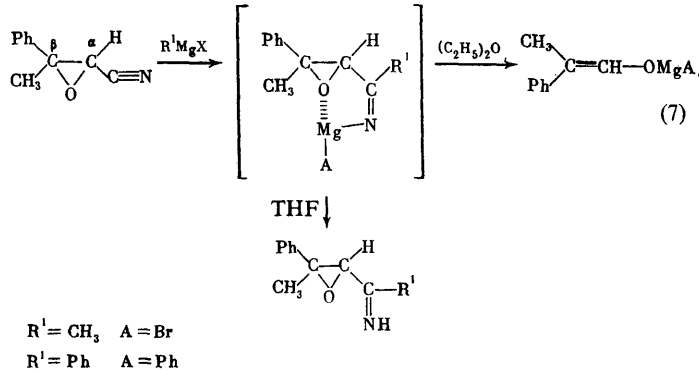
The above isomerisation reaction is accompanied, according to the authors,[122–125] by the simultaneous "normal" nucleophilic opening of the ring. The isomerisation of epoxides by organomagnesium compounds is fully inhibited in highly basic solvents.

It is sometimes possible to isolate the epoxide isomerisation products themselves. An α-hydroxyketone has been identified[126,127] in the reaction mixture produced by the interaction of α-epoxycyclopentanones with RMgX:



The above scheme shows that the products of the reaction are determined by the temperature of the reaction mixture. An increase in temperature enhances the acid properties, i.e. leads to isomerisation.

The species inducing the isomerisation of certain epoxides are alkyl(aryl)magnesium imines:[128–130]

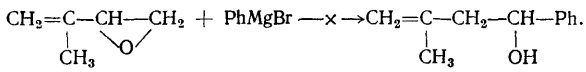


(7)

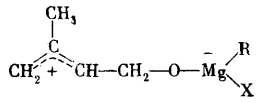
$R^1 = CH_3$ A = Br
$R^1 = Ph$ A = Ph

Scheme (7) shows that the acid properties of magnesium-containing conglomerates are responsible for the possibility of isomerisation.

The cleavage of isopropenyloxiran by phenylmagnesium bromide has been investigated,[131] but the epoxide isomerisation products were not detected in the reaction mixture:



In our view, in the given instance a carbonium-like state with a primary carbon atom is not produced because of the higher stability of a carbonium-like transition state with a secondary carbon atom stabilised by $\pi-\pi$ conjugation:



We believe that isomerisation proceeds because the epoxide molecule can be cleaved into two stable oppositely charged fragments within the molecule, which rapidly and irreversibly isomerise to ketones or aldehydes. The carbonyl compounds formed combined with an RMgX molecule and are converted into carbinols.

(e) The cleavage of carbinols and alkoxides. After introduction with RMgX in weakly solvating solvents, many ketones form the products of the "anomalous" reaction: after the "normal" addition to the carbonyl group, the magnesium alkoxide formed reacts with another RMgX molecule and is cleaved at the C–O σ-bond[132–137] (Table 7):

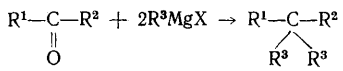
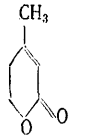
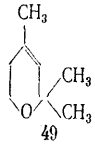
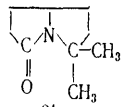
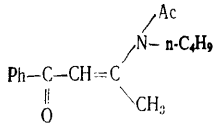
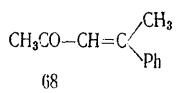
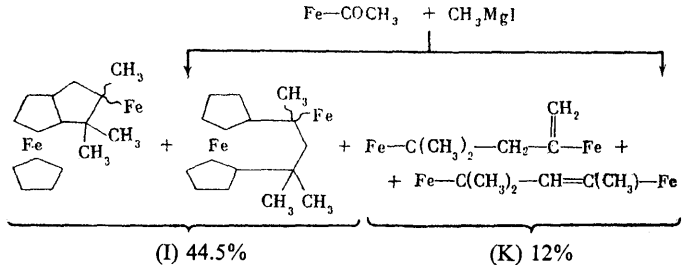


Table 7. The yields of the products of the cleavage of carbinols and alkoxides.

Substrate	Reagent	Yield of product, %	Refs.
	CH_3MgI	 49	[132]
	CH_3MgBr	 21	[133]
	CH_3MgI	 68	[134]
	RMgX		[135]
$FcC(CH_3)_2OH$	CH_3MgI	$FcC(CH_3)_2$ 14	[136, 137]

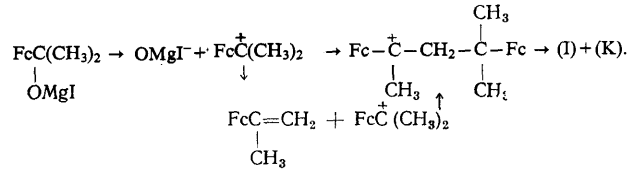
All the substrates listed in Table 7 contain in the α-position relative to the carbonyl carbon atom potential stabilisers of the α-carbonium ion—nitrogen and oxygen atoms and the ferrocenyl group. On the other hand, the oxygen ion stabilised by the MgX^+ counterion is converted into a readily eliminated group and thus the lability of the C–O σ-bond in such alkoxides becomes understandable.

The isolation of products of the intramolecular homo- and heteroannular alkylation of the ferrocenyl substituent and also of ferrocene-containing alkenes from the reaction mixture produced by the interaction of acetylferrocene and methylmagnesium iodide supports the view that the reactions of the organic compounds of the classes considered proceed via a stage in which a carbonium ion (a carbonium-like transition state) is formed:



(I) 44.5% (K) 12%

It is believed[136,137] that the reactions discussed above proceed via the C–O σ-bond ionisation stage with formation of the dimethylferrocenylcarbonium ion:



3. The cleavage of the C–Cl bond

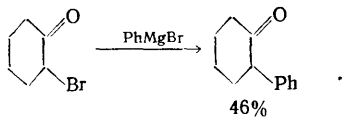
Certain chlorine-containing compounds undergo heterolysis at the C–Cl σ-bond by Grignard reagents. Table 8 presents examples of such reactions.

It is striking that all the cleaved compounds can give rise to a stable carbonium ion and a stable anion and that, in the presence of two chlorine atoms in the substrate molecule (two readily eliminated groups) (Table 8, examples 1 and 6), the $C^{\alpha}-Cl^{\beta}$ σ-bond is cleaved (Table 8, example 1).

Arbuzov et al.[138] noted that the stereochemical results of the interaction of 2,3-dichlorotetrahydropyran with RMgX can be explained by the intermediate formation of an oxocarbonium ion.

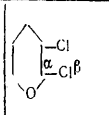
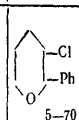
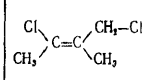
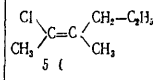
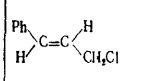
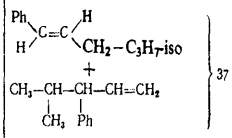
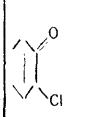
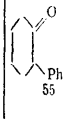
It has been noted[142] that the substitution of the chlorine atom in (*Z*)-3-chloro-1-phenylpropene takes place only in ether; in THF, the products of the C–Cl heterolysis—(*Z*)-4-methyl-1-phenylpent-1-ene and (*Z*)-4-methyl-3-phenylpent-1-ene—are not formed. Although this fact was not explained,[142] we believe that in the given instance the weakening of the Lewis acid properties of RMgX in THF prevents the fragmentation of the chlorine-containing alkene.

Grignard reagents also cleave bromine-containing compounds. The cleavage of the C–Br σ-bond has been described:[140]



Apparently iodine- and fluorine-containing compounds can also be cleaved by RMgX.

Table 8. The yields of the products of the cleavage of chlorine-containing compounds.

No.	Substrate	Reagent	Yield of product, %	Refs.
1		PhMgBr	 5–70	[138–140]
2		C_4H_9MgBr	 5 (	[141]
3		iso-C_3H_7MgB	 37	[142]
4	$CH_2CH{=}C(Cl){-}CH_2Cl$	CH_3MgI	$CH_3{-}CH{=}C(Cl){-}CH_2 + CH_3{-}CH(CH_3){-}C(Cl){=}CH_2$ 50 18	[143]
5	$CH_3CH{=}CH{-}CH_2Cl$	PhMgBr	$CH_3CH(Ph){-}CH{=}CH_2$ 59	[144]
6		PhMgBr	 55	[145]

4. The cleavage of compounds of different classes

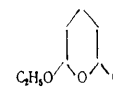
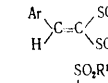
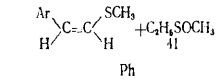
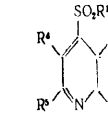
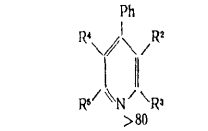
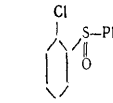
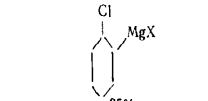
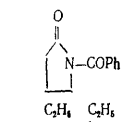
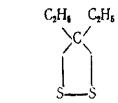
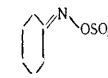
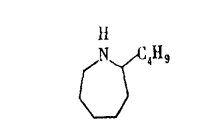
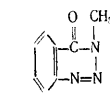
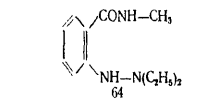
Isolated examples involving the heterolysis of a carbon–element σ-bond by organomagnesium compounds derived from organic compounds of different classes can be found in the literature. Examination of examples 1–7 (Table 9) shows that these are related reactions, since the yield of the products indicated in Table 9 depends on the solvating capacity of the solvent and also on the stability of the fragments of the molecules of the initial compound into which they can cleave heterolytically by RMgX at the carbon–element bond.

Examples 8–10 (Table 9) show that the heterolysis of the carbon–element σ-bond examined in the present review is a special aspect of a wide range of reactions involving the cleavage of element–element bonds by Grignard reagents.

IV. Conclusion

In conclusion of the review, it is essential to note that the heterolysis of a carbon–element σ-bond is hardly likely to be very important for organic synthesis, in the first place because well tried synthetic methods for the preparation of stable carbonium ions or carbanions already exist. Using the latter as the starting materials, it is possible to obtain fairly readily the required products without resorting to the cleavage by RMgX of substrates comprising the species under consideration [a carbonium ion (and its counterion) and the carbanion (and its counterion)].

Table 9. Yields of the products of the cleavage of different class of organic compounds.

No.	Substrate	Reagent	Yield of product, %	Refs.
1		PhMgBr	$Ph{-}CH(OC_2H_5){-}(CH_2)_3{-}CH(OH){-}Ph$ 100	[146]
2	$R{-}S{-}C{\equiv}N$	R^1MgX	$R{-}S{-}R^1$ >40	[147]
3		C_2H_5MgBr	 41	[148]
4		PhMgBr	 >80	[149]
5		PhMgBr	 85%	[150]
6	$(CH_3)_2N{-}CH(SCH_3)_2$	PhMgBr	$(CH_3)_2N{-}CH(Ph)_2$ 30	[151]
7		n-$C_6H_{13}MgBr$	n-$C_6H_{13}CO(CH_2)_3NH{-}COPh$	[152]
8		CH_3MgI	$(C_2H_5)_2C(CH_2SCH_3)SH$ 86	[153]
9		C_4H_9MgI	 57	[154]
10		C_2H_5MgI	 64	[155]

However, the possibility of the heterolysis of a carbon–element (element–element) σ-bond by organomagnesium compounds must always be taken into account for compounds which can fragment into stable charged species.[156–158]

Thus reactions in which carbon–element bonds are apparently cleaved have been described in the literature, although the authors of the communications quoted did not describe the identification of the following compounds [the products of the heterolytic reactions (8)–(10) respectively]:

$(C_2H_5)_2N—CH_2C\equiv C—CH_2—N(C_2H_5)_2$, $(CH_3)_2N—CH_2CH_3$, $PhCH(OCH_3)$ Ph.

$(C_2H_5)_2N—CH_2—C\equiv CMgI + ClSi(CH_3)_3 \rightarrow (C_2H_5)_2N—CH_2—C\equiv C—Si(CH_3)_3$ (Ref.156). (8)

$$(CH_3)_2N—CH_2—CH(Ph)—CO—CH_3 + CH_3MgI \rightarrow \rightarrow (CH_3)_2N—CH_2CH(Ph)—C(CH_3)_2 \quad \text{(Ref.157)} \qquad (9)$$
$$\qquad\qquad\qquad

57. V N Postnov, Yu N Polivin, V A Sazonova *J. Organomet. Chem.*, 1985, **288** 197
58. Yu N Polivin *Materialy Konferentsii Molodykh Uchenykh Khimicheskogo Fakul'teta MGU. 1984* (Proceedings of the Conference of Young Scientists at the Faculty of Chemistry of Moscow State University. 1984), p. 508. Deposited at the All-Union Institute of Scientific and Technical Information (VINITI). 30. 08. 84. No. 6054
59. V N Postnov, Yu N Polivin, V A Sazonova *Dokl. Akad. Nauk SSSR*, 1983, **271** 1399
60. Yu N Polivin *Materialy Konferentsii Molodykh Uchenykh UDN im. P Lumumby. 1988* (Proceedings of the Conference of Young Scientists at the P Lumumba Friendship Among Peoples University. 1988), p. 151. Deposited at the All-Union Institute of Scientific and Technical Information (VINITI). 1.07.88 No. 5304
61. N C Deno, J J Jaruzelsky, A Schriesheim *J. Am. Chem. Soc.*, 1955, **77** 3044
62. L Angiolini, P Bizzazzi, G Soapini *Tetrahedron*, 1981, **37** 2137
63. W Shuhua, P Yingqi *Huaxue Xuebao*, 1982, **40** 267; *Chem. Abs.*, 1982, **96** 217408 f
64. F Eiden, M Schmidt *Arch. Pharm.*, 1987, **320**(2) 130
65. H Ahlbrecht, H Döllinger *Synthesis*, 1985, (8) 743
66. A N Nesmeyanov, N A Vol'kenau, E G Perevalova *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1951, 699
67. A N Nesmeyanov, V F Lavrushina, T N Shmaeva *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1956, 309
68. A N Nesmeyanov, E G Perevalova, N A Vol'kenau *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1951, 692
69. R Fosse *Ann.*, 1909, Ser. 8, 400
70. H G Kraft, R M Rode *Z. Naturforsch.*, 1979, **34** 886
71. D G Cox *J. Am. Chem. Soc.*, 1974, **96** 6823
72. T V Petrenko, V T Novikov *Zh. Obshch. Khim.*, 1983, **53** 2516
73. J Mirek, S Rachwal, B Kawalek *J. Organomet. Chem.*, 1983, **248** 107
74. L Lochman, M Sorm *Collect. Czech. Commun.*, 1976, **38** 3449
75. V N Postnov, Yu N Polivin, V A Sazonova *Tezisy III Vsesoyuznoi Konferentsii po Metalloorganicheskoi Khimii. Ufa. 1985* (Abstracts of Reports at the IIIrd All-Union Conferences on Organometallic Chemistry. Ufa. 1985), p. 218
76. C M Hill, D E Simmons, M E Hill *J. Am. Chem. Soc.*, 1955, **77** 3889
77. C M Hill, D E Simmons, M E Hill *J. Am. Chem. Soc.*, 1953, **75** 5408
78. C M Hill, R M Prigmore, G J Moore *J. Am. Chem. Soc.*, 1955, **77** 352
79. F Mann, F Stewart *J. Chem. Soc.*, 1954, 4127
80. J P Mason, M Zief *J. Am. Chem. Soc.*, 1940, **62** 1450
81. H Walther, L Haase, H Gross *J. Prakt. Chem.*, 1980, **322** 902
82. H Stetter, E Reske *Chem. Ber.*, 1970, **103** 643
83. G Courtois, P Miginiac *Bull. Soc. Chim. Fr.*, 1982, Pt. II 395
84. F Barbot, L Poncini *J. Chem. Res. Synop.*, 1981, **11** 343
85. L Poncini *N. Z. J. Sci.*, 1983, **26**(1) 31
86. L Poncini *J. Org. Chem.*, 1984, **49**(11) 2031
87. H Betmann, G Wolfen, K Meclerer *Synthesis*, 1987, (9) 848
88. C S Combs, T S Wills, R D Giles *J. Org. Chem.*, 1971, **36** 2027
89. C R Hauser, P Superstcin, J C Shivers *J. Am. Chem. Soc.*, 1948, **70** 606
90. R T Arnold, R W Liggett, S Searles *J. Am. Chem. Soc.*, 1948, **70** 3938
91. R T Arnold, R W Liggett *J. Am. Chem. Soc.*, 1945, **67** 357
92. R T Arnold, R W Liggett *J. Am. Chem. Soc.*, 1942, **64** 2875
93. R T Arnold, S Searles *J. Am. Chem. Soc.*, 1949, **71** 2021
94. R C Fuson, D E Brasure, J A Fuller *J. Am. Chem. Soc.*, 1955, **77** 3131
95. R C Fuson, H L Jackson, J A Fuller *J. Am. Chem. Soc.*, 1954, **76** 499
96. R T Arnold, H Bank, R W Liggett *J. Am. Chem. Soc.*, 1941, **63** 3444
97. K W Wilson, J D Roberts, W G Yong *J. Am. Chem. Soc.*, 1949, **71** 2019
98. L F Fieser, H Heymann *J. Am. Chem. Soc.*, 1942, **64** 376
99. B Miller, J Haggerty *J. Chem. Soc., Chem. Commun.*, 1984, **23** 1617
100. T Goto, Y Hirata, G H Stout *Problems in Advanced Organic Chemistry* (Translated into Russian), Izd. Mir, Moscow, 1971, p. 145
101. N P Volynskii *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1981, 187
102. K T Mizuch, Ts M Gel'fer *Dokl. Akad. Nauk SSSR*, 1950, **70** 637
103. K T Mizuch *Zh. Obshch. Khim.*, 1946, **16** 1471
104. R Fuson, A Rachlin *J. Am. Chem. Soc.*, 1942, **64** 1564
105. R P Houghton, A D Morgan *J. Chem. Soc., Perkin Trans. 1*, 1981, 756
106. B A Trofimov, A S Atavin, S E Orlova *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1966, 2023
107. B A Trofimov, A S Atavin, S E Orlova *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1967, 2727
108. B A Trofimov, A S Atavin, S E Orlova *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1969, 1343
109. M F Shostakhovskii, A S Atavin, B A Trofimov *Zh. Obshch. Khim.*, 1964, **34** 2089
110. M F Shostakhovskii, A S Atavin, B A Trofimov *Zh. Org. Khim.*, 1964, **1** 1170
111. C Blomberg, A Vreugdenhil, T Hansa *Recl. Trav. Chim.*, 1963, **82** 355
112. S S Sabirov, L M Gnevasheva, M I Ismailov *Dokl. Akad. Nauk Tadzh. SSSR*, 1984, **27** 243
113. A A Mel'nitskii, O F Glukhova, T K Kiladze, et al. *Dokl. Akad. Nauk SSSR*, 1987, **292**(6) 1390
114. G Westera, C Blomberg, Bickelhaupt *J. Organomet. Chem.*, 1974, **82** 291
115. S F Karaev, I A Shikhiev, A K Khibidova *Azerb. Khim. Zh.*, 1977, 661
116. O A Reutov, I P Beletskaya, K P Butin *CH-Kisloty* (CH Acids), Izd. Nauka, Moscow, 1980, p. 64
117. A D Abell, R A Massy-Westropp *Aust. J. Chem.*, 1985, **38** 1031
118. E Eliel, F Nader *J. Am. Chem. Soc.*, 1970, **92** 584
119. A Morgan, R Houghton *J. Chem. Soc., Perkin Trans. 1*, 1981, 756
120. P D Bartlett, C M Berry *J. Am. Chem. Soc.*, 1934, **56** 2683
121. N G Gaylord, L D Caul *J. Am. Chem. Soc.*, 1955, **77** 3132
122. P I Kazaryan, N I Khizaptsyan, A A Gevorkyan *Khim. Geterotsikl. Soedin.*, 1984, (2) 267
123. R Clous, M Schlesser *Helv. Chim. Acta*, 1984, **67**(6) 1470
124. J R Schander, A Krief *Tetrahedron Lett.*, 1982, **23**(42) 4389
125. L Crombie, R Hardy, D Knight *J. Chem. Soc., Perkin Trans. 1*, 1985, (7) 1373
126. S Sepulveda, S Soto, R Mestres *Bull. Soc. Chim. Fr.*, 1983, **11** 5237

127. N L Lysenko, A N Bobrov *Ukr. Khim. Zh. (Russ. Ed.)*, 1983, **49**(10) 1113
128. J M Normant, J Cantacuzene *Tetrahedron Lett.*, 1971, 2405
129. J Cantacuzene, D Richard, M Theze *Tetrahedron Lett.*, 1967, 1365
130. J Cantacuzene, A Katamat, *Bull. Soc. Chim. Fr.*, 1968, **11** 4540
131. A A Gevorkyan, P I Kazaryan, S V Avakyan *Khim. Geterotsikl. Soedin.*, 1985, (4) 450
132. M S Sargosyan, K A Petrosyan, S A Mkrtumyan *Arm. Khim. Zh.*, 1987, **40** 705
133. K Takahashi, A Brossi *Heterocycles* 1988, **27**(10) 2475
134. C Kashima, Y Yamamoto, S Tsukyba *Heterocycles*, 1982, **19**(7) 1211
135. N Marquardt, J Lehnmann *Synthesis*, 1987, (12) 1064
136. W H Horspool, P Stanley, R Sutherland *J. Chem. Soc. C*, 1971, (8) 1365
137. W H Horspool, R Sutherland, J R Sutton *Can. J. Chem.*, 1969, **47** 3085
138. B A Arbuzov, E I Klimovitskii, L K Yuldashev, et al. *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1974, (2) 377
139. C Leslie, R Hardy *J. Chem. Soc., Perkin Trans. 1*, 1981, (9) 1971
140. B Giancarlo, G Catelani, M Anwar *Tetrahedron*, 1986, **42**(14) 3973
141. G M Mkryan, A M Mkrtychan, S V Avakyan *Arm. Khim. Zh.*, 1981, **34**(10) 847
142. K Maraoka, M Nojima, S Kasabayashi *J. Chem. Soc., Perkin Trans. 2*, 1986, (5) 761
143. E Voskanyan, O Akopyan, A Mkrtychan *Arm. Khim. Zh.*, 1988, **41**(7) 411
144. A Onistchenko, P Buchholz, H Stamm *Tetrahedron*, 1987, **43**(3) 565
145. M Hori, T Kataoka, H Shimizu *Chem. Pharm. Bull.*, 1986, **34**(9) 3599
146. L N Kralina, R I Kruglikova, G I Tarulina *Khim. Geterotsikl. Soedin.*, 1970, 311
147. A Sature *J. Am. Chem. Soc.*, 1920, 2369
148. K Ogura, K Arai, G Tsuchihashi *Bull. Chem. Soc. Jpn.*, 1982, **55**(11) 3669
149. N Fuzukawa, T Fujiwara, M Tsuvuoka, Japanese P. 61 280 474; *Chem. Abs.*, 1987, **107** 77 643 x
150. F Naomishi, S Tadao, F Nasashi *Tetrahedron Lett.*, 1987, **28**(2) 2727
151. A Anand, J Singh *Tetrahedron Lett.*, 1988, **44**(19) 5975
152. A Giovannini, D Savoia *J. Org. Chem.*, 1989, **54**(1) 228
153. M Tazaki, S Nagahama, M Takag *Chem. Lett.*, 1982, (8) 1339
154. G Makata, Japanese P. 58 162 558; *Chem. Abs.*, 1984, **100** 85 604f
155. J Campbell, S Noyee, R Storr *J. Chem. Soc., Chem. Commun.*, 1983, 1344
156. A Khuttier, H Sheat *J. Chem. Res. Synop.*, 1987, **6** 184
157. P Papadaki-Valiraki, T Siatra *Chem. Crom.*, 1987, **16**(2) 63
158. S Murata, K Yamabe, K Tashiro *Chem. Express*, 1988, **3**(6) 363