Translated from *Uspekhi Khimii*, **44**, 75-103 (1975) U.D.C. 547.2 : 547.422

The Cleavage of the Carbon-Oxygen Bond by Organomagnesium Compounds

B.A.Trofimov and S.E.Korostova

Studies on reactions involving the cleavage of the C-O bond by organomagnesium compounds (OMC) (Grignard and Norman reagents and Iotsich complexes), including the behaviour of ethers, open-chain acetals, and cyclic acetals in relation to the OMC, are reviewed. The mechanism of the cleavage of the ether linkage by OMC is discussed, attention being concentrated on the reaction of 1,3-dioxacyclanes with OMC, the complex-formation processes in the reaction of 1,3-dioxolans with Grignard reagents and Iotsich complexes, and also the mode of the cleavage of asymmetrically substituted 1,3-dioxacyclanes by these reagents.
The bibliography includes 183 references.

CONTENTS

I. Introduction 41
II. Ethers 41
III. Open-chain acetals and their structural analogues 44
IV. Cyclic acetals (1,3-dioxacyclanes) and their analogues 47

I. INTRODUCTION

Since the publication of the last review[1] on the cleavage of the C-O bond by organomagnesium compounds (OMC) the number of studies in this field has doubled and continues to grow. This is particularly due to the discovery of new preparative syntheses and also the fact that they yield additional information about the structure of OMC and the role of electrophilic catalysis and complex formation in reactions of OMC.

The available information about the chemistry of the O-C bond has been appreciably amplified by studies on the cleavage of cyclic acetals and some of their analogues by Grignard, Iotsich, and Norman reagents carried out in recent years in the USSR[2-27] and abroad[28-34]. Until recently it was not clear whether the Chichibabin-Elgazin-Spath reaction[35-43] can be applied in the series of 1,3-diheterocyclanes. The recommendation[44] that certain cyclic acetals be used as solvents for Grignard syntheses appeared to suggest a high stability of such acetals in relation to OMC. Nevertheless the wide distribution of cyclic acetal systems in nature, the systematic use of acetal protecting groups in carbohydrate and steroid chemistry, and the high and many-sided physiological activities of certain 1,3-dioxacyclanes impart urgency to the solution of these problems: the reactions of the cyclic acetal group leads to new ways of synthesising and modifying important groups of organic compounds. After the development of an industrial method for the synthesis of 2-methyl-1,3-dioxolan[45], the possibility of its employment as a useful chemical starting material became apparent. Against the background of continually expanding research on the polymerisation of trioxan and cyclic acetals and ethers, analysis of the conditions and characteristics of the cleavage of the C-O bond has acquired special importance. Such cleavage is the initial stage in any method of polymerising oxygen-containing heterocycles.

Studies published from 1960 to 1962 and partly in 1973 are discussed critically in the present review. Of the earlier publications, only those which had not been considered in previous reviews[1,46,47] are quoted.

Attention has been concentrated on the reactions of OMC with cyclic acetals, which reflect the trend which is at present dominant in this field. The review does not deal with the behaviour of OMC in relation to 1,4-dioxans, 1,3,5-trioxans, and derivatives of morpholines and orthoesters, since no new data appear to have been published on this subject in the above period. It also seemed undesirable to include in the review the reactions of esters and lactones, since the cleavage of their C-O bonds on interaction with OMC appears to be a secondary process for such compounds, which is not part of the reactions under consideration.

II. ETHERS

1. Reaction Mechanism

In principle, the R'-O-R'' molecule can be cleaved when either of two C-O bonds is acted upon by OMC. If, developing further the ideas described by Houben-Weyl[47], the reaction is regarded as the usual bimolecular nucleophilic substitution (S_N2) at the carbon atom of the group R':

$$R'—OR'' + \overset{-\delta}{R'''}—\overset{+\delta}{Mg}X \rightarrow R'—R''' + R''—OMgX\,, \qquad (1)$$

then one must naturally expect that this entails the rupture of the C-O bond where the carbon atom has a lower electron density or there is a greater scope for the distribution of the charge of the attacking anion. Unfortunately, the mode and mechanisms of the cleavage reactions of ethers have not been analysed so far in the literature, although the relevant facts are available (see previous reviews[1,46,47]). If account is taken of all the examples at present available, the conclusion reached is fairly unexpected: the cleavage of asymmetric ethers by OMC involves preferentially the C-O bond in which the carbon atom has the maximum electron density. In other words, the cleavage involves the formation of the most favourable carbonium ion. This is illustrated by examples (2)-(8):[1,48-53]

$$CH_3OC_6H_5 + CH_3MgI \rightarrow C_7H_8 + C_6H_5OMgI\,, \qquad (2)$$

$$C_2H_5OC_6H_5 + C_5H_{11}MgBr \rightarrow C_2H_4 + C_5H_{12} + C_6H_5OMgBr\,, \qquad (3)$$

$$n\text{-}C_8H_{17}OCH_2CH{=}CH_2 + C_6H_5MgBr \rightarrow C_6H_5CH_2CH{=}CH_2 + n\text{-}C_8H_{17}OMgBr\,, \qquad (4)$$

$$C_2H_5OCH_2C_6H_5 + C_6H_5MgBr \rightarrow C_6H_5CH_2C_6H_5 + C_2H_5OMgBr\,, \qquad (5)$$

$$CH_2{=}CHCH_2OC_6H_5 + C_6H_5MgBr \rightarrow CH_2{=}CHCH_2C_6H_5 + C_6H_5OMgBr\ , \quad (6)$$

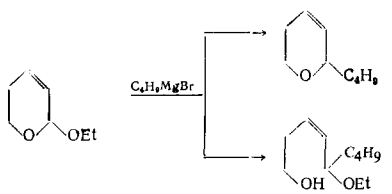
$$C_4H_9OCH_2CH{=}CHC_6H_5 + C_7H_{15}MgBr \rightarrow C_6H_5CH{=}CHCH_2C_7H_{15} + C_4H_9OMgBr\ , \quad (7)$$

$$(C_6H_5)_2COCH_2C \equiv CH + (C_6H_5)_2COCH_2C \equiv CMgBr \rightarrow$$
$$\rightarrow (C_6H_5)_2CC \equiv CCH_2OC(C_6H_5)_2 + HC \equiv CCH_2OMgBr\ . \quad (8)$$

Certain $\alpha\beta$-unsaturated ethers[54-56], which are sometimes cleaved on the side of the double bond, apparently constitute an exception. However, the contradictory information on this problem and also the known specificity of the chemical behaviour of such ethers preclude fairly definite conclusions. Thus it has been reported[55] that the ether $C_6H_5C(OC_2H_5){=}CH_2$ reacts with phenyl- and *p*-methoxyphenylmagnesium bromides, forming respectively $(C_6H_5)_2C{=}CH_2$ and $p\text{-}CH_3OC_6H_4(C_6H_5)C{=}CH_2$. It has also been shown[56] that alkyl vinyl ethers with different alkyl substituents in the α- and β-positions in the vinyl group are cleaved by Grignard reagents (GR) via the reaction

$$RCH{=}C(R')OR'' + R'''MgBr \rightarrow [RCH{=}C(R')OH] \rightarrow RCH_2COR'\ , \quad (9)$$

where R = H, $n\text{-}C_3H_7$, $n\text{-}C_5H_{11}$, or $n\text{-}C_6H_{13}$, R′ = H, $n\text{-}C_4H_9$, $n\text{-}C_5H_{11}$, or $n\text{-}C_6H_{13}$, R″ = C_2H_5 or $n\text{-}C_4H_9$, and R‴ = C_4H_9. Ultimately ketones formed. The reactants are heated in petroleum ether for 12–30 h.[56] For example, 5-undecanone was obtained in 76% yield from $C_5H_{11}CH{=}C(C_4H_9)OC_4H_9$ and butylmagnesium bromide. The results of the study by Quelet and d'Angelo[57] [reaction (10)] are consistent with this finding:



(10)

On the other hand, according to other data[58] β-alkyl-substituted vinyl ethers react with OMC to form primary alcohols and olefins. Similarly the reaction of unsubstituted vinyl ethers, in particular butyl vinyl ether, with phenylmagnesium bromide results in the formation of butanol and styrene in 60 and 30% yields respectively[56]. It has been suggested[56] that the yield of propenylmagnesium bromide, obtained in vinyl ethers, is influenced by its reaction with the solvent.

There are data on the polymerisation of vinyl ethers under the influence of Grignard reagents[59,60] showing that the polymerisation proceeds in the presence of an alkyl vinyl ether[60]. On the other hand, in the presence of an excess of the Grignard reagent, the initial ether is recovered unchanged even after heating and only a small amount of oligomers and products of the hydration of the vinyl ethers are formed under these conditions. Therefore, despite earlier studies[56,58], it was concluded[60] that alkoxy-groups adjoining the double bond are relatively immobile, like a halogen atom, and are not exchanged for the group in the OMC. These results for $\alpha\beta$-unsaturated ethers are nevertheless consistent with the conclusion that the majority of ethers react with OMC apparently via an S_N1 mechanism. However, since spontaneous dissociation of the C–O bond is unlikely under these conditions, the classical S_N1 mechanism must of course be rejected. The following explanation is probable. In all the known cases of the cleavage of the C–O bonds under the influence of OMC the reaction mixture contains Lewis acids (MgX_2 and CoX_2; here and henceforth X is a halogen), which are coordinated to the oxygen atom and probably ultimately cleave the C–O bond. This can occur simultaneously with attack by an anion†, for example R_2Mg:

$$Mg(R)_2 \longrightarrow R\overset{\curvearrowright}{O}{:}\,MgX_2\ . \quad (11)$$

In order to explain the observed mode of cleavage of asymmetric ethers, a decisive role must be attributed to the electrophilic attack $X_2Mg{\rightarrow}{:}O\langle$ in the dissociation of the C–O bond. Thus the process must be classified as nucleophilic substitution with electrophilic catalysis. As will be shown below, the majority of the characteristics of the dissociation of the C–O bond by OMC known at the present time can be explained satisfactorily by the proposed mechanism.

2. Cyclic Ethers

Like open-chain ethers, cyclic ethers are relatively unreactive in relation to OMC. It is not fortuitous that tetrahydrofuran (THF), 2-methyltetrahydrofuran, and tetrahydropyran occupy a special position as solvents for Grignard syntheses[44]. The following new facts can be added to the information available from previous reviews[1,46,47] on the behaviour of cyclic ethers in the presence of OMC. Many reactions involving OMC take place in THF without the cleavage of its ring[28,61,62]. Nevertheless it has been stated[63] that THF is cleaved when butylmagnesium bromide is synthesised in it. On the other hand, according to other data[44,64-67] THF begins to react with Grignard reagents only at about 200°C, forming primary alcohols:

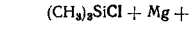


$$+ RMgX \rightarrow R(CH_2)_4OMgX\ , \quad (12)$$

where

$$R{=}C_2H_5\,(Br),\ C_4H_9\,(Cl),\ (C_6H_5)_3C\,(Br);\quad X{=}Cl,\ Br\ .$$

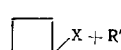
Chlorotrimethylsilane and magnesium react in THF[68] via the mechanism



$$(CH_3)_3SiCl + Mg + \rightarrow (CH_3)_3Si(CH_2)_4OMgCl\ . \quad (13)$$

The reaction between dihydropyran and OMC leads to the formation of an unsaturated alcohol in 35–40% yield[69].

The reaction of 2-halogeno-substituted cyclic ethers with a Normal reagent can proceed in different ways. Thus, when $CH_3CH{=}CHMgBr$ interacts with 2-chlorotetrahydrofuran and 2-chlorotetrahydropyran, the unsaturated alcohols $CH_3CH{=}CHCH{=}CH(CH_2)_2OH$ and $CH_3CH{=}CHCH{=}CH(CH_2)_3OH$ are formed respectively[70]. On the other hand, another mode of this reaction has been described[71]:



$$+ R'MgBr \rightarrow + MgXBr\ , \quad (14)$$

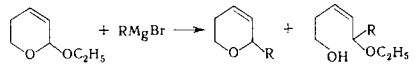
where R = H or CH_3, R′ = $CH_2{=}CH$ or $CH_3CH{=}CH$, and X = Cl or Br. The yield of the reaction products is 50%.

The reaction of 2-alkoxytetrahydropyrans with OMC has been studied[68,72] and the cleavage of the C–O bond in the pyran ring has been reported[69,73-76]. For example,

† One cannot rule out the possibility that this attack occurs in certain cases as a one-electron transfer.

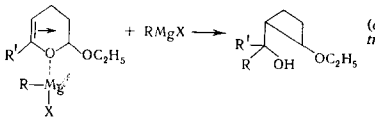
when 2-ethoxy-2,3-dihydro-γ-pyran is heated in toluene (85–90°C, 90 min) with an excess of a Grignard reagent, a mixture of *cis*- and *trans*-alkyl (or aryl)(2-ethoxycyclobutyl)methanols is formed in yields up to 48%.[74] The authors[74] suggest that the reaction proceeds via a mechanism involving cyclic electron transfer.

The reactions of the following cyclic ethers [reactions (15)–(20)] have also been described[28,57,77]:



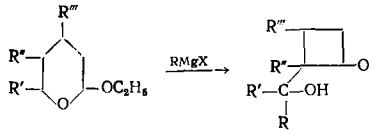
(15)

where R = CH_3, C_2H_5, n-C_4H_9, or C_6H_5;



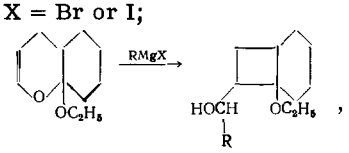
(16)

where R = CH_3, n-$C_4H_9C{\equiv}C$, or t-C_4H_9, R′ = H or CH_3, and X = Br or I;

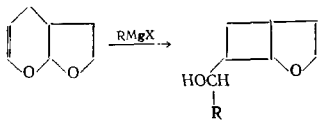


(17)

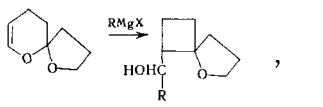
where R = CH_3, C_2H_5, or C_4H_9, R′ = R″ = H, R‴ = CH_3 or C_6H_5, and X = Br or I;



(18)



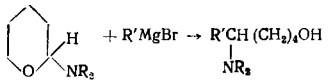
(19)



(20)

where R = C_2H_5 or C_4H_9 and X = Br.

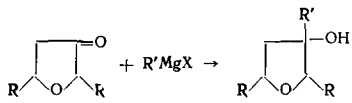
The interaction of 2-dialkylaminotetrahydropyrans with a Norman reagent leads to aminoalcohols[65]:



(21)

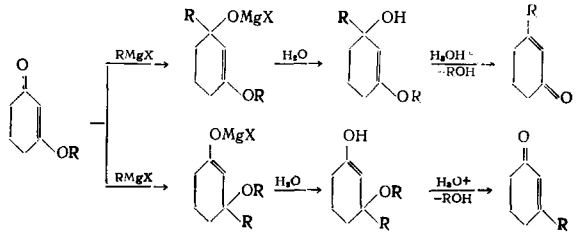
where R = C_2H_5 and R′ = $CH_2{=}CH$ or $CH_3CH{=}CH$.

Cyclic ketoethers react with OMC via the carbonyl group[78–80] [reactions (22) and (23)]:



(22)

where R = H or CH_3, R′ = CH_3, C_2H_5, C_3H_7, C_5H_{11}, or C_6H_5, and X = Br or Cl, and



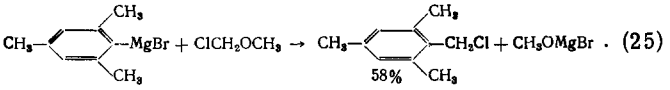
(23)

3. Ethers with Other Functional Groups

Full glycol ethers are fairly resistant to the action of OMC[81–83]. Thus the diethyl and dibutyl ethers of ethylene glycol[82], the diethyl and dibutyl ethers of diethylene glycol[66], and also the ethers of polyethylene glycols of the type $R(OCH_2CH_2)_nOR$ have been suggested[64] as high-boiling solvents for Grignard syntheses. The cleavage of the C–O bond under the influence of OMC was not observed in the dimethyl ether of ethylene glycol[81] even on heating at 70°C for 3.5 h. However, this ether is known to be cleaved appreciably[84] after 3 h at 95°C:

$$CH_3OCH_2CH_2OCH_3 + C_4H_9C{\equiv}CMgBr \rightarrow CH_3OCH_2CH_2C{\equiv}CC_4H_9 + CH_3OMgBr. \quad (24)$$

Halogenoethers. Without repeating the references quoted in Pokonova's monograph[85] and Summers' review[86], we shall examine the characteristic reactions of OMC with halogenoethers using some new examples. α-Chloroethers are known[85] to exchange their halogen readily for the hydrocarbon group in OMC, as a rule without the cleavage of the C–O bond. According to Shostakovskii et al.,[87] aryl α-chloroisopropyl ethers behave in this way. The reaction with Norman[88] and Iotsich[89–92] reagents proceeds similarly. Both halogen atoms are substituted without much difficulty in bis-(α-halogenomethyl) ethers[83]. However, under the influence of di-o-substituted arylmagnesium halides, the α-halogenoether is cleaved at the C–O bond[93,94]:



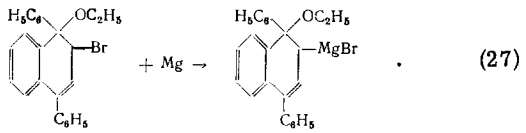
(25)

o-Halogenoethers form Grignard reagents[95]. When an attempt is made to prepare OMC from β-halogenoethers, the C–O bond is usually cleaved with the liberation of an olefin[96]:

$$CH_3O(CH_2)_2Cl + Mg \xrightarrow[THF]{ether} CH_3OMgCl + \rangle C{=}C\langle . \quad (26)$$

However, according to Shostakovskii et al.,[61] β-bromoethyl phenyl ether can react normally with magnesium.

Another instance of the formation of OMC from a β-halogenoether is also known[97]:



(27)

A Grignard reagent could not be obtained from γ-bromobutyl vinyl ether (in diethyl ether and THF as solvents), dimerisation and dehydrobromination products being detected[23,98]:

$$CH_2{=}CHO(CH_2)_3CHBrCH_3 + Mg \rightarrow CH_2{=}CHO(CH_2)_2CH{=}CHCH_3 + CH_2{=}CHO(CH_2)_3(CH_3)CHCH(CH_3)(CH_2)_3OCH{=}CH_2. \quad (28)$$

Only δ-bromobutyl vinyl ether reacts with magnesium without appreciable complications, forming the corresponding Grignard reagent[23,98].

A Norman reagent does not disrupt the C–O bond in $\alpha\beta$-dibromoethers[99,100] and certain Iotsich complexes behave similarly with respect to β-bromoethyl chloromethyl ether[101].

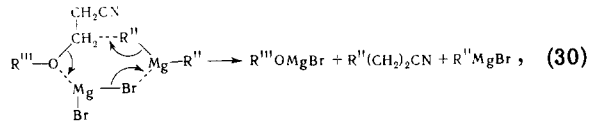
Certain trihalogenoalkyl ethers merely exchange their α-halogen atom for the alkyl group on reaction with a Grignard reagent and the C–O bond remains unaffected[28,102].

Ethers with active functional groups react with OMC in accordance with the general rule, i.e. via the most reactive fragment[28,103-106].

Cyanoethers. In contrast to α-alkoxynitriles, which react with OMC in the usual way, β-alkoxynitriles are wholly cleaved by the latter at the C–O bond[107]:

$$CH_2{=}CHOR'O(CH_2)_2C{\equiv}N + R''MgBr \rightarrow CH_2{=}CHOR'OMgBr\ , \qquad (29)$$

where R′ = $(CH_2)_2$ or $(CH_2)_2O(CH_2)_2$ and R″ = C_2H_5, C_4H_9, or C_6H_5. The reaction proceeds with evolution of heat. It has been suggested[107,108] that it involves the intermediate complex illustrated below:



$$\longrightarrow R'''OMgBr + R''(CH_2)_2CN + R''MgBr\ , \qquad (30)$$

where R‴ = CH_2 or CHOR′.

The cyano-product obtained on cleavage of the ether is then converted into a ketiminate and which then polymerises:

$$R''(CH_2)_2CN \rightarrow \left[\begin{array}{c} -C(R'')-NH- \\ | \\ (CH_2)_2R'' \end{array}\right]_n^- \ . \qquad (31)$$

When the β-cyanoethyl ether of 2-methyl-4-trimethylsilylbut-3-yn-2-ol reacts with ethylmagnesium bromide[109,110], the main process is the cleavage of the C–O bond:

$$(CH_3)_3SiC{\equiv}CC(CH_3)_2OCH_2CH_2CN + C_2H_5MgBr \rightarrow$$
$$\rightarrow (CH_3)_3SiC{\equiv}CC(CH_3)_2OH + (CH_3)_3SiC{\equiv}C(CH_3)_2OCH_2CH_2\underset{22\%}{\underset{\|}{C}}C_2H_5 \qquad (32)$$
$$O$$

Aminoethers. The exchange of the alkoxy-groups in certain aminoethers for the substituent in Grignard and Norman reagents has been described[111-115] [reactions (33)–(36)]:

$$H_2NOCH_3 + RMgX \rightarrow RNH_2 + CH_3OMgX\ , \qquad (33)$$

where R = C_2H_5, i-C_5H_{11}, i-C_4H_9, or t-C_4H_9 and X = Cl, Br, or I;

$$C_6H_5CH_2ONH_2 + RMgX \rightarrow RNH_2 + C_6H_5CH_2OMgX\ , \qquad (34)$$

where R = C_2H_5, i-C_5H_{11}, cyclo-C_6H_{11}, C_6H_5, $C_6H_5CH_2$, p-BvC_6H_4 or α-naphthyl and X = Cl, Br, or I;

$$R_2NCH_2OR + R''MgCl \rightarrow R_2NCH_2R'' + ROMgCl\ , \qquad (35)$$

$$R_2NCH(R')OR'' + R'''MgBr \rightarrow R_2NCH(R')R''' + R''OMgBr\ , \qquad (36)$$

where R = CH_3, C_2H_5, C_4H_9, C_5H_{11}, R′ = H, R″ = C_2H_5, C_4H_9, or C_6H_5, R‴ = $CH_3CH{=}CH$, $CH_2{=}CHCH_2$; $CH_2{=}CH$, $(CH_3)_2CH$, $(CH_3)_2C{=}CH$, i-C_5H_{11}, C_4H_9, or α-naphthyl, and X = Cl, Br, or I.

III. OPEN-CHAIN ACETALS AND THEIR STRUCTURAL ANALOGUES

Many acetals are very resistant to the reaction of OMC and it is difficult to make them undergo exchange reactions with the latter.

1. Formals

Dimethyl and diethyl formals nevertheless exchange alkoxy-groups for the substituent in the Grignard reagent at high temperatures, forming ethers[116-118]:

$$ROCH_2OR + C_6H_5MgBr \rightarrow C_6H_5CH_2OR + ROMgBr\ , \qquad (37)$$

where R = CH_3 or C_2H_5.

Saturated symmetrical formals derived from alcohols ranging from propanol upwards hardly react with OMC under these conditions. The method of synthesis of a number of OMC[119] in di-isopropyl or di-isobutyl formals is based on this finding. Mixed unsaturated formals[60] are more reactive than saturated symmetrical formals towards Grignard reagents. Alkoxy-groups containing multiple bonds then undergo exchange:

$$ROCH_2OR' + C_6H_5MgX \rightarrow R'OCH_2C_6H_5 + ROMgX\ , \qquad (38)$$

where R = C_2H_5 or C_4H_9 and R′ = $C(CH_3)_2CH{=}CH_2$, or $CH{\equiv}C(CH_3)_2C$.

The above data are consistent with the proposed mechanism (see Section I, 1), since of the two most probable intermediate cations of the type $ROC\overset{+}{H}_2$ the more stable is the one containing a group with more marked electron-donating properties (i.e. in the present case an aliphatic group). When an OMC acts on the diformals $ROCH_2OCH_2OR$, the corresponding formaldehyde acetals are formed in yields up to 50%:[120]

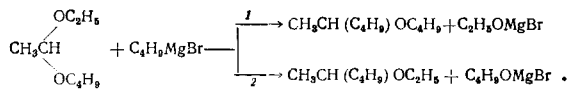
$$ROCH_2OCH_2OR + R'MgX \rightarrow ROCH_2OCH_2R' + ROMgX\ , \qquad (39)$$

where R = C_2H_5, C_4H_9, i-C_5H_{11}, or C_6H_{13}, R′ = $CH_2C_6H_5$ or n-C_6H_{13}, and X = Cl. This reaction proved to be convenient for the synthesis of formals with a β-phenylethyl alcohol residue, which has a flowery scent.

2. Acetaldehyde Acetals

In the reaction of symmetrical dialkyl and di(arylalkyl) acetals[121] with Grignard reagents the alkoxy-groups can be arranged in the following sequence in terms of the ease of their exchange: $OC_6H_5 > OAlk > OCH_2C_6H_5$. This sequence might have been foreseen on the basis of the ideas described in Section I. 1. The available data on the reactivities of dialkyl acetals in relation to Grignard reagents are contradictory. Thus as early as 1961 Blomberg and Vrengdenhill[122] observed in the synthesis of Grignard reagents in boiling dialkyl acetals the cleavage of the latter with formation of ethers and alkoxymagnesium halides. However, in 1964 Shostakovskii et al.[123] suggested that diethyl and dibutyl acetals may be used as the medium for the synthesis of OMC, since according to their data, these acetals do not interact with Grignard reagents even at 150°C. Grinberg[124] obtained ethers derived from alkyl(aryl)hexylmethanols and diaryl(alkyl)hexylmethanes by the reaction between the acetal of oenanthaldehyde and OMC. Thus not only the acetal but also the ether formed from it are cleaved in this case.

If the alkyl groups in asymmetric acetals do not differ appreciably in their structures, the reaction proceeds in two ways[59]:



$$+ C_4H_9MgBr \xrightarrow{1} CH_3CH(C_4H_9)OC_4H_9 + C_2H_5OMgBr$$
$$\xrightarrow{2} CH_3CH(C_4H_9)OC_2H_5 + C_4H_9OMgBr\ . \qquad (40)$$

Pathway *1* is dominant, i.e. the less electron-donating alkoxy-group again undergoes exchange more readily. As expected, in mixed alkyl aryl acetals[59] the aryloxy-group

is split off preferentially. On the basis of the mechanism discussed in Section I.1, the symmetrisation of the mixed acetals in the course of these reactions might have been predicted. Such symmetrisation has in fact been observed in the reaction of ethylmagnesium bromide with butyl ethyl and benzyl ethyl acetals[59]. The reaction of acetals with a Iotsich complex leads to the formation of acetylenic ethers[84,125,126]:

$$CH_3CH(OR)_2 + HC\equiv CMgBr \xrightarrow[1-3\ h]{95^\circ} HC\equiv CCH(CH_3)OR + ROMgBr\ , \quad (41)$$

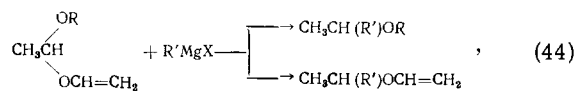
$$2CH_3CH(OC_4H_9)_2 + BrMgC\equiv CMgBr \rightarrow CH_3CH(OC_4H_9)C\equiv CCH(OC_4H_9)CH_3 + 2C_4H_9OMgBr\ . \quad (42)$$

The Iotsich complex obtained from ethynyldimethylmethanol is also reactive[127]:

$$CH_3CH(OC_4H_9)_2 + BrMgC\equiv CC(CH_3)_2OMgBr \xrightarrow{90-95^\circ} \rightarrow (CH_3)_2C(OH)C\equiv CCH(CH_3)OC_4H_9 + C_4H_9OMgBr\ . \quad (43)$$

The reactivity of C–O bonds in relation to the Iotsich complex increases sharply on passing from acetals to ketals[84]. It will be shown below that this rule holds fairly clearly also in other versions of the reaction of OMC with acetals or with their close analogues. This is yet another piece of evidence for the electrophilic nature of the rate-limiting stage in the cleavage of the C–O bond under the influence of OMC. Presumably, the interaction C–O←MgX_2, and not the nucleophilic attack $R^{\ominus}$→C–O, is decisive. Otherwise the enhancement of the electron-donating properties of the group joined to the oxygen atom on passing from acetals to ketals would have reduced the reactivity of the reacting C–O bonds. In reality the C–O bonds in ketals are more reactive than in acetals.

The acetals of unsaturated alcohols react with OMC like the acetals of saturated alcohols. The interaction of alkyl vinyl acetals with Grignard reagents[127,128] leads mainly to the formation of saturated ethers:



$$+ R'MgX \rightarrow \begin{cases} \rightarrow CH_3CH(R')OR \\ \rightarrow CH_3CH(R')OCH=CH_2 \end{cases}\ , \quad (44)$$

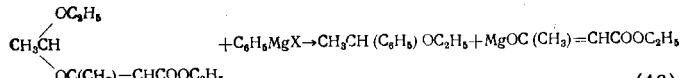
where R = alkyl or CH = CH, R′ = C_6H_5, and X = Br.

The yield of the corresponding alkyl vinyl ethers is about 30%, i.e. as in αβ-unsaturated formals[60], the C–O bond on the side of the more strongly electron-accepting group is the first to be broken, which is equivalent to the formation of the most stable carboxonium ion.

Divinyl acetals[127] involved in an exchange reaction with OMC form vinyl ethers:

$$CH_3CH(OCH=CH_2)_2 + RMgX \rightarrow CH_3CH(R)OCH=CH_2 + CH_2=CHOMgX\ . \quad (45)$$

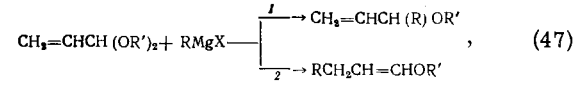
It is surprising that the reaction of the acetal derived from the β-hydroxycrotonic ester with a phenylmagnesium halide[129] proceeds without affecting the ester group.



$$+ C_6H_5MgX \rightarrow CH_3CH(C_6H_5)OC_2H_5 + MgOC(CH_3)=CHCOOC_2H_5\ . \quad (46)$$

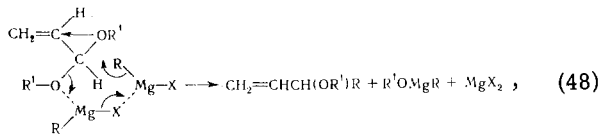
3. Acetals of Unsaturated Aldehydes

Acrolein acetals[130] give rise to a mixture of allyl and vinyl ethers on reaction with OMC:

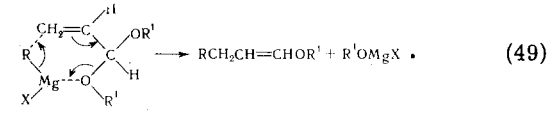


$$CH_2=CHCH(OR')_2 + RMgX \rightarrow \begin{cases} \xrightarrow{1} CH_2=CHCH(R)OR' \\ \xrightarrow{2} RCH_2CH=CHOR' \end{cases}\ , \quad (47)$$

where R = CH_3, C_2H_5, C_3H_7, i-C_3H_7, C_4H_9, i-C_4H_9, $CH_3(C_2H_5)CH$, $(CH_3)_3C$, cyclo-C_6H_{11}, C_6H_5, $CH_3CH=CH$, or $C_4H_9C\equiv C$, R′ = CH_3, C_2H_5, i-C_3H_7, or $CH(CH_3)_2$, and X = Br, Cl or I. At elevated temperatures (100–120°C) pathway *1* predominates (the yield of allyl ether is 93%). The reaction is carried out in ether, THF, toluene, xylene, or decalin in the course of 1.5–2 h. The following reaction mechanisms have been proposed[130]:



$$\rightarrow CH_2=CHCH(OR^I)R + R^IOMgR + MgX_2\ , \quad (48)$$

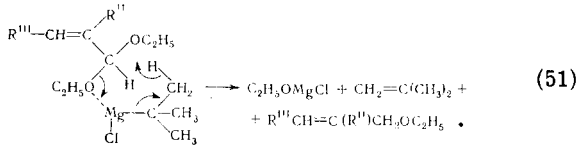


$$\rightarrow RCH_2CH=CHOR^I + R^IOMgX\ . \quad (49)$$

The homologues of the propenal acetal[131] react with OMC as follows:

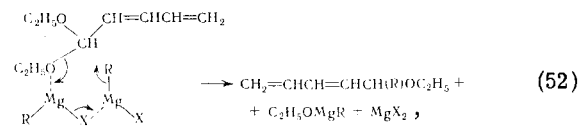
$$R^{IV}CH=CR^{III}CR^{II}(OR^I)_2 + RMgX \rightarrow R^{IV}CH=CR^{III}CR^{II}(R)OR^I + RR^{IV}CHR^{III}C=C(R^{II})OR^I, \quad (50)$$

where R = C_2H_5, n-C_4H_9, $(CH_3)_3C$, C_6H_5, $C_6H_5CH_2$, or $C_6H_5CH_2CH_2$, R^I = C_2H_5, R^{II} = H or CH_3, R^{III} = H, C_2H_5, or i-C_3H_7, R^{IV} = H, and X = Br or Cl. The following reaction mechanism is discussed in the same study[131]:



$$\rightarrow C_2H_5OMgCl + CH_2=C(CH_3)_2 + R^{III}CH=C(R^{II})CH_2OC_2H_5\ . \quad (51)$$

Quelet and d'Angelo[57] proposed the mechanism



$$\rightarrow CH_2=CHCH=CHCH(R)OC_2H_5 + C_2H_5OMgR + MgX_2\ , \quad (52)$$

where R = CH_3, n-C_4H_9, or t-$C_4H_9C\equiv C$, and X = Br. Similar reactions are discussed in Normant's review[28].

Ethers with an acetylenic linkage have been obtained from propargyl acetals[132,133].

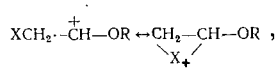
4. Halogenocetals

The acetals of halogenoaldehydes with a halogen atom in the β-position relative to the ethylidene group undergo an exchange reaction with OMC, forming β-halogenoethers[102]:

$$XCH_2CH(OR)_2 + R'MgX \rightarrow XCH_2CH(R')OR + ROMgX\ , \quad (53)$$

where R = n-C_4H_9, R′ = C_6H_5 or C_4H_9, and X = Br.

Under these conditions, the exchange takes place more readily than for the usual acetals. At first sight this finding is inconsistent with the fact that the C–O bond is ruptured before a new C–C bond is formed. However, when account is taken of the possibility of the anchimeric cooperation by the halogen atom,



$$\quad (54)$$

the contradiction is removed.

In reactions with Iotsich complexes, bromoacetaldehyde acetals exchange their alkoxy-groups for the ethynyl group[125]. The bromine atom is not substituted under these conditions:

$$BrCH_2CH(OC_4H_9)_2 + HC\equiv CMgBr \rightarrow BrCH_2CH(C\equiv CH)OC_4H_9 + C_4H_9OMgBr, \quad (55)$$

$$2\,BrCH_2CH(OC_4H_9)_2 + BrMgC\equiv CMgBr \rightarrow 2C_4H_9OMgBr + \\ + BrCH_2CH(OC_4H_9)C\equiv CCH(OC_4H_9)CH_2Br. \quad (56)$$

The reactions of chlorodiphenylacetaldehyde with phenylmagnesium bromide, leading to acetals derived from carbon monoxide [$C(OR)_2$] and $\alpha\beta$-unsaturated ethers, have been described[134,135]:

$$(C_2H_5O)_2CHC(C_6H_5)_2Cl + C_6H_5MgBr \rightarrow (C_2H_5O)_2CHC(C_6H_5)_2MgBr + C_6H_5Cl \rightarrow \\ \rightarrow C(OC_2H_5)_2 + CH(C_6H_5)_2MgBr, \quad (57)$$

$$(C_6H_5O)_2CHC(C_6H_5)_2Cl + C_6H_5MgBr \rightarrow (C_6H_5O)_2CHC(C_6H_5)_2MgBr + C_6H_5Cl \rightarrow \\ \rightarrow C_6H_5OCH{=}C(C_6H_5)_2 + C_6H_5OMgBr. \quad (58)$$

However, studies by other workers[136] failed to confirm the existence of $C(OC_2H_5)_2$.

The interaction of the dibutyl acetal of bromoacetaldehyde with metallic magnesium leads mainly to butyl vinyl ether[60]:

$$BrCH_2CH(OC_4H_9)_2 + Mg \rightarrow CH_2{=}CHOC_4H_9 + C_4H_9OMgBr. \quad (59)$$

Similar reactions have been reported in other communications[137-139].

When α-bromoacrolein acetals are heated with Grignard reagents at 90–95°C for 3 h, unsaturated bromoethers are formed[131]:

$$CH_2{=}CHBrCH(OR')_2 + RMgX \rightarrow \begin{cases} \rightarrow RCHCBr{=}CHOR' \\ \rightarrow CH_2{=}CBrCH(R)OR' \end{cases}, \quad (60)$$

where R = C_4H_9, R′ = C_2H_5, and X = Br.

When a Grignard reagent reacts with the diethyl acetal of bromoacetaldehyde, β-bromovinyl ethyl ether is formed in 53% yield[28]:

$$Br_2CHCH(OC_2H_5)_2 \xrightarrow{i\text{-}C_5H_{11}MgCl} trans\text{-}CHBr{=}CHOC_2H_5. \quad (61)$$

The dimethyl acetal of α-bromo-β-chloropropionaldehyde exchanges only the methoxy-group in the cold for the group in the Grignard reagent[102]:

$$ClCH_2CHBrCH(OCH_3)_2 + RMgX \rightarrow ClCH_2CHBrCH(R)OCH_3 + CH_3OMgBr, \quad (62)$$

where R = n-C_3H_7 or n-C_4H_9.

The halogen in the acetals of chloropropiolaldehyde may be substituted by the group of the Grignard reagent with formation of acetals of $\alpha\beta$-acetylenic aldehydes in 40–70% yield[139]:

$$ClC\equiv CCH(OR)_2 + R'MgX \rightarrow R'C\equiv CCH(OR)_2 + MgXCl, \quad (63)$$

where R = C_2H_5 or C_4H_9, R′ = n-C_3H_7, i-C_3H_7, n-C_4H_9, i-C_4H_9, n-C_6H_{13}, n-C_9H_{19}, C_6H_5, or α-$C_{10}H_7$ and X = Br.

The acetals of halogenoalcohols as a rule exchange their halogen atom for the group of the OMC in the first place. Thus the reaction

$$CH_3CH(OR)OCH_2CH_2Cl + R'MgX \rightarrow \begin{cases} \rightarrow CH_3CH(R')OCH_2CH_2Cl \\ \rightarrow CH_3CH(OR)OCH_2CH_2R' \\ \rightarrow CH_3CH(R)OCH_2CH_2R', \end{cases} \quad (64)$$

where R = C_2H_5 or C_4H_9, R′ = C_6H_5 or $C_6H_5CH_2$, and X = Cl or Br, has been described[140]. The reaction temperature is higher than the boiling point of β-chloroethyl acetal.

When di-(β-chloroethyl) acetal reacts with benzylmagnesium chloride, both chlorine atoms are substituted by benzyl residues with formation of di-(γ-phenylpropyl) acetal[141-143]:

$$CH_3CH(OCH_2CH_2Cl)_2 + 2\,RMgX \rightarrow CH_3CH(OCH_2CH_2R)_2 + 2MgClX, \quad (65)$$

where R = C_6H_5 or $C_6H_5CH_2$ and X = Br or Cl.

Asymmetric alkyl β-chloroethyl acetals react similarly with Grignard reagents[141], but the yield of substitution products does not exceed 8%. The authors[141] note that chlorine in the β-position relative to the alkoxy-group makes the latter relatively immobile.

After prolonged heating with magnesium in ether, alkyl β-chloroethyl acetals give rise to a mixture of three products[60]:

$$2CH_3CH(OC_4H_9)OCH_2CH_2Cl + Mg \rightarrow \begin{cases} 1 \rightarrow CH_3CH(OC_4H_9)OCH_2CH_2CH(CH_3)OCH_2CH_2Cl \\ 2 \rightarrow CH_3CH(OC_4H_9)OCH_2CH_2CH_2CH_2OCH(OC_4H_9)CH_3 \\ 3 \rightarrow ClCH_2CH_2OCH(CH_3)CH(CH_3)OCH_2CH_2Cl. \end{cases} \quad (66)$$

The third pathway predominates.

5. Acetals with Other Functional Groups and Heteroatoms

The acetals of methoxyacetaldehyde[106] form glycol ethers with OMC:

$$CH_3OCH_2CH(OCH_3)_2 + RMgCl \rightarrow CH_3OCH_2CH(R)OCH_3. \quad (67)$$

The reaction of the ethoxyacetals $C_6H_5[CH(OC_2H_5)CH_2]_n.CH(OC_2H_5)_2$ with $ArCH_2MgCl$ has been discussed[144,145] as a possible pathway to the synthesis of arylated polyene hydrocarbons, which are used as organic phosphors.

Carbamoyl- and cyano-acetals react with OMC via their functional groups[106,129,146]:

$$R_2NCOCH(OC_2H_5)_2 + CH_3MgI \rightarrow R_2NC(OH)(CH_3)CH(OC_2H_5)_2 \rightarrow (C_2H_5O)_2CHCCH_3, \quad (68)$$

$$CNCH(OR)_2 + R'MgX \rightarrow R'COCH(OR)_2, \quad (69)$$

where R = C_2H_5 or C_6H_5 and R′ = C_2H_5, i-C_3H_7, n-C_5H_{11}, n-C_7H_{15}, C_6H_5, or cyclo-C_6H_{11}. The yield of ketoacetals in the latter reaction is 79–95%.

At 36°C 1-acetoxy-1-butoxyethane reacts with Grignard reagents primarily via the ester group[140,147], which is ultimately exchanged for the group attached to the Grignard reagent.

Mono- and di-thioacetals can be involved in exchange reactions with OMC[148,149] [reaction (70)]. Monothioacetals initially split off the alkoxy-group under the influence of the Grignard reagent:

$$CH_3CH(OR')(SR'') + RMgX \rightarrow CH_3CH(R)SR'' + R'OMgX, \quad (70)$$

where R = C_4H_9 or C_6H_5. The reaction of dithioacetals with Grignard reagents is much more difficult.

The reaction of organosilicon acetals with OMC has been described[110,140,150]. The alkoxy-group containing the silicon atom is exchanged regardless of whether it is linked to oxygen directly or is more remote. This mode of reaction is difficult to explain. The corresponding ethers are usually obtained in yields up to 70%.

The capacity of organosilicon groups in acetals for exchange decreases in the sequence[150] $OSi(CH_3)_3 > OSi(C_2H_5)_3 > OCH(CH{=}CH_2)CH_2Si(CH_3)_2C_2H_5$.

In organogermanium acetals the germanium-containing groups are also exchanged for the group of the Grignard reagent[60].

IV. CYCLIC ACETALS (1,3-DIOXACYCLANES) AND THEIR ANALOGUES

Cyclic acetals play an important role in synthetic organic chemistry. The protection of vicinal hydroxy-groups of carbohydrates and sugars by acetal groups is widely known. The protection of the carbonyl group by the acetal group has been used successfully in the industrial synthesis of steroids and terpenoids.

Although 1,3-dioxacyclanes do not differ in principle in any way from open-chain acetals, nevertheless their cyclic structure is responsible for one characteristic feature which justifies the consideration of the reactions of 1,3-dioxacyclanes with OMC in a separate section. This feature is that 1,3-dioxacyclanes do not lose their oxygen-containing fragment on cleavage of the C–O bond by OMC in the way that open-chain acetals do.

As shown above, the exchange reactions of acyclic acetals with OMC have been investigated in fair detail. On the other hand, systematic studies on the analogous reactions of 1,3-dioxacyclanes began only recently. It appeared for a long time that 1,3-dioxacyclanes are fully resistant to the action of OMC. This was indicated by many facts. Thus 1,3-dioxolans with methyl substituents at $C_{(4)}$[44] or at $C_{(4)}$ and $C_{(5)}$[34] were suggested as solvents for Grignard syntheses. According to Nazarov[151], a bicyclic acetal with a complex structure, consisting of two 1,3-dioxolan fragments, does not react with OMC under the usual conditions. Many examples are known in which 1,3-dioxacyclanes containing functional groups react with OMC only via these functional groups without the cleavage of the C–O bonds in the acetal ring. In particular, the methylation of the terminal acetylenic group in 2-but-3-ynyl-2-methyl-1,3-dioxolan by ethylmagnesium bromide and methyl iodide in THF has been described[152]. The cleavage of the C–O bond has not been observed either in reactions of various carbonyl derivatives of 1,3-dioxolans with OMC[31,153-155].

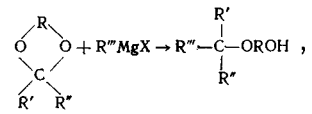
The interaction of 2-methoxy-1,3-dioxolans with OMC on heating leads to 2-alkyl(aryl)dioxolans[156]. The formation of OMC from cyclic five-membered acetals derived from saturated and unsaturated halogenoketones, including aromatic and heteroaromatic ketones, has been described[99,144,157].

The ethylene acetal of chloral is reduced by Grignard reagents to the dichloroacetaldehyde acetal in 74% yield[28].

When cyclic acetals of certain dihalogenoketones are treated with metallic magnesium, a three-membered ring is formed. The C–O bonds are not then affected[106]. All the data quoted above appear to have created a psychological barrier to studies on the cleavage of 1,3-dioxacyclanes by OMC. A few early studies[158-161] at the beginning of the century, in which the formation of the monoethyl ether of catechol from its formal on prolonged heating with methylmagnesium iodide was mentioned, were not developed further and were undeservedly essentially forgotten until the 1960's.

1. The Cleavage of 1,3-Dioxacyclanes by Grignard Reagents

Reactions involving the opening of the ring in various cyclic acetals by OMC [reaction (71)], leading to glycol monoethers (cellosolves), have been described almost simultaneously and independently by two research teams[2,34]:

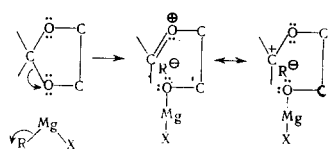


(71)

where R = $(CH_2)_2$, $(CH_3)CHCH_2$, $(CH_3)CHCH_2CH_2$, R′ = H, CH_3, or C_2H_5, R″ = H, C_2H_5, C_3H_7, or n-C_4H_9, R‴ = CH_3, C_2H_5, n-C_4H_9, C_6H_5, or CH_2=$CHCH_2$, and X = Br or I.

Cellosolves are usually obtained by the addition of alcohols to epoxyalkanes. The reaction is carried out in the presence of various catalysts[162] or by heating in an autoclave[163]. A mixture of ethers of mono-, di-, and tri-alkylene glycols, which are capable of interconversions under the reaction conditions, is as a rule formed[163]. The reaction of 1,3-dioxacyclanes with Grignard reagents made it possible to develop a fundamentally new method[5,6] for the preparation of a wide variety of glycol monoethers. The reaction is carried out at 60–130°C in solvents (benzene, toluene, or xylene) or in an excess of the acetal itself. The yield of hydroxyalkyl ethers depends on the structure and nature of the initial reactants, their proportions, the duration of heating, and the medium, reaching 82%.

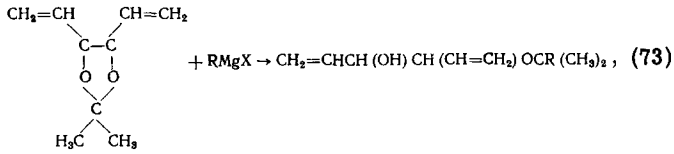
More than 30 different glycol monoethers obtained in this way have been described[22-24]. Cyclic formals are resistant to the action of Grignard reagents under the conditions investigated. As alkyl substituents accumulate in the 2-position, the reaction accelerates and the yield of cellosolves increases[22-24]. This behaviour is consistent with data for the influence of substituents on the hydrolysis[164,165] of 1,3-dioxacyclanes and also on their cleavage by halogenoacyls[166-170] and is probably due to similar causes: a change in electron density at the oxygen atoms which are the object of the primary electrophilic attack and in the stability of the intermediate carboxonium ion[24]. This finding conflicts with the concept of the primary nucleophilic attack on the $C_{(2)}$ atom, since under such conditions the electron-donating substituents in the 2-position should have retarded the process. The facilitation of the reaction with increase of the electron-donating capacity of substituents in the 2-position shows that the $C_{(2)}$–O bond dissociates before the formation of a new $C_{(2)}$–R bond (R is the group attached to OMC). The following mechanism has been proposed for the opening of the 1,3-dioxolan ring by OMC[34]:



(72)

According to mechanism (72), an increase in the electron-donating influence of the alkyl substituents in the 2-position should facilitate the cleavage of the acetal ring. The results of Blomberg at al.[34] indicate that ethylmagnesium bromide hardly reacts at room temperature with 2-methyl-1,3-dioxolan, while 2-ethyl- and 2-n-propyl-1,3-dioxolans form hydroxyethers under these conditions in yields of 39 and 78% respectively. The bulk of the alkyl groups in the Grignard reagent is reflected in the course of the reaction only when the dioxolan ring contains fairly bulky substituents[34]. The corresponding hydroxyethers have been obtained from the ethylene ketal of cyclohexanone on treatment with two equivalents of a Grignard

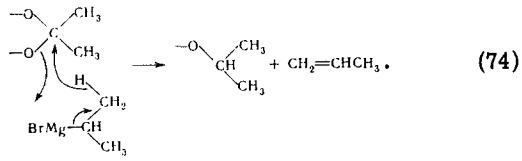
reagent in 91% yield (75°C, 16 h, benzene).[33] The reaction of 4-alkoxymethyl-2,2-dialkyl-1,3-dioxolans with ethylmagnesium bromide leads to the corresponding glycerol ethers[171]. The reactions of 2,2,4,4-substituted 1,3-dioxolans with various Grignard reagents [reactions (73)–(76)] have been described[29]‡:



(73)

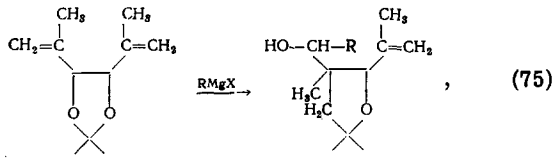
where R = CH_3 (X = I), C_2H_5, i-C_3H_7, or C_6H_5 (X = Br).

When R = i-C_3H_7, a reduction takes place:

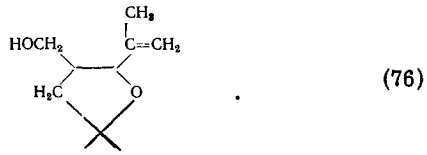


(74)

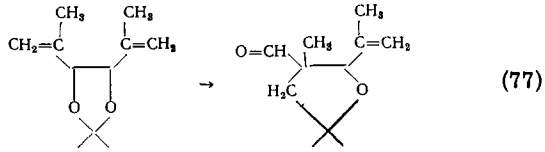
cis-Isomers undergo isomerisation:


(75)

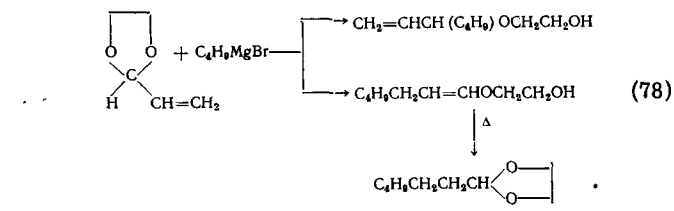
a primary alcohol being obtained with i-C_3H_7MgBr:


(76)

A rearrangement of similar acetals to furan aldehydes is known[173]:


(77)

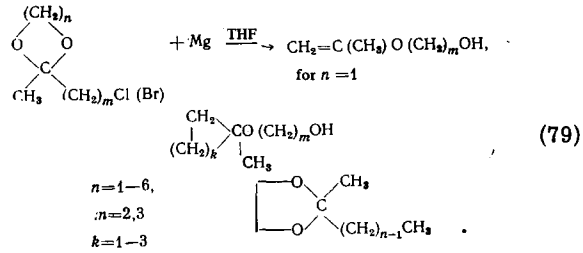
The latter are probably intermediates in the isomerisation described by Mousset[29]. When butylmagnesium bromide reacts with the cyclic acrolein acetal, the vinyl group is alkylated in addition to the normal mode of reaction [reaction (78)]. The process is accompanied by a prototropic rearrangement[130]:



(78)

‡ These problems are discussed in greater detail by Mousset[172].

The reactions of ω-halogenoalkyl-1,3-dioxolans with metallic magnesium have been considered[28,96,174]:

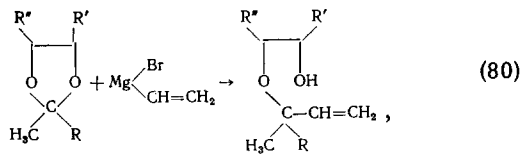


(79)

When $n = 3$, the formation of hydroxyethers is already accompanied by the reduction of the ω-halogenoalkyl substituent, which leads to the appearance in the reaction mixture of the corresponding 2-alkyl-2-methyl-1,3-dioxolans; when $n = 5$ or 6, the reduction becomes the only pathway followed in the process.

2. The Cleavage of 1,3-Dioxacyclanes by Vinylmagnesium Bromide and the Iotsich Reagent

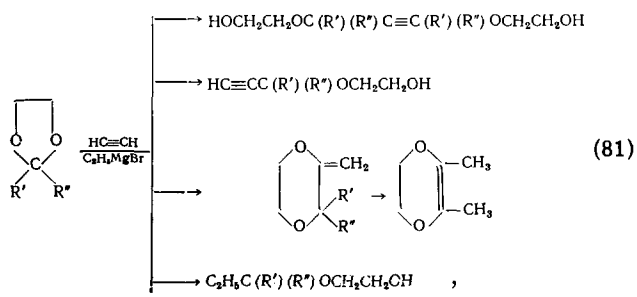
Compared with saturated OMC, which readily rupture the C–O bonds of cyclic acetals and ketals, vinylmagnesium bromide is much less reactive in relation to these compounds[14]. Thus 2-ethyl-2-methyl-1,3-dioxolan begins to react with vinylmagnesium bromide only under relatively severe conditions (120°C, xylene):


(80)

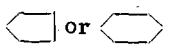
where R = H, C_2H_5, C_3H_7, or C_4H_9, R′ = CH_3, and R″ = CH_3.

β-Hydroxyalkyl ethers of ethylenic alcohols are obtained in yields of about 10%. 2-Butyl-2-methyl-, 2-ethyl-2,4-dimethyl-, and 2-ethyl-2,4,5-trimethyl-1,3-dioxolans were introduced into the reaction. Unsaturated β-hydroxyalkyl ethers could not be isolated in the case of 2-methyl- and 4-methyl-2-propyl-1,3-dioxolans, i.e. here too the conclusion that the reactivity of 1,3-dioxolans is reduced as the electron-donating properties of the substituents in the 2-position are weakened remains valid.

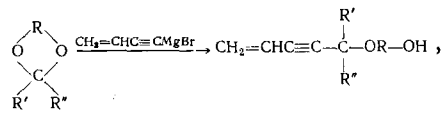
The cleavage of cyclic acetals by ethynylmagnesium bromide [reaction (81)] is accompanied by side reactions. A complex mixture containing, according to gas–liquid chromatographic and infrared spectroscopic data, various cyclisation products of the expected ethynyl ethers in addition to the ethers themselves as well as saturated hydroxyethers corresponding to the opening of the dioxolan ring by the initial Grignard reagent, is formed as a rule[19,22–24]:



(81)

where R′ = H or CH_3, R″ = CH_3 or C_2H_5, and R′,R″ =  or .

A number of hydroxyalkyl ethers derived from vinylethynylmethanols have been obtained in yields up to 80% by the reaction of various 1,3-dioxolans with vinylethynylmagnesium bromide (VEMB)[4,6,8,10,15,16]:



(82)

where R = $(CH_2)_2$ or $CH_2CH(CH_3)$, R′ = H or CH_3, and R″ = H, CH_3, C_2H_5, C_3H_7, or C_6H_{13}. In this process too the reactivity of 1,3-dioxolans increases somewhat with increase of the number and electron-donating capacity of substituents in the 2-position. Thus, whereas the yields of the hydroxyethyl ethers from 2-methyl- and 2-ethyl-2-methyl-1,3-dioxolans were 44.3 and 58.3% under comparable (but not optimal) conditions, unsubstituted 1,3-dioxolan could not be cleaved at all by VEMB.

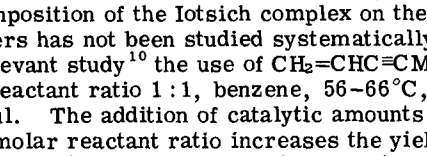
The introduction of the methyl group in the 4- or 5-position does not affect the reactivity of 1,3-dioxolan quite so significantly, although the latter is also apparently somewhat activated. One of the most important factors affecting the yields of hydroxyalkyl ethers derived from vinylethynyl alcohols is the reactant ratio[10] (see Table).

Variation of the yield of the vinyloxyethyl ether derived from methylvinylethynylmethanol with the initial reactant ratio.

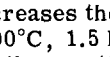
Molar ratio 2-methyl-1,3-dioxolan : VEMB	Yield (w.r.t. VEMB), %
1:2	80
1:1	39.2
2:1	21.9

The yield of hydroxyethers depends no less significantly on the solvent. In ethyl ether the yield does not exceed 10%. When all the stages of the synthesis, including the preparation of the Grignard reagent, are carried out in the reacting acetal, it was possible to obtain the hydroxyether in yields up to 45%.[10] The effect of the halogen entering into the composition of the Iotsich complex on the yield of hydroxyethers has not been studied systematically. In the only relevant study[10] the use of $CH_2{=}CHC{\equiv}CMgI$ instead of VEMB (reactant ratio 1 : 1, benzene, 56–66°C, 2 h) was unsuccessful. The addition of catalytic amounts of $CoCl_2$ for an equimolar reactant ratio increases the yield to 57% compared with 39% (benzene, 80–90°C, 1.5 h). Higher $CoCl_2$ concentrations do not favour the reaction[10].

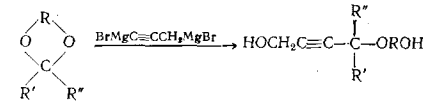
A number of β-hydroxyethyl ethers derived from secondary and tertiary phenyl-substituted acetylenic alcohols were obtained[7] from 1,3-dioxolans and phenylethynylmagnesium bromide:



40–60% (83)

where R = $(CH_2)_2$ or $(CH_2)_3$, R′ = H or CH_3, R″ = CH_3, C_2H_5, or C_3H_7, and R′ = R″ = . The reaction proceeds at 60–80°C. Iotsich complexes can be used under these conditions in the form of ether adducts with subsequent distillation of the ether, but they can be formed just as conveniently directly in the reacting cyclic acetal. To prevent the competing process, involving the saturated organomagnesium compound used to prepare the Iotsich complex, the intermediate Grignard reagent must then be synthesised at the lowest possible temperature (not above 40°C). Unsubstituted 1,3-dioxolan is resistant to the action of phenylethynylmagnesium bromide even at 100–120°C (xylene).

β-Hydroxyalkyl ethers of asymmetric acetylenic glycols were obtained by the reaction of certain 1,3-dioxolans with propynylenedimagnesium dibromide[3,24]:

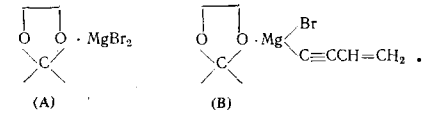


(84)

where R = $(CH_2)_2$ or $CH(CH_3)CH(CH_3)$, R′ = H or CH_3, and R″ = CH_3, C_2H_5, or C_3H_7.

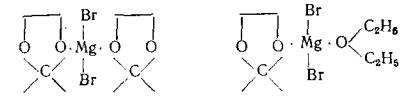
3. Complex Formation Processes

Like 1,4-dioxan, 1,3-dioxolans[175,176] can precipitate MgX_2 and RMgX from OMC solutions[8,10]. In the case of VEMB[8,10] the precipitate consists mainly of a mixture of the dioxolanates (A) and (B) in proportions of approximately 2 : 1:



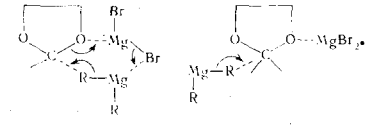
(85)

Small amounts of solvates of the type



(86)

were detected in the precipitate in addition to the complexes (A) and (B).[8,10] Thus ether adducts of Iotsich complexes probably have the same structure as the ether adducts of saturated magnesium halides and can be regarded as a mixture of $(CH_2{=}CHC{\equiv}C)_2Mg$ (40%), $MgBr_2$ (40%), and $CH_2{=}CHC{\equiv}CMgBr$ (20%). The reaction most probably proceeds via a synchronous electron transfer in cyclic or linear complexes[8,10]:



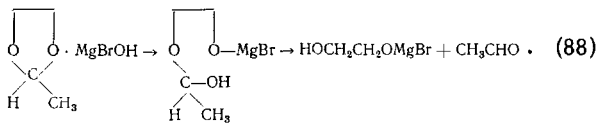
(87)

In such concerted nucleophilic substitution, the coordination O → $MgBr_2$ should play the most significant role. If the nucleophilic attack C_2 ← R were the most important factor, then electron-donating substituents at $C_{(2)}$ would hinder the reaction. The proposed mechanism gives a completely natural explanation of the requirement of at least a twofold excess of the Iotsich complex for the attainment of the maximum yield of hydroxyethers. A similar mechanism has been proposed for the cleavage of certain unsaturated acetals by OMC.[130]

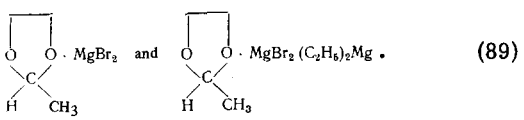
Insoluble complexes with certain 1,3-dioxolans are also formed by ethylmagnesium bromide. The principal components of the complexes are $MgBr_2$, C_2H_5MgBr, and

the corresponding dioxolan. The composition of the complexes is not constant and depends on the structure of the initial acetal, the reactant ratio, temperature, and the time of contact between the solid phase and the solution. It has been established for unsubstituted 1,3-dioxolan[10,11] that a decrease of temperature reduces the content of OMC in the precipitate. Gradual binding of 2-methyl-1,3-dioxolan by anhydrous $MgBr_2$ was observed[11]. The infrared spectrum of this complex hardly differs from that of the complex obtained from ethylmagnesium bromide at −20°C.

Basic magnesium salts are also capable of coordination interaction with cyclic acetals. However, the resulting complexes are unstable and tend to undergo further reactions (particularly on heating) with ring opening:

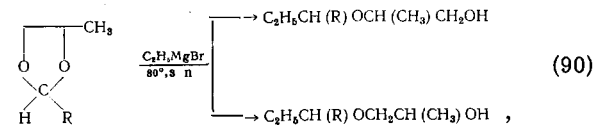

(88)

The rate of change of the OMC concentration in solution in the reaction between ethylmagnesium bromide and 2-methyl-1,3-dioxolan at 18°C has been measured[11]. The sharp decrease of the OMC concentration at the beginning of the reaction corresponds to the precipitation of the complex [the OMC concentration probably falls not only as a result of the binding of C_2H_5MgBr but also as a result of the adsorption of $(C_2H_5)_2Mg$ at the instant of the formation of the precipitate]; subsequently the OMC concentration over the precipitate changes much more slowly. Presumably the consumption of the OMC in this stage is due to the ring opening reaction itself. However, gas–liquid chromatographic analysis of the products of the hydrolysis of the reaction mixture failed to reveal even traces of the expected β-hydroxyethyl ether. The results correspond to the consecutive formation of complexes of two types:


(89)

4. The Mode of Cleavage of Asymmetrically Substituted 1,3-Dioxacyclanes

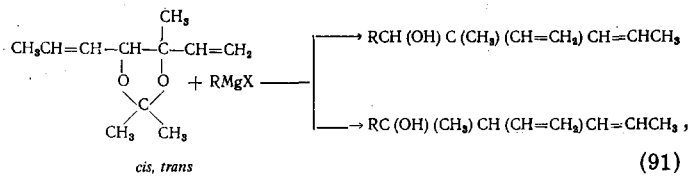
When 4-alkyl- and 2,4-dialkyl-1,3-dioxolans react with Grignard reagents[9], the products may be two structurally isomeric β-hydroxyalkyl ethers differing only by the position of the hydroxy-group—at the first carbon atom in one and at the second carbon atom in the other:


(90)

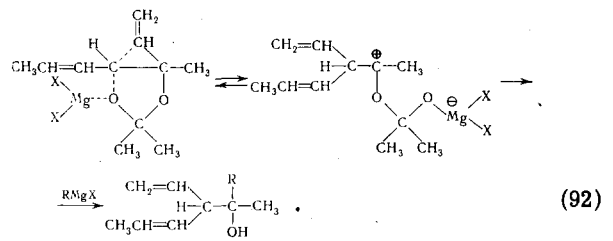
where R = CH_3 or C_3H_7.

However, it was found[9] that the reaction results in the almost exclusive formation of 2-hydroxy-1-methylethyl ethers. The admixture of the second isomer is slight, amounting to about 4% of the first.

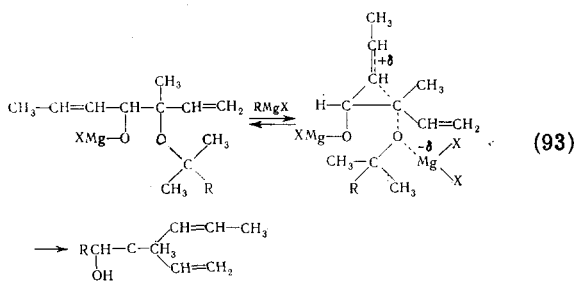
Interesting rearrangements were discovered[30] in the following reaction:


(91)

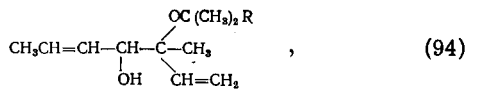
where R = CH_3 (X = I), C_2H_5, or C_6H_5 (X = Br). The formation of the tertiary alcohol begins with the rupture of the $O_{(1)}-C_{(5)}$ bond:


(92)

The cleavage of the $O_{(1)}-C_{(2)}$ bond leads to a secondary alcohol:

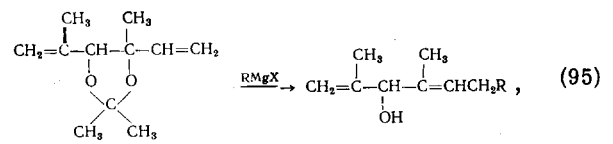

(93)

Thus both the tertiary and secondary alcohols are products of the attack by the OMC on the $O_{(1)}$ oxygen atom. The formation of hydroxyethers with the ether function at the tertiary carbon atom having the structure


(94)

which should have been obtained as a result of attack on the $O_{(3)}$ atom, was never observed in these reactions[30].

The cleavage of the C–O bond under the influence of a Grignard reagent in another 1,3-dioxolan with a structure very similar to that considered above was accompanied by the alkylation of one of the double bonds and its subsequent migration to the centre of the molecule[30]:

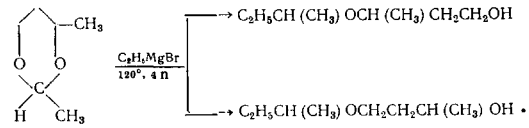

(95)

where R = CH_3 (X = I), C_2H_5, or C_6H_5 (X = Br).

The *cis*- and *trans*-isomers of 2,3-dimethyl and 4-methyl-2-propyl-1,3-dioxolans are cleaved by Grignard reagents at different rates[9]. The *cis*-isomers proved to be more reactive. This shows that the $O \rightarrow MgBr_2$ bond is oriented in space at a certain angle to the plane of the dioxolan ring, since otherwise the isomers of 2,4-dialkyl-1,3-dioxolans would be sterically indistinguishable in the formation of the intermediate complex[9]. These data, demonstrating a lower reactivity of 1,3-dioxolans with the

trans-disposition of the substituents with respect to the Grignard reagent, were subsequently confirmed in another study[30].

In contrast to asymmetrically substituted 1,3-dioxolans, 2,4-dimethyl-1,3-dioxan is cleaved by ethylmagnesium bromide with formation of two possible isomeric hydroxyethers in proportions of approximately 1 : 1[17]:



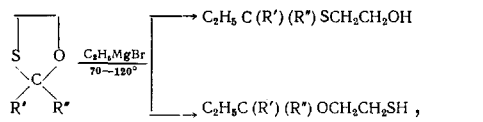
(96)

The change in the structural specificity of the cleavage of acetal rings on passing from five- to six-membered rings is associated with the conformations of the compounds. In contrast to the almost planar 1,3-dioxolans, 2,4-dimethyl-1,3-dioxan has the chair conformation with the *cis*-equatorial disposition of the CH_3 groups[17]. The 1 : 1 ratio of the isomeric hydroxyethers formed from this acetal shows that the *cis-e,e*-conformation to a large extent eliminates the steric hindrance to the interaction $O \rightarrow MgBr_2$, which is the initial stage in the cleavage of the 1,3-dioxacyclane.

However, the degree of structural specificity of the reaction depends on the bulk of the OMC molecules. When branched groups and bulky halogen atoms are present, the above effect of steric descreening of the $O_{(3)}$ atom in the 1,3-dioxan ring is insufficient for a preferential cleavage of the $O_{(1)} - C_{(2)}$ bond, of the kind observed in the cleavage of 2,4-dimethyl-1,3-dioxan by isobutylmagnesium bromide[17]. Thus the mode of cleavage of asymmetrically substituted 1,3-dioxolans and 1,3-dioxans is determined not only by the ring conformation but also to a similar extent by the steric characteristics of the OMC components[17].

5. The Cleavage of 1,3-Oxaheterocyclanes by OMC

1,3-Oxathiolans are cleaved by ethylmagnesium bromide with formation of 2-ethylthioethanols only[18,24]:

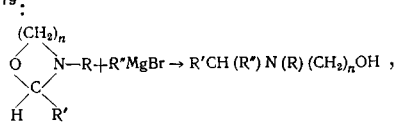


(97)

where R′ = H or CH_3 and R″ = H, CH_3, C_2H_5, or C_3H_7.

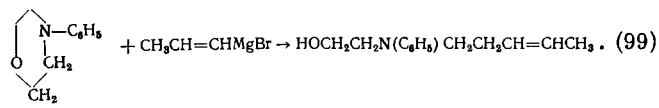
The unsubstituted ring is stable in the experimental temperature range (70–120°C). Compared with the corresponding 1,3-dioxolans, 1,3-oxathiolans are less reactive with respect to OMC[18]. Yet another feature of the reaction has been noted[18,23,24]: in contrast to 1,3-dioxolans, the introduction of two alkyl groups in the 2-position increases the stability of the 1,3-oxathiolan ring. 2-Monoalkyl-1,3-oxathiolans are the most reactive. This influence of substitution is evidence that in this instance the dissociation of the C–O bond does not precede appreciably the formation of the C–R bond, i.e. the reaction approaches the S_N2 type[18].

1,3-Oxazolidines are also cleaved by OMC at the C–O bond[115,177–179]:



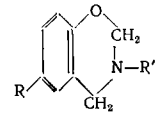
(98)

where R = H, CH_3, n-C_4H_9, i-C_4H_9, $(CH_3)_2CHCH_2$, or C_6H_5, R′ = H, CH_3, i-C_3H_7, or C_6H_5, and R″ = CH_3, $C_6H_5CH_2$, $(CH_3)_2CH$, CH_2=CH, or CH_3CH=CH_2. The yield of amino-alcohols reaches 80% in some cases. The reaction between 1,4-oxazolidines and propenylmagnesium bromide proceeds similarly[115]:



(99)

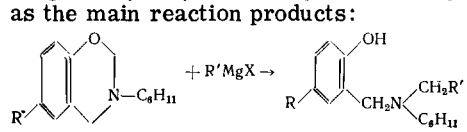
It has been found[180] that 2-oxazolidines of the type



(100)

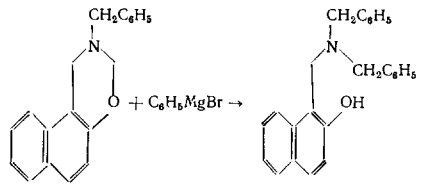
unsubstituted in the 2-position, do not react with CH_3MgI. However, later it was observed[181] that, when oxazines of similar structure are acted upon by a large excess of C_6H_5MgBr, the cleavage products are nevertheless formed in 8% yield.

When OMC interact with certain 1,3,2-dibenzoxazines, the benzoxazine ring is ruptured with formation of the corresponding 4-alkyl(aryl)-2-dialkylaminomethylphenols[74,101] as the main reaction products:



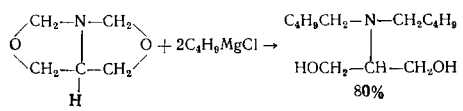
(101)

where R = $C(CH_3)_3$ or C_6H_5, R′ = CH_3, $(CH_3)_2CHCH_2$, C_6H_{11}, $C_6H_5CH_2$, or CH_2=$CHCH_2$ and X = Br, Cl, or I. The reaction is carried out in the presence of an excess of OMC. A similar reaction



(102)

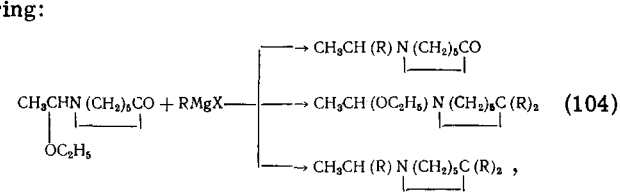
has been described[181]. The reaction



(103)

takes place at room temperature in the course of 24 h.[177]

N-(1-Ethoxyethyl)lactams[182,183] initially exchange preferentially the ethoxy-group for the group in the OMC and then the reaction involves the C=O bond with retention of the ring:

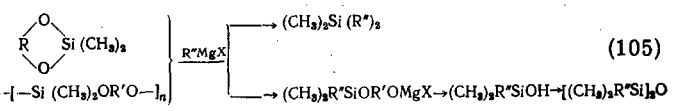


(104)

where R = C_3H_7, C_4H_9, or i-C_5H_{11} and X = Br.

1,3-Dioxa-2-silacyclanes and their oligomers[20,25] readily undergo ring opening under the influence of alkyl-(aryl)magnesium halides at a temperature as low as 30–40°C with formation of trialkyl(diaryl)silylglycol monoethers. In addition, the second Si–O bond is also ruptured with formation of tetra-alkyl(trialkylaryl)silanes, whose yields increase in the presence of an excess of the

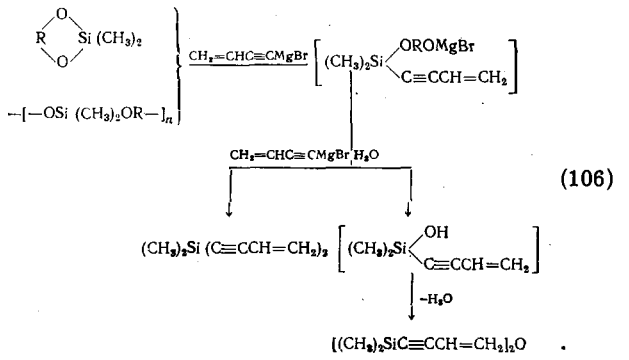
Grignard reagent and on raising the reaction temperature to 70–80°C:



(105)

where $R' = (CH_2)_2$, $(CH_2)_2O(OCH_2)_2$, or $(CH_2)_4$ and $R'' = C_6H_5$, C_3H_7, C_4H_9, or C_6H_5.

The cleavage of cyclic alkoxysilanes or the elementary units in the corresponding oligomers by VEMB proceeds as follows:[22,25]



(106)

The reaction occurs at 60–90°C. The above examples show that the Si–O bond is more reactive with respect to OMC than the C–O bond.

REFERENCES

1. S. T. Ioffe and A. N. Nesmeyanov, "Metody Elementoorganicheskoi Khimii" (Methods in the Organic Chemistry of the Elements), Izd. Akad. Nauk SSSR, Moscow, 1963, p. 324.
2. M. F. Shostakovskii, A. S. Atavin, and B. A. Trofimov, Zhur. Obshch. Khim., 34, 2089 (1964).
3. M. F. Shostakovskii, A. S. Atavin, S. E. Orlova, and B. A. Trofimov, Zhur. Org. Khim., 1, 1170 (1965).
4. S. E. Orlova, A. S. Atavin, B. A. Trofimov, and E. P. Vyalykh, "Tezisy Dokladov Konferentsii po Khimii Atsetilena" (Abstracts of Reports at the Conference on Acetylene Chemistry), Izd. Akad. Nauk SSSR SO IrIOKh Sovet Nar. Khoz. Vost.-Sib. Ekonomicheskogo r-na Irk. Otd. Vses. Khim. Obshch. im. Mendeleeva, Irkutsk, 1965, p. 24.
5. M. F. Shostakovskii, A. S. Atavin, B. A. Trofimov, and S. E. Orlova, USSR P. 178 813; Byul. Izobret., No. 4 (1966).
6. M. F. Shostakovskii, A. S. Atavin, B. A. Trofimov, E. P. Vyalykh, and S. E. Orlova, USSR P. 188 959; Byul. Izobret., No. 3 (1966).
7. A. S. Atavin, B. A. Trofimov, and S. E. Orlova, Zhur. Org. Khim., 2, 206 (1966).
8. B. A. Trofimov, A. S. Atavin, and S. E. Orlova, Izv. Akad. Nauk SSSR, Ser. Khim., 2023 (1966).
9. B. A. Trofimov, A. S. Atavin, S. E. Orlova, E. I. Kositsina, and V. V. Keiko, Izv. Akad. Nauk SSSR, Ser. Khim., 2727 (1967).
10. B. A. Trofimov, A. S. Atavin, and S. E. Orlova, Zhur. Org. Khim., 4, 264 (1968).
11. A. S. Atavin, M. F. Shostakovskii, S. E. Orlova, and B. A. Trofimov, Izv. Akad. Nauk SSSR, Ser. Khim., 2599 (1968).
12. S. E. Orlova, M. F. Shostakovskii, A. S. Atavin, and B. A. Trofimov, "Tezisy Dokladov 2-oi Konferentsii po Voprosam Stroeniya i Reaktsionnoi Sposobnosti Atsetalei" (Abstracts of Reports at the Second Conference on the Problems of the Structure and Reactivity of Acetals), Izd. ILIM, Frunze, 1967, p. 82.
13. B. A. Trofimov, A. S. Atavin, and S. E. Orlova, "Tezisy Dokladov 2-oi Konferentsii po Voprosam Stroeniya i Reaktsionnoi Sposobnosti Atsetalei" (Abstracts of Reports at the Second Conference on the Problems of the Structure and Reactivity of Acetals), Izd. ILIM, Frunze, 1967, p. 81.
14. M. F. Shostakovskii, A. S. Atavin, S. E. Korostova, and B. A. Trofimov, Izv. Akad. Nauk SSSR, Ser. Khim., 1904 (1968).
15. S. E. Orlova, A. S. Atavin, B. A. Trofimov, and E. P. Vyalykh, Symposium, "Khimiya Atsetilena" (The Chemistry of Acetylene), Izd. Nauka, Moscow, 1968, p. 2527
16. A. S. Atavin, B. A. Trofimov, and S. E. Orlova, Izv. Akad. Nauk SSSR, Ser. Khim., 109 (1968).
17. A. S. Atavin, B. A. Trofimov, S. E. Korostova, G. A. Kalabin, V. V. Keiko, and E. I. Kositsina, Izv. Akad. Nauk SSSR, Ser. Khim., 1343 (1969).
18. M. F. Shostakovskii, B. A. Trofimov, A. S. Atavin, and S. E. Korostova, Izv. Akad. Nauk SSSR, Ser. Khim., 1149 (1970).
19. M. F. Shostakovskii, B. A. Trofimov, A. S. Atavin, S. E. Korostova, L. P. Nekrasova, and V. V. Keiko, Izv. Akad. Nauk SSSR, Ser. Khim., 668 (1970).
20. M. F. Shostakovskii, A. S. Atavin, E. P. Vyalykh, B. A. Trofimov, N. A. Vodbol'skaya, and V. V. Keiko, Izv. Akad. Nauk SSSR, Ser. Khim., 1283 (1966).
21. M. F. Shostakovskii, A. S. Atavin, E. P. Vyalykh, and B. A. Trofimov, Izv. Akad. Nauk SSSR, Ser. Khim., 943 (1967).
22. B. A. Trofimov, Candidate's Thesis, Irkutsk State University, Irkutsk, 1965.
23. B. A. Trofimov, Doctoral Thesis, Leningrad State University, Leningrad, 1971.
24. S. E. Korostova, Candidate's Thesis, Irkutsk State University, Irkutsk, 1969.
25. E. P. Vyalykh, Candidate's Thesis, Irkutsk State University, Irkutsk, 1968.
26. M. F. Shostakovskii, A. S. Atavin, and B. A. Trofimov, Zhur. Obshch. Khim., 34, 2088 (1964).
27. A. S. Atavin, S. E. Orlova, and B. A. Trofimov, "Materialy Konferentsii Oblastnogo Otdeleniya Vsesoyuznogo Khimicheskogo Obshchestva im. Mendeleeva, Irkutsk, 1967" (Proceedings of the Conference of the Regional Division of the Mendeleev All-Union Chemical Society, Irkutsk, 1967), p. 100.
28. H. Normant, Bull. Soc. chim. France, 2161 (1972).
29. G. Mousset, Bull. Soc. chim. France, 4097 (1971).
30. G. Mousset, Bull. Soc. chim. France, 1983 (1972).
31. R. Meric and J.-P. Vigneron, Bull. Soc. chim. France, 327 (1973).
32. G. Giusti, Bull. Soc. chim. France, 383 (1973).
33. R. A. Mallory, S. Rovinsky, and I. Scheer, J. Chem. Soc., 5526 (1964).
34. C. Blomberg, A. D. Vreugdenhil, and T. J. Homsma, Rec. Trav. chim., 82, 355 (1963).
35. A. E. Chichibabin and S. E. Elgazin, Zhur. Russ. Fiz. Khim. Obshch., 46, 39 (1914).
36. A. E. Chichibabin and S. E. Elgazin, Zhur. Russ. Fiz. Khim. Obshch., 46, 802 (1914).

37. A. E. Chichibabin and S. E. Elgazin, Ber., **47**, 48 (1914).
38. A. E. Chichibabin and S. E. Elgazin, Ber., **47**, 1843 (1914).
39. E. Späth, Monatsh., **34**, 1967 (1913).
40. E. Späth, Ber., **47**, 766 (1914).
41. E. Späth, Monatsh., **35**, 463 (1914).
42. E. Späth, Monatsh., **35**, 3196 (1914).
43. E. Späth, Monatsh., **36**, 1 (1915).
44. R. B. Carlin and L. O. Smith, J. Amer. Chem. Soc., **69**, 2007 (1947).
45. R. D. Yakubov, B. A. Trofimov, and A. S. Atavin, see Ref. 12, p. 65.
46. R. L. Burwel, Chem. Rev., **54**, 615 (1954).
47. Houben-Weyl, "Methoden der organischen Chemie. Sauerstoffverbindungen", I, Vierte Auflage Herausgegeben von Eugen Müller, Georg Thieme Verlag, Stuttgart, 1965, Vol. VI/3, p. 160.
48. A. Lüttringhaus, G. v. Sääf, and K. Hauschild, Ber., **71**, 1673 (1938).
49. H. Simons and P. Remmert, Ber., **47**, 269 (1914).
50. V. Grignard, Compt. rend., **151**, 322 (1910).
51. C. M. Hill, L. Haynes, D. E. Simmons, and M. E. Hill, J. Amer. Chem. Soc., **75**, 5408 (1953).
52. K. Zeill and H. Meyer, Ber., **75**, 356 (1942).
53. C. M. Hill, L. Haynes, D. E. Simmons, and M. E. Hill, J. Amer. Chem. Soc., **80**, 3623 (1958).
54. C. M. Hill, D. E. Simmons, and M. E. Hill, J. Amer. Chem. Soc., **77**, 3889 (1955).
55. C. M. Hill, R. A. Walker, and M. E. Hill, J. Amer. Chem. Soc., **73**, 1663 (1951).
56. C. M. Hill, R. M. Prigmore, and G. J. Moore, J. Amer. Chem. Soc., **77**, 352 (1955).
57. R. Quelet and J. d'Angelo, Bull. Soc. chim. France, 3390 (1967).
58. C. M. Hill, R. Woodberry, D. E. Simmons, M. E. Hill, and L. Haynes, Amer. Chem. Soc., **80**, 4602 (1958).
59. M. F. Shostakovskii, A. M. Khomutov, and A. P. Alimov, Izv. Akad. Nauk SSSR, Otd. Khim., Nauk, 1843 (1963).
60. M. R. Kulibekov, Doctoral Thesis, Azerbaijan State University, Baku, 1964.
61. M. F. Shostakovskii, B. A. Sokolov, O. N. Khil'ko, G. G. Balezina, and G. M. Alekseeva, Izv. Sibir. Otd. Akad. Nauk SSSR, Ser. Khim., **11**, 92 (1963).
62. W. Zeil and J. Winter, Tagungsbericht Chemische Gesellschaft DDR, 77, 1955 (1954); Chem. Zentr., 9270 (1962).
63. L. D. Assarson, Acta Chem. Scand., **10**, 1510 (1956).
64. H. Normant, Bull. Soc. chim. France, 1444 (1957).
65. H. Normant, French P. 656 917; Compt. rend., **239**, 1510 (1954).
66. F. R. Jensen and R. L. Bedard, J. Org. Chem., **24**, 874 (1959).
67. H. Normant, Bull. Soc. chim. France, 728 (1957).
68. W. Steudel and H. Gilman, J. Amer. Chem. Soc., **82**, 6129 (1960).
69. C. M. Hill, J. Senter, L. Haynes, and M. Hill, J. Amer. Chem. Soc., **76**, 208 (1955).
70. H. Normant, Compt. rend., **240**, 1111 (1955).
71. J. Ficini, Bull. Soc. chim. France, 119 (1956).
72. J. Buendia, Bull. Soc. chim. France, 3598 (1966).
73. C. Glacet and A. Gaumeton, Compt. rend., **241**, 208 (1955).
74. R. Quelet and J. d'Angelo, Compt. rend., **264**, 216 (1967).
75. J. Colonge and J. Buendia, Compt. rend., **261**, 1699 (1965).
76. K. G. Mizuch, Zhur. Obshch. Khim., **23**, 861 (1953).
77. J. d'Angelo, Bull. Soc. chim. France, 181 (1969).
78. Yu. K. Yur'ev, E. M. Lukina, and I. K. Korobitsina, Zhur. Obshch. Khim., **24**, 1238 (1954).
79. Yu. I. Yur'ev, E. G. Rozantsev, and S. M. Godovikova, Zhur. Obshch. Khim., **28**, 2168 (1958).
80. A. Spassky-Pasteur and H. Riviere, Bull. Soc. chim. France, 811 (1969).
81. L. I. Zakharkin, K. B. Bilevich, and O. Yu. Okhlobystin, Dokl. Akad. Nauk SSSR, **152**, 338 (1963).
82. US P. 2 416 717; Chem. Abs., **45**, 9079 (1951).
83. M. Pavlovskii, Zhur. Russ. Fiz. Khim. Obshch., **43**, 214 (1911).
84. A. E. Kranzfelder and R. R. Vogt, J. Amer. Chem. Soc., **60**, 1714 (1938).
85. Yu. V. Pokonova, "Galoidefiry" (Halogenoethers), Izd. Khimiya, Leningrad, 1966.
86. L. Summers, Chem. Rev., **55**, 301 (1955).
87. M. F. Shostakovskii, E. P. Gracheva, and N. K. Kul'bovskaya, Zhur. Obshch. Khim., **28**, 2341 (1958).
88. H. Normant, Compt. rend., **240**, 314 (1955).
89. I. A. Shikhiev, B. M. Guseinzade, I. A. Aslanov, N. T. Mekhmandarova, B. G. Yusufov, M. I. Shikhiev, E. M. Isaev, G. S. Askerov, M. Nasirova, and S. Rzaeva, Zhur. Org. Khim., **3**, 558 (1966).
90. I. A. Shikhiev, M. F. Shostakovskii, and N. V. Komarov, "Novye Kislorodsoderzhashchie Kremniiorganicheskie Soedineniya" (New Oxygen-containing Organosilicon Compounds), Azerneftneshr, Baku, 1960.
91. I. A. Shikhiev, "Khimiya Elementoorganicheskikh Soedinenii" (The Chemistry of Organic Derivatives of the Elements), Maarif, Baku, 1965.
92. Cauthier, Ann. Chim. Phys., [8], **16**, 334 (1909).
93. I. I. Lapkin and O. M. Lapkina, Zhur. Obshch. Khim., **21**, 108 (1951).
94. I. I. Lapkin and O. M. Lapkina, Zhur. Obshch. Khim., **22**, 1602 (1952).
95. Yu. K. Yur'ev, "Prakticheskie Raboty po Organicheskoi Khimii" (Practical Organic Chemistry), Izd. Moskov. Gos. Univ., 1961, p. 227.
96. C. Feugeas and H. Normant, Bull. Soc. chim. France, 1441 (1963).
97. J. Ficini and J.-Cl. Depezay, Tetrahedron Letters, 4795 (1969).
98. A. V. Gusarov, Candidate's Thesis, Irkutsk State University, Irkutsk, 1969.
99. H. Normant, Compt. rend., **239**, 1811 (1954).
100. H. Normant and G. Martin, Bull. Soc. chim. France, 429 (1957).
101. I. A. Shikhiev, E. M. Isaev, and I. A. Aslanov, Zhur. Org. Khim., **4**, 552 (1968).
102. R. Quelet and P. Pineau, Compt. rend., **222**, 1237 (1946).
103. I. N. Nazarov, I. V. Torgov, and G. P. Verkholetova, Dokl. Akad. Nauk SSSR, **112**, 1067 (1957).
104. H. Normant, "Advances in Organic Chemistry" (Translated into Russian), Izd. Mir., Moscow, 1964, Vol. 2, pp. 22, 25 [Translated from "Advances in Organic Chemistry" (Edited by R. A. Raphael, E. C. Taylor, and H. Wynberg), Interscience, New York, 1960, Vol. 2, p. 1 (Ed. of Translation)].
105. H. Normant, Compt. rend., **240**, 1435 (1955).
106. Houben-Weyl, see Ref. 47, 1954, Vol. II, 7/1, p. 103.
107. V. I. Lavrov, Candidate's Thesis, Irkutsk State University, Irkutsk, 1967.
108. M. F. Shostakovskii, A. S. Atavin, V. I. Lavrov, and B. A. Trofimov, Dokl. Akad. Nauk SSSR, **171**, 887 (1965).

109. M. F. Shostakovskii, L. M. Kaliberdo, and N. V. Komarov, Izv. Akad. Nauk SSSR, Otd. Khim., Nauk, 703 (1961).
110. M. F. Shostakovskii, N. V. Komarov, V. B. Pukhnarevich, and A. M. Sklyanova, Izv. Akad. Nauk SSSR, Otd. Khim., Nauk, 1019 (1962).
111. N. I. Sheverdina and K. A. Kocheshkov, Zhur. Obshch. Khim., 8, 1825 (1938).
112. N. I. Sheverdina and K. A. Kocheshkov, Izv. Akad. Nauk SSSR, Otd. Khim. Nauk., 75 (1941).
113. G. M. Robinson and R. Robinson, J. Chem. Soc., 532 (1923).
114. M. Senkus, J. Amer. Chem. Soc., 67, 1515 (1945).
115. C. Ficini and H. Normant, Bull. Soc. chim. France, 1454 (1957).
116. Sh. Mamedov and O. Osipov, Izv. Akad. Nauk Azerb. SSR, No. 4, 67 (1948).
117. Sh. Mamedov and A. Niazov, Izv. Akad. Nauk Azerb. SSR, No. 9, 30 (1948).
118. Sh. Mamedov and A. I. Abdullaev, Symposium, "Trudy Instituta Khimii AN AzSSR" (Transactions of the Institute of Chemistry of the Academy of Sciences of Azerbaijan SSR), Baku, 1956, No. 15, p. 99.
119. M. F. Shostakovskii, M. R. Kulibekov, A. K. Gorban', and S. M. Shostakovskii, Zhur. Obshch. Khim., 34, 760 (1964).
120. M. R. Kulibekov and Sh. Mamedov, Zhur. Obshch. Khim., 26, 3020 (1956).
121. M. F. Shostakovskii and M. R. Kulibekov, Zhur. Obshch. Khim., 28, 951 (1958).
122. C. B. Blomberg and A. D. Vrengdenhill, Rec. Trav. chim., 81, 238 (1961); Chem. Abs., 57, 5784 (1962).
123. M. F. Shostakovskii, M. R. Kulibekov, A. K. Gorban', and S. M. Shostakovskii, Zhur. Obshch. Khim., 34, 2618 (1964).
124. I. V. Grinberg, Soobshch. o Nauchno-Issledov. Rabote Kievskogo Industrial'nogo Instituta, Kiev, 2, 30 (1930); Ref. Zhur. Khim., IV, No. 2, 41 (1941).
125. M. R. Kulibekov, Dokl. Akad. Nauk Azerb. SSR, 5, 20 (1964).
126. I. A. Shikhiev, M. R. Kulibekov, I. T. Mekhmandarova, and I. A. Aslanov, Azerb. Khim. Zhur., No. 2, 73 (1964).
127. M. R. Kulibekov, Azerb. Khim. Zhur., No. 4, 91 (1963).
128. R. Quelet, C. Broguet, and J. d'Angelo, Compt. rend., (C) 264, 1316 (1967).
129. M. R. Kulibekov, Uch. Zap. Azerb. Gos. Univ., 1, 67 (1967).
130. R. Quelet, P. Bercot, and J. d'Angelo, Bull. Soc. chim. France, 3258 (1966).
131. R. Quelet and J. d'Angelo, Bull. Soc. chim. France, 1503 (1967).
132. J. Grard, Ann. chim., 13, 336 (1930).
133. J. Grard, Compt. rend., 189, 541 (1929).
134. H. Scheibler and A. Schmidt, Ber., 67, 1514 (1934).
135. H. Scheibler and M. Depher, Ber., 68, 2154 (1935).
136. F. Adickes, W. Simson, and P. P. Peckelhoff, Ber., 67, 1436 (1934).
137. Cl. Feugeas, Bull. Soc. chim. France, 2568 (1963).
138. P. Freundler and P. Lebru, Compt. rend., 140, 795 (1905).
139. A. I. Zakharkin, Dokl. Akad. Nauk SSSR, 105, 985 (1955).
140. M. R. Kulibekov, Azerb. Khim. Zhur., No. 1, 63 (1964).
141. M. F. Shostakovskii and A. N. Bogdanova, "Trudy Konferentsii po Voprosam Stroeniya i Reaktsionnoi Sposobnosti Atsetalei" (Proceedings of the Conference on the Problems of the Structure and Reactivity of Acetals), Izd. Akad. Nauk Kirghiz. SSR, Frunze, 1963, p. 21.
142. M. F. Shostakovskii, M. R. Kulibekov, and A. K. Gorban', Zhur. Obshch. Khim., 28, 2839 (1958).
143. M. R. Kulibekov and A. K. Gorban', Izv. Akad. Nauk SSSR, Otd. Khim. Nauk, 763 (1963).
144. B. M. Mikhailov and L. S. Povarov, Izv. Akad. Nauk SSSR, Otd. Khim. Nauk, 839 (1959).
145. B. M. Mikhailov and L. S. Povarov, Izv. Akad. Nauk SSSR, Otd. Khim. Nauk, 1948 (1959).
146. R. Dulou and D. Savostianoff, Compt. rend., (C) 262, 564 (1966).
147. M. F. Shostakovskii and M. R. Kulibekov, Zhur. Obshch. Khim., 28, 2339 (1958).
148. M. F. Shostakovskii, M. R. Kulibekov, and A. K. Gorban', USSR P. 159 836; Byul. Izobret., No. 8 (1964).
149. M. F. Shostakovskii, M. R. Kulibekov, and A. K. Gorban', Zhur. Obshch. Khim., 34, 2837 (1964).
150. M. F. Shostakovskii, M. R. Kulibekov, and I. A. Shikhiev, Zhur. Obshch. Khim., 23, 1539 (1958).
151. I. N. Nazarov, Izv. Akad. Nauk SSSR, Otd. Khim. Nauk., 208 (1940).
152. C. Feugeas, Bull. Soc. chim. France, 2579 (1963).
153. B. G. Kovalev and A. A. Shamshurin, see Ref. 12, p. 31.
154. N. K. Kochetkov, E. E. Nifantf'ev, and A. N. Nesmeyanov, Izv. Akad. Nauk SSSR, Otd. Khim. Nauk., 949 (1957).
155. N. K. Kochetkov, E. E. Nifantf'ev, and V. N. Shibaev, Khim. Nauka i Prom., 4, 808 (1959).
156. S. Tanimoto, S. Shiniojo, and R. Oda, J. Synth. Org. Chem. Japan, 26, 435 (1968).
157. H. Normant, Bull. Soc. chim. France, 1434 (1963).
158. E. Späth, Monatsh., 35, 327 (1914).
159. E. Späth, Ber., 60, 702 (1927).
160. K. Kafuka, J. Pharm. Soc. Japan, No. 521, 1 (1925); Chem. Zentr., I, 69 (1926).
161. K. Kafuka and R. Kato, J. Pharm. Soc. Japan, No. 533, 56 (1926); Chem. Zentr., II, 2721 (1926).
162. E. Fourneau and J. Ribas, Bull. Soc. chim. France, 1584 (1926).
163. French P. 697 786 (1931); Chem. Abs., 1, 2394 (1931).
164. R. Lentner, Monatsh., 60, 317 (1932).
165. P. Solomaa and A. Kankaanperä, Acta Chem. Scand., 15, 871 (1961).
166. A. D. Atavin, B. A. Trofimov, S. E. Orlova, and V. V. Keiko, Izv. Sibir. Otd. Akad. Nauk SSSR, 11, 111 (1965).
167. M. F. Shostakovskii, A. S. Atavin, B. A. Trofimov, S. E. Orlova, and V. V. Keiko, Zhur. Obshch. Khim., 34, 2089 (1964).
168. A. S. Atavin, B. A. Trofimov, G. I. Kagan, S. E. Orlova, and V. V. Keiko, Khim. Geterotsikl. Soed., 462 (1966).
169. A. S. Atavin, M. F. Shostakovskii, B. A. Trofimov, and S. E. Orlova, USSR P. 172 303; Byul. Izobret., No. 13 (1965).
170. E. Arundale and L. A. Mikeska, Uspekhi Khim., 23, 223 (1954) [probably translated from Chem. Rev., 51, 505 (1952) (Ed. of Translation)].
171. R. I. Dubova, Candidate's Thesis, Irkutsk State University, Irkutsk, 1968.

172. G. Mousset, These Doc. Sci., Universite de Clermont-Ferrand, 1970.
173. P. Martinet and G. Mousset, Bull. Soc. chim. France, 4093 (1971).
174. C. Feugeas, Bull. Soc. chim. France, 2568 (1963).
175. W. Schlenk and W. Schlenk, Jnr., Ber., **62**, 920 (1929).
176. W. Schlenk, Ber., **64**, 734 (1931).
177. M. Sehkus, J. Amer. Chem. Soc., **67**, 1515 (1945).
178. L. H. Goodson and H. Christopher, J. Amer. Chem. Soc., **72**, 358 (1950).
179. Houben-Weyl, see Ref. 47, Vol. II, "Amine", XI/I, p. 816.
180. W. J. Burke and C. Weatherbee, J. Amer. Chem. Soc., **72**, 4691 (1950).
181. W. J. Burke, M. J. Kolbezen, and C. W. Stephens, J. Amer. Chem. Soc., **74**, 3601 (1952).
182. M. R. Kulibekov, Uch. Zap. Azerb. Gos. Univ., **2**, 15 (1964).
183. M. R. Kulibekov, Azerb. Khim. Zhur., No. 5, 91 (1962).

Irkutsk Institute of Organic Chemistry,
Siberian Division of the USSR
Academy of Sciences