

Mechanisms of Ionic Reactions in the Gas Phase. Formation, Rearrangement, and Fragmentation of Oxygen-, Sulfur- and Nitrogen-Stabilized Carbocations. High-Order Hydride Shifts

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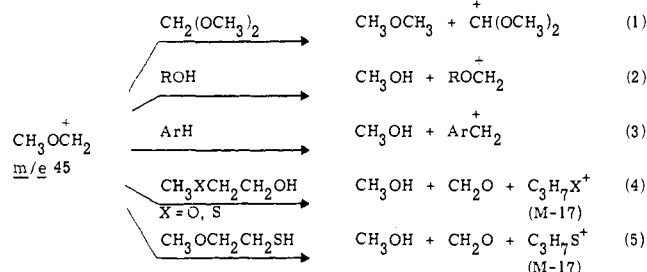
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Abstract: An ion cyclotron resonance study of the low-pressure gas-phase reactions of methoxymethyl cations $\text{CH}_3\text{OCH}_2^+$ with alcohols, thiols, and amines is described. Condensation with loss of methanol was observed for most of the neutral reactants used. However, alcohols reacted rapidly only when substituted with alkoxy, alkylthio, or amino groups. Likewise, product ions, ROCH_2^+ , RSC_2^+ , and R_2NCH_2^+ dissociated by elimination of $\text{CH}_2=\text{O}$ (or $\text{CH}_2=\text{NR}$) provided that the R group carried an alkoxy, alkylthio, or alkylamino substituent. The particular mode of dissociation depended on the substituent. In the specific cases of $\text{CH}_3\text{OCH}_2\text{CH}_2\text{SCH}_2^+$ and $\text{CH}_3\text{OCH}_2\text{CH}_2\text{NHCH}_2^+$, dissociation of $\text{CH}_2=\text{O}$ was preceded by a 1,6-hydride transfer. Still higher order hydride transfers were detected in the ion chemistry of 3-methoxypropanethiol and 3-methoxybutanethiol. Experiments designed to detect related rearrangements and fragmentations in the corresponding solvated ions generated under solvolytic conditions gave no evidence of hydride transfer or fragmentation. The results of this study underscore the difference in behavior of gaseous and solvated ions. We suggest that their structures are not strictly comparable and that the reactions of the gaseous ions can be attributed to the effects of internal solvation and product stability.

Alkoxyethyl cations have long been recognized as intermediates in solvolysis reactions of compounds of the type ROCH_2X such as acetals,¹ alkoxyethyl esters,² and chloromethyl ethers.³ They have been observed directly by NMR methods starting with halomethyl ethers in $\text{SbF}_5\text{-SO}_2$ at -60°C ,⁴ and both their spectral and chemical properties support a hybrid structure for these ions comprised of carbenium and oxonium forms, $\text{RO}-\text{CH}_2^+ \leftrightarrow \text{RO}=\text{CH}_2^+$.

In the gas phase, structurally similar ions are readily formed by electron impact fragmentation of molecules having the structural feature $\text{ROCH}_2\text{R}'$.⁵ Alkoxyethyl ions have also been recognized as products of gas-phase ion-molecule reactions observed by the methods of chemical ionization mass spectrometry⁶ and low-pressure ion cyclotron resonance.⁷⁻¹¹ The work described in the present paper was occasioned by our interest in the chemistry of both gaseous and solvated alkoxyethyl cations, our long range objectives being the determination of how solvation, or the lack of solvation, influences the behavior of organic ions.

Reports on the gas-phase behavior of methoxymethyl cations $\text{CH}_3\text{OCH}_2^+$ have appeared in connection with ion cyclotron resonance (ICR) studies of the ion chemistry of ethers,^{7,8} acetals,^{8b,9} alcohols,¹⁰ and arenes.¹¹ The dominant reaction of the gaseous ion is hydride abstraction with ethers and acetals (reaction 1), and substitution by loss of methanol with alcohols and aromatic hydrocarbons (reactions 2 and 3).



In the course of an investigation of the ion-molecule chemistry of 2-methoxyethanol by ICR techniques, we observed that methoxymethyl cations react with the parent alcohol to give product ions of composition $\text{C}_3\text{H}_7\text{O}^+$ corresponding to the loss of 17 mass units (OH) from the parent molecule (reaction 4). This reaction, which was also observed

with 2-methylthioethanol ($\text{X} = \text{S}$), did not seem remarkable in the case of alcohols, but we were surprised to find that the isomeric 2-methoxyethanethiol also reacted with $\text{CH}_3\text{OCH}_2^+$ to give an (M - 17) ion as a major product (reaction 5). Because we could not readily explain how the methoxymethyl cation could strip the equivalent of ^-OH from the thiol, we investigated the reaction in more detail. The investigation was not limited to thiols, and we now report on the scope and mechanisms of the reactions of methoxymethyl cations with simple and substituted alcohols, thiols, and amines. Evidence will be presented to show that gaseous carbocations can rearrange by long-range hydride shifts that apparently have no precedent in solution chemistry.

Results and Discussion

Instrumentation. The gas-phase reactions were achieved using pulsed ion cyclotron resonance spectroscopy at sample pressures in the region of 10^{-6} - 10^{-5} Torr in a trapped-ion analyzer cell.¹² The precursor ions for each product ion were identified by double resonance experiments. In cases of ambiguity, as when ions of different structure but having the same mass-to-charge ratio were involved, isotopically labeled substrates were used. The spectrometer was equipped with a dual inlet system so that mixtures of compounds at known pressures could be introduced into the analyzer cell. Reactant methoxymethyl cations were the primary fragment ions of neutral reactants of structure $\text{CH}_3\text{O}(\text{CH}_2)_n\text{XH}$ with $\text{X} = \text{S}$ or O . In other cases, methyl ethers, $\text{CH}_3\text{OCH}_2\text{CH}_3$ or $\text{CH}_3\text{O}(\text{CH}_2)_n\text{OCH}_3$, were introduced into the analyzer cell specifically as a source of $\text{CH}_3\text{OCH}_2^+$.

Methoxymethyl Cations with Alcohols. Condensation of $\text{CH}_3\text{OCH}_2^+$ (m/e 45) with alcohols, as in reaction 2, can be described as a substitution of methoxy for alkoxy and could proceed by an addition-elimination pathway (eq 6) or by methyl transfer (eq 7). Both pathways have precedent. Route 6 is the commonly observed A-1 mechanism for solution-phase hydrolysis of acetals, ketals and, ortho esters,¹ whereas route 7 has been observed in the related gas-phase reactions of hydroxyalkyl cations R_2^+COH with alcohols.¹³ Also, methoxymethyl cations are known to transfer a methyl cation to neutral ethers;⁷ therefore it is reasonable to suppose that a similar methyl transfer could occur to an alcohol.

Table I. Condensation and Elimination Reactions of Alcohols with Methoxymethyl Cations and Related Ions

$\text{CH}_3\text{OCH}_2^+ + \text{ROH} \xrightarrow{-\text{CH}_3\text{OH}} \text{ROCH}_2^+ \xrightarrow{-\text{CH}_2\text{O}} \text{R}^+$			
Reactant ion (<i>m/e</i>) ^a	Neutral alcohol	Condensation ion (<i>m/e</i>), M + 13	Elimination ion (<i>m/e</i>), M - 17
CH ₃ O=CH ₂ ⁺ (45)	CH ₃ CH ₂ OH CH ₃ CH ₂ CH ₂ OH CH ₃ CH ₂ CH ₂ CH ₂ OH (CH ₃) ₂ CHOH CH ₃ CH ₂ CH(OH)CH ₃ (CH ₃) ₃ COH CH ₃ OCH ₂ CH ₂ OH CD ₃ OCH ₂ CH ₂ OH CH ₃ OCH ₂ CD ₂ OH	<i>b</i>	
CD ₃ OCH ₂ ⁺ (48) ^c	CH ₃ OCH ₂ CH ₂ OH	CH ₃ OCH ₂ CH ₂ O=CH ₂ ⁺ (89)	CH ₃ OC ₂ H ₄ ⁺ (59)
CH ₃ OCD ₂ ⁺ (47) ^d	CH ₃ OCH ₂ CH ₂ OH	CD ₃ OCH ₂ CH ₂ O=CH ₂ ⁺ (92)	CD ₃ OC ₂ H ₄ ⁺ (62)
CH ₃ ¹⁸ OCH ₂ ⁺ (47) ^e	CH ₃ OCH ₂ CH ₂ OH	CH ₃ OCH ₂ CD ₂ O=CH ₂ ⁺ (91)	CH ₃ OC ₂ H ₂ D ₂ ⁺ (61)
	CH ₃ OCH ₂ CH ₂ OH	CH ₃ OCH ₂ CH ₂ O=CH ₂ ⁺ (89)	CH ₃ OC ₂ H ₄ ⁺ (59)
	CH ₃ SCH ₂ CH ₂ OH	CH ₃ OCH ₂ CH ₂ O=CD ₂ ⁺ (91)	CH ₃ OC ₂ H ₄ ⁺ (59)
	CD ₃ SCH ₂ CH ₂ OH	CH ₃ OCH ₂ CH ₂ O=CH ₂ ⁺ (89)	CH ₃ OC ₂ H ₄ ⁺ (59)
	H ₂ NCH ₂ CH ₂ OH	CH ₃ SCH ₂ CH ₂ O=CH ₂ ⁺ (105)	CH ₃ SC ₂ H ₄ ⁺ (75)
	CH ₃ NHCH ₂ CH ₂ OH	CD ₃ SCH ₂ CH ₂ O=CH ₂ ⁺ (108)	CD ₃ SC ₂ H ₄ ⁺ (78)
	ClCH ₂ CH ₂ OH	H ₂ NCH ₂ CH ₂ O=CH ₂ ⁺ (74)	
	BrCH ₂ CH ₂ OH	CH ₃ NHCH ₂ CH ₂ O=CH ₂ ⁺ (88)	
	CH ₃ CH ₂ OCH ₂ CH ₂ OH	CH ₃ CH ₂ OCH ₂ CH ₂ O=CH ₂ ⁺ (103)	CH ₃ CH ₂ OC ₂ H ₄ ⁺ (73)
	CH ₃ CH ₂ SCH ₂ CH ₂ OH	CH ₃ CH ₂ SCH ₂ CH ₂ O=CH ₂ ⁺ (119)	CH ₃ CH ₂ SC ₂ H ₄ ⁺ (89)
	CH ₃ OCH ₂ CH(CH ₃)OH	CH ₃ OCH ₂ CH(CH ₃)O=CH ₂ ⁺ (103)	CH ₃ OC ₃ H ₆ ⁺ (73)
	CH ₃ OCH ₂ C(CH ₃) ₂ OH		CH ₃ OC ₄ H ₈ ⁺ (87)
	CH ₃ OCH(CH ₃)CH ₂ OH	CH ₃ OCH(CH ₃)CH ₂ O=CH ₂ ⁺ (103)	CH ₃ OC ₃ H ₆ ⁺ (73)
	CH ₃ OCH ₂ CH ₂ CH ₂ OH	CH ₃ OCH ₂ CH ₂ CH ₂ O=CH ₂ ⁺ (103)	CH ₃ OC ₃ H ₆ ⁺ (73)
	CH ₃ SCH ₂ CH ₂ CH ₂ OH	CH ₃ SCH ₂ CH ₂ CH ₂ O=CH ₂ ⁺ (119)	CH ₃ SC ₃ H ₆ ⁺ (89)
	CH ₃ OCH ₂ CH ₂ CH ₂ CH ₂ OH	CH ₃ OCH ₂ CH ₂ CH ₂ CH ₂ O=CH ₂ ⁺ (117)	CH ₃ OC ₄ H ₈ ⁺ (87)
	CH ₃ OCH ₂ CH ₂ CH ₂ CH ₂ CH ₂ OH		
CH ₃ O=CHCH ₃ (59)	CH ₃ OCH ₂ CH ₂ OH	CH ₃ OCH ₂ CH ₂ O=CHCH ₃ ⁺ (103)	
CH ₃ CH ₂ O=CH ₂ ⁺ (59)	CH ₃ OCH ₂ CH ₂ OH	CH ₃ OCH ₂ CH ₂ O=CH ₂ ⁺ (89)	CH ₃ OC ₂ H ₄ ⁺ (59)
CH ₃ S ⁺ =CH ₂ ⁺ (61)	CH ₃ OCH ₂ CH ₂ OH	CH ₃ OCH ₂ CH ₂ O=CH ₂ ⁺ (89)	
CH ₃ CH ₂ S ⁺ =CH ₂ ⁺ (75)	CH ₃ OCH ₂ CH ₂ OH	CH ₃ OCH ₂ CH ₂ O=CH ₂ ⁺ (89)	

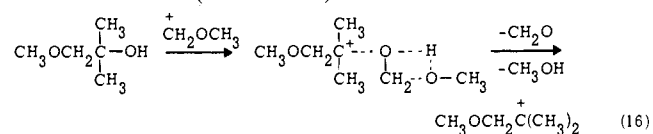
^a The reactant ion is the precursor for both condensation and elimination product ions. It is formed from the neutral alcohol or from added methoxyethane or 1,2-dimethoxyethane on electron impact. ^b No observable reaction. ^c From CD₃OCH₂CH₂OCD₃. ^d From CH₃OCD₂-CH₂OCH₃ or CH₃CD₂OCH₃. ^e From CH₃¹⁸OCH₂CH₃.

that excitation of (M + 13) can lead to dissociation by loss of CH₂O. If the reactant ion is labeled as CD₃OCH₂⁺, CH₃OCD₂⁺, or CH₃¹⁸OCH₂⁺, the label is *not* found in the product (M - 17) ion. If the neutral alcohol is labeled either as CD₃OCH₂CH₂OH or CH₃OCH₂CD₂OH, the label is *retained* in the product (M - 17) ion. These results are summarized in Table I. Entirely comparable results were obtained from the reaction of CH₃SCH₂CH₂OH with CH₃OCH₂⁺.

The structures of the product ions in Scheme 1 are presumed to be as shown. In particular, we assign a cyclic oxonium or sulfonium structure to the (M - 17) ions to account for the dependence of the reaction sequence on the presence of a neighboring oxygen or sulfur substituent. Further discussion of ion structure is given at the conclusion of the paper.

The reaction sequence of Scheme 1 was quite general for methoxy-substituted alcohols and was prominent with increasing chain length in CH₃O(CH₂)_nOH from n = 2-4. However, when n = 5, reaction to give either (M + 13) or (M - 17) ions was not observed. Secondary and tertiary methoxy-substituted alcohols also reacted with CH₃OCH₂⁺ to give (M - 17) ions, although the precursor (M + 13) ions were not always visible. For example, in the ion-molecule chemistry of CH₃OCH₂C(CH₃)₂OH, the dominant product ion corresponds to (M - 17) and has *m/e* 87. However, the main route to this ion is by way of dissociation of the protonated parent formed from the acidic fragment ion (CH₃)₂C=OH⁺ (*m/e* 59). On providing a source of CH₃OCH₂⁺ by the addition of 1,2-dimethoxyethane to the cell, a low-intensity (M + 13) ion of *m/e* 117 was detected, but the (M - 17) ion (*m/e* 87) showed a definite double resonance response on irradiation of

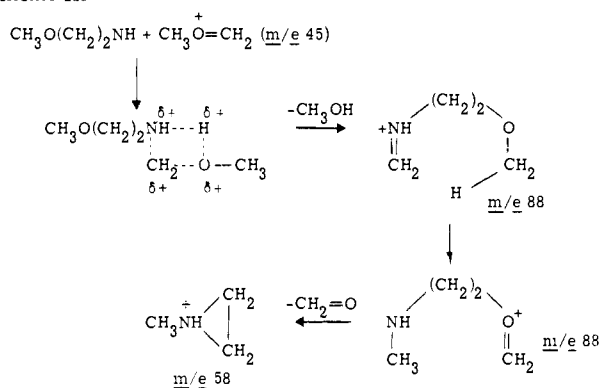
CH₃OCH₂⁺. We conclude that the tertiary alcohol may still react by the sequence of Scheme 1 but that the dissociation to (M - 17) occurs more rapidly than intermediate (M + 13) ions can be stabilized (reaction 16).



Several of the alcohols studied condensed with CH₃OCH₂⁺ or CH₃SCH₂⁺ to give (M + 13) ions that did *not* dissociate by loss of formaldehyde. 2-Aminoethanol and 2-(*N*-methylamino)ethanol are examples (see Table I). When the reactant ion was either CH₃OCHCH₃⁺ or RSCH₂⁺, 2-methoxyethanol underwent initial condensation but the product ions did not dissociate further. With few exceptions, dissociation of ions of structure RO⁺=CR'₂ appears facile in the gas phase only when the leaving group is formaldehyde (R' = H), when R⁺ is a reasonably stable ion, and when the condensation that forms RO⁺=CH₂ is sufficiently exothermic to support dissociation to R⁺ and CH₂=O. The exothermicity of condensation with RSCH₂⁺ is evidently insufficient to cause dissociation.

Methoxymethyl Cations with Thiols. There are some interesting differences between thiols and alcohols in their reactions with CH₃OCH₂⁺. Condensation of simple thiols ethanethiol and 2-propanethiol with methoxymethyl cations occurred readily whereas no comparable reaction was observed for the corresponding alcohols (compare Tables I and II). Also, product ions of structure RSCH₂⁺ did *not* dissociate by loss

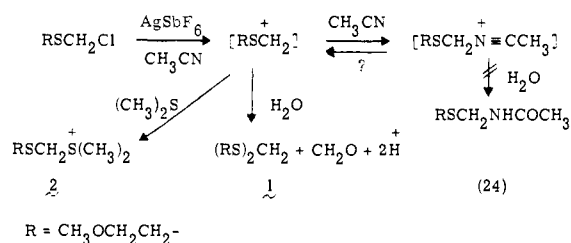
Scheme III



place but the $(M + 13)$ ion was stable and did not eliminate either $\text{CH}_2=\text{S}$ or $\text{CH}_2=\text{NH}$. In fact, elimination of $\text{CH}_2=\text{S}$ was not observed under any circumstances, and the overall results place the relative gas-phase mobilities of formaldehyde, thioformaldehyde, and methylenimine as leaving groups in the order $\text{CH}_2=\text{O} > \text{CH}_2=\text{NH} > \text{CH}_2=\text{S}$.

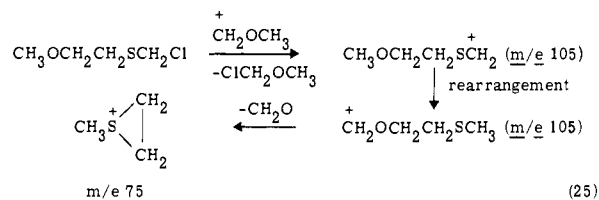
Formation and Behavior of $\text{CH}_3\text{OCH}_2\text{CH}_2\text{SCH}_2^+$ in Solution. The 1,6-, 1,7- and 1,8-hydride transfers implicated in the rearrangement and dissociation of gaseous ions of structure $\text{CH}_3\text{O}(\text{CH}_2)_n\text{SCH}_2^+$ ($n = 2-4$) are of uncommonly high order. In solution, hydride transfers of higher order than 1,5 are seldom observed in acyclic ions although high order transannular shifts are well known.¹⁴ However, Saunders and Stofko¹⁵ made the interesting observation that 1,5-hydride shifts are more facile than 1,3 or 1,4 shifts in acyclic carbocations in $\text{FSO}_3\text{H}-\text{SO}_2$, and Olah and Sommer have reported hydride shifts and oxonium ion formation in diprotonated alkoxy alcohols.¹⁶ We therefore considered the possibility that high-order hydride shifts in $\text{CH}_3\text{O}(\text{CH}_2)_n\text{SCH}_2^+$ might be comparably facile in solution as in the gas phase. To test this idea, several solution-phase reactions designed to generate the ions of interest as reactive intermediates were investigated and carefully analyzed for products of rearrangement.

It has been established by kinetic studies that chloromethyl sulfides RSCH_2Cl react by an $\text{S}_\text{N}1$ mechanism under solvolytic conditions.³ We therefore attempted to generate $\text{CH}_3\text{OCH}_2\text{CH}_2\text{SCH}_2^+$ by reaction of the chloride $\text{CH}_3\text{OCH}_2\text{CH}_2\text{SCH}_2\text{Cl}$ with AgSbF_6 in acetonitrile. We anticipated a type of Ritter reaction which would lead to amides¹⁷—possibly of rearranged structure if a hydride shift to give the oxonium isomer occurred. In actuality, silver chloride was instantly formed but the organic product was bis(2-methoxyethylthio)methane (**1**) (reaction 24). Evidently, the intermediate cation presumably formed was trapped by a sulfur nucleophile rather than by the solvent. When methyl sulfide was added to the reaction mixture, the product was the sulfonium salt **2**. The importance of the reaction is not the nature of the products but the fact that they are of *unrearranged* structure. No 1,6-hydride transfer was indicated.

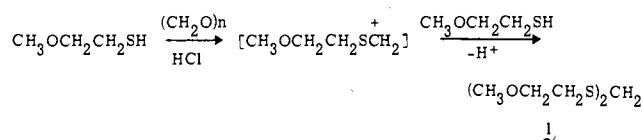


In striking contrast, the gas-phase ion chemistry of $\text{CH}_3\text{OCH}_2\text{CH}_2\text{SCH}_2\text{Cl}$ was dominated by a chloride-abstraction reaction involving the fragment ion $\text{CH}_3\text{OCH}_2^+$ (m/e 45) to give $\text{CH}_3\text{OCH}_2\text{CH}_2\text{SCH}_2^+$ (m/e 105) or its oxonium

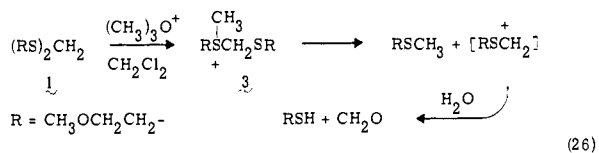
isomer that dissociated to give $\text{CH}_3\text{SC}_2\text{H}_4^+$ (m/e 75) (see reaction 25 and Figure 1d).



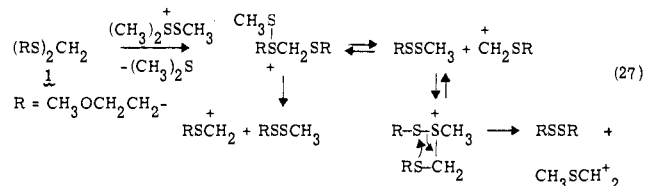
Using another approach, we reasoned that acid-catalyzed formation or hydrolysis of the thioacetal **1** might proceed by way of $\text{CH}_3\text{OCH}_2\text{CH}_2\text{SCH}_2^+$, if such reactions proceed by an A-1 mechanism commonly observed with acetals. Thioacetal **1** was prepared in 60% yield from 2-methoxyethanethiol and paraformaldehyde in dioxane and concentrated HCl. No acetal products of rearranged structure were found which means that, if the sulfonium ion were formed, it did not rearrange.



Thioacetals are difficult to hydrolyze by the acidic conditions effective for acetals,¹⁸ and they usually require metal halide catalysis¹⁹ or powerfully electrophilic alkylating agents.²⁰ Therefore, we reacted **1** with Meerwein's reagent, $(\text{CH}_3)_3\text{O}^+\text{BF}_4^-$, to labilize the S-C-S bonding. NMR analysis indicated that the product of methylation was the sulfonium salt **3**. The spectrum in methylene chloride was broad and temperature dependent indicating a rapid rate process, either by a degenerate S-methyl transfer²¹ or by a dissociative equilibrium (see eq 27), but, irrespective of the nature of this process, the salt hydrolyzed to give only normal unrearranged products. If $\text{CH}_3\text{OCH}_2\text{CH}_2\text{SCH}_2^+$ was a reaction intermediate, it did not rearrange (reaction 26).

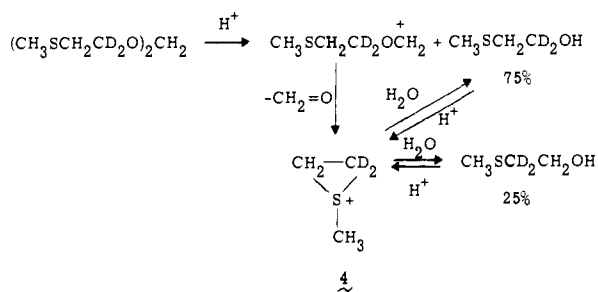


A powerful electrophile that rapidly cleaves thioacetals is methylthiodimethylsulfonium fluoroborate $(\text{CH}_3)_2\text{SSCH}_3^+\text{BF}_4^-$.^{22,23} This reagent was used to methylthiolate thioacetal **1** and, based on previous work with this reagent,²³ we anticipated a facile cleavage of the S-C-S bonds in **1** to give $\text{CH}_3\text{OCH}_2\text{CH}_2\text{SCH}_2^+$. However the only products isolated from this reaction besides methyl sulfide were disulfides RSSR and RSSCH_3 , where $\text{R} = 2$ -methoxyethyl (reaction 27). There was no evidence of rearrangement by way of hydride transfer although the reaction does involve some interesting 1,2 rearrangements, probably by way of $\text{CH}_3\text{OCH}_2\text{CH}_2\text{SCH}_2^+$.



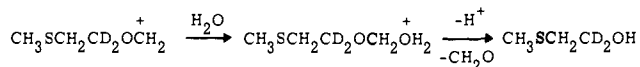
Elimination of Formaldehyde from ROCH_2^+ in Solution. The present ICR results show that *gaseous* ROCH_2^+ ions readily lose formaldehyde provided that the R group carries a neighboring alkoxy or alkylthio substituent. The substituent may therefore participate in the elimination and we infer from this that the product ions are probably cyclic. There is considerable

Scheme IV



evidence for neighboring-group participation in solvolysis reactions²⁴ and to some extent in gas-phase reactions,¹⁰ but, to our knowledge, internal displacement of formaldehyde from alkoxyethyl cations by a neighboring group is not a common circumstance in solution. To explore the possibility of dissociation of solvated $\text{CH}_3\text{SCH}_2\text{CH}_2\text{OCH}_2^+$ ions, we investigated the acid-catalyzed hydrolysis of bis(2-methylthioethoxy-1,1- d_2)methane ($(\text{CH}_3\text{SCH}_2\text{CD}_2\text{O})_2\text{CH}_2$) in sulfuric acid solution. Assuming that acid hydrolysis proceeds by an A-1 mechanism, ions of structure $\text{CH}_3\text{SCH}_2\text{CD}_2\text{OCH}_2^+$ will be formed as intermediates and, if they dissociate by loss of CH_2O , would almost certainly result in the formation of the cyclic sulfonium ion **4**. The symmetry of **4** would then lead to scrambling of the CD_2 label in the product 2-methylthioethanol. Exclusive reaction by this route (Scheme IV) would lead to a product distribution of 75% $\text{CH}_3\text{SCH}_2\text{CD}_2\text{OH}$ and 25% $\text{CH}_3\text{SCD}_2\text{CH}_2\text{OH}$. The extent to which **4** is formed by the reversible dissociation of the alcohol product can only increase the amount of label scrambling. The figure of 25% $\text{CH}_3\text{SCD}_2\text{CH}_2\text{OH}$ is therefore a lower limit if Scheme IV is applicable.

Hydrolysis was achieved by heating the labeled acetal in a 1:9 mixture (by volume) of concentrated sulfuric acid and water for 18 h. The products were isolated and analyzed by NMR to determine the label distribution. At 60 °C, only 14% of the product alcohol contained deuterium at C-2. At 80 °C, 36% had deuterium at C-2. Because the degree of label scrambling at 60 °C was *less* than the lower limit of 25% predicted by Scheme IV, we have to conclude that Scheme IV cannot be the exclusive pathway in the acetal hydrolysis. This result makes it doubtful that $\text{CH}_3\text{SCH}_2\text{CH}_2\text{OCH}_2^+$ fragments to give **4** under these conditions. At 80 °C, the amount of scrambling was *greater* than predicted by Scheme IV, which means that the alcohol product rearranged significantly by way of **4** under these conditions. This was confirmed independently by subjecting $\text{CH}_3\text{SCH}_2\text{CD}_2\text{OH}$ to the hydrolysis conditions. In summary, although we cannot rule out Scheme IV entirely, it cannot be the sole route to 2-methylthioethanol. A plausible alternative is addition-elimination without the participation of the neighboring group.



Summary and Conclusions

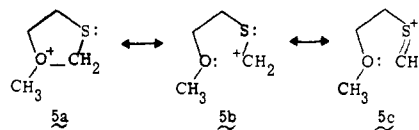
The observation that alcohols ROH react with gaseous methoxymethyl cations only when substituted with alkoxy, alkylthio, and amino substituents implies that the substituent influences the energetics of reaction. This is so for the initial condensation to give ROCH_2^+ ($M + 13$) ions as well as for the subsequent dissociation of formaldehyde to give R^+ ($M - 17$) ions. The evidence is negative that a similar dissociation of alkoxyethyl cations occurs under solvolytic conditions.

A second major point of difference between gaseous and solvated ions is that high-order hydride transfers for ions of structure $\text{CH}_3\text{O}(\text{CH}_2)_n\text{SCH}_2^+$ ($n = 2-4$) and $\text{CH}_3\text{O}-$

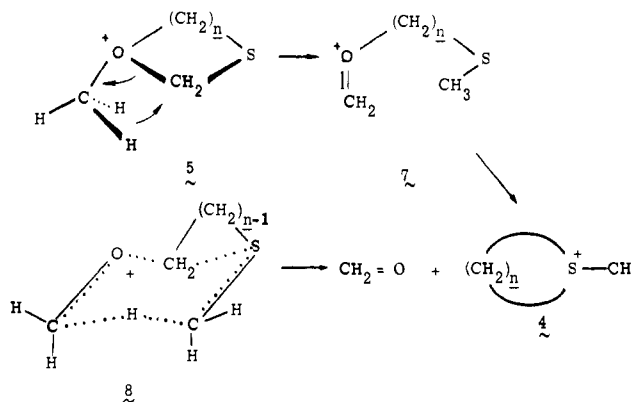
$(\text{CH}_2)_n\text{NHCH}_2^+$ are observed in the gas phase only. We are led to the conclusion that the gaseous ions are not strictly comparable in structure to the solvated ions, and that it is an oversimplification to represent them as ROCH_2^+ and the like.²⁵ In solution, ionic intermediates described as alkoxy-methyl or alkylthiomethyl ions are not free ions but are closely associated with solvent molecules, the leaving group, or counterions. The conformations, the charge distribution, and hence the reactions of the solvated ions must therefore be influenced by the external medium. The corresponding gaseous ions are not stabilized by associated solvent molecules and cannot be influenced by counterion effects. Whatever degree of stabilization by charge delocalization exists in the free gaseous ion can only be achieved intramolecularly. Hence, it seems likely that, in the absence of external solvent, alkoxy-methyl and related ions acquire stability through internal solvation—specifically by electron donation from neighboring groups.

Unusual rearrangements and fragmentations involving seemingly remote functions are not uncommon in mass spectrometry, especially with bifunctional molecules.^{9b,26} Many mass spectral reactions are remarkably regiospecific and appear to be the result of interaction (internal solvation²⁷) between the site of charge and a distant functional group, and it has been pointed out that there is a close analogy between mass spectral rearrangements, fragmentations, and ion-molecule reactions.²⁵ As one example emerging from the present study, the most abundant *fragment* ion in the ICR spectrum of $\text{CH}_3\text{CD}_2\text{OCH}_2\text{CH}_2\text{OH}$ was found to have m/e 73 corresponding to the loss of HDO from the molecular ion m/e 92. There is no m/e 74 ion, meaning that fragmentation is a highly selective 1,4 elimination by way of a six-membered cyclic transition state.²⁸

In the present work, we visualize certain of the bifunctional gaseous ions as having a cyclic conformation, or possibly a fully covalent structure, such that the maximum charge stabilization can be achieved. As a specific example, the gaseous ion, hitherto written as $\text{CH}_3\text{OCH}_2\text{CH}_2\text{SCH}_2^+$, may be better described as a hybrid of three-valence-bond structures **5a-c**.



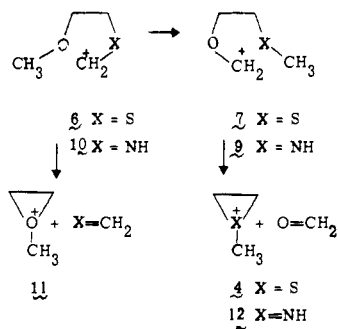
By describing **5** as a cyclic structure, it becomes easier to visualize how hydride shifts from *O*-methyl to give *S*-methyl could be facile because the cyclic structure brings the *O*- CH_3 group in a position to transfer hydride to the ring methylene. However, transfer by way of a four-center transition state as in **5** \rightarrow **7** implies retention of configuration at the migration terminus which, by orbital-symmetry considerations, is forbidden. Alternatively, a strong covalent bond between the methylene carbon and the donor atom (oxygen) may not be



formed, as implied in **5**, in which case orbital symmetry considerations may not apply. Another possibility is that hydride transfer and elimination of $\text{CH}_2=\text{O}$ are concurrent events by way of a transition state such as **8**.

An important point regarding hydride transfer from *O*-methyl to give *S*-methyl is that it appears to be contrathermodynamic. Recent evidence from gas-phase studies^{29,30} and ab initio calculations³¹ indicate that positive carbon is better stabilized by electron donation from neighboring sulfur than from neighboring oxygen. That is to say, the sulfonium ions are preferred over oxonium ions.

On this basis, rearrangement might have been expected in the direction **7** \rightarrow **6** rather than **6** \rightarrow **7**. This apparent anomaly can be understood if the rearrangement is concerted with elimination (i.e., **8** \rightarrow $\text{CH}_2=\text{O}$ + **4**) or if the reaction pathway is controlled by the stability of the final products rather than by the stability of the intermediate ions. Thus, the most exothermic pathway for dissociation is by way of **7** to give $\text{CH}_2=\text{O}$ and a sulfonium ion **4**; the energetically less favorable pathway via **6** would give $\text{CH}_2=\text{S}$ and an oxonium ion. The actual energy difference between the two reaction paths is not known accurately because the heats of formation of the product ions are uncertain. Nevertheless, there is no doubt that the combination $\text{CH}_2=\text{O}$ + **4** is more stable than $\text{CH}_2=\text{S}$ + **11**.³²



Similar arguments can be advanced in the analogous nitrogen vs. oxygen rearrangements. The observed hydride transfer in the rearrangement of the immonium ion **10** to the oxocarbenium ion **9** is contrathermodynamic, but the dissociation products of **9** are more stable ($\text{O}=\text{CH}_2$ and ammonium ion **12**) than those from **10** ($\text{H}_2\text{C}=\text{NH}$ and oxonium ion **11**).³³

In the case of the sulfur analogue $\text{CH}_3\text{SCH}_2\text{CH}_2\text{NHCH}_2^+$, no hydride transfer is indicated and the products of dissociation, $\text{CH}_2=\text{NH}$ and sulfonium ion **4**, are presumably a more stable combination than the alternative products, $\text{CH}_2=\text{S}$ and the ammonium ion **12**, which were not observed.

Although we have indicated that the product ions **4**, **11**, and **12** have a cyclic structure, this is a presumption on our part as the ICR data give no direct evidence as to ion structure. The assignment is quite reasonable for sulfonium and ammonium ions based on their mode of formation and the known stability of R_3S^+ and R_4N^+ ions. The situation with respect to the oxonium ion is less certain. It is relevant that recent studies^{10,50} on the structures of gaseous ions $\text{C}_3\text{H}_7\text{S}^+$ and $\text{C}_3\text{H}_7\text{O}^+$ support a cyclic structure for the sulfur ion and an acyclic structure for the oxygen ion.

Experimental Section

Methoxyethane-¹⁸O was obtained by the acid hydrolysis of triethyl phosphate with 43% ¹⁸O-enriched water by the procedure of Blumental and Herbert³⁸ to give ethanol-¹⁸O followed by methylation with methyl iodide and silver oxide in dimethylformamide. The methoxyethane prepared in this manner was 26% enriched in ¹⁸O. Sources of deuterium-labeled methoxymethyl cations were **1,2-(dimethoxy-*d*₆)ethane** (prepared by methylation of the monosodium salt of 1,2-ethanediol with methyl-*d*₃ iodide followed by a second

methylation step using methyl-*d*₃ iodide and silver oxide in dimethylformamide), **1,2-dimethoxyethane-1,1-*d*₂** (prepared by lithium aluminum deuteride reduction of methyl methoxyacetate or methoxyacetyl chloride³⁹ followed by $\text{CH}_3\text{I}-\text{Ag}_2\text{O}$ methylation in dimethylformamide), and **methoxyethane-1,1-*d*₂** (prepared by the reduction of methyl acetate with lithium aluminum deuteride followed by methylation of ethanol-1,1-*d*₂). Conversion of ethanol-1,1-*d*₂ to iodoethane-1,1-*d*₂ with phosphorus and iodine followed by treatment with 1,2-ethanediol and silver oxide in dimethylformamide gave **2-(ethoxy-1,1-*d*₂)ethanol**.

2-Methylthioethanol-1,1-*d*₂ was prepared in 67% yield by lithium aluminum deuteride reduction of ethyl methylthioacetate and was converted to **bis(2-methylthioethoxy-1,1-*d*₂)methane** by heating with paraformaldehyde and concentrated sulfuric acid at 40 °C for 12 h.⁴⁰ The yield of thioacetal was 46%, bp 118–123 °C (3 mm) and ¹H NMR (CCl_4 , unlabeled product) δ 2.09 (singlet 6-H of two SCH_3), 2.60 (triplet, $J = 7$ Hz, 4 H of two SCH_2), 3.66 (triplet, $J = 7$ Hz, 4 H of two OCH_2), 4.61 (singlet CH_2). The labeled thioacetal showed no ¹H resonance at δ 3.66. **Bis(2-methoxyethylthio)methane** was prepared from 2-methoxyethanethiol and paraformaldehyde on refluxing in dioxane and concentrated HCl for 1 h.⁴¹ The product was obtained in 60% yield and had bp 125–127 °C (4 mm) and ¹H NMR (CCl_4) δ 2.74 (triplet, $J = 7$ Hz, 4 H of two SCH_2), 3.30 (singlet, 6 H of two OCH_3), 3.53 (triplet, $J = 7$ Hz, 4 H of two OCH_2), 3.70 (singlet, CH_2).

2-Methoxyethanethiol,⁴² **2-methylthioethanol**,⁴³ **3-methylthioethanol**,⁴⁴ **2-(*N*-methylamino)ethanol**,⁴⁵ **2-methylthioethylamine**,⁴⁶ and **2-mercaptoethylamine**⁴⁷ were prepared by literature procedures. **2-(Methoxy-*d*₃)ethylamine** was prepared from the picrate of aziridine by refluxing the salt with methanol-*d*₃ for 2 h.⁴⁸ The product picrate salt was dissolved in aqueous hydrochloric acid and isolated as the hydrochloride salt from which the free amine was obtained in 10% yield by neutralization with sodium methoxide in methanol.⁴⁸

2-Methoxyethyl chloromethyl sulfide was prepared from 2-methoxyethanethiol, paraformaldehyde, and dry hydrogen chloride gas in dichloromethane solution at –20 °C.⁴⁹ The product was obtained in 63% yield and had bp 54–56 °C (4 mm) and ¹H NMR (CCl_4) δ 2.89 (triplet, $J = 7$ Hz, SCH_2), 3.33 (singlet, OCH_3), 3.63 (triplet, $J = 7$ Hz, OCH_2), 4.76 (singlet, CH_2Cl).

2-(Methoxy-*d*₃)ethanethiol was prepared from 1,2-ethanediol by monomethylation to **2-(methoxy-*d*₃)ethanol** with methyl-*d*₃ iodide followed by conversion to the chloride with thionyl chloride in ether and tri-*n*-butylamine then displacement with hydrogen sulfide in KOH and methanol.

Adaptation of the method used for the preparation of 2-methoxyethanethiol⁴² gave **2-ethoxyethanethiol**, **3-methoxypropanethiol**, **4-methoxybutanethiol**, and **5-methoxypentanethiol**.

1-Methoxy-2-propanol and **2-methoxy-1-propanol** were prepared from propylene oxide and methanol using an acid catalyst. Separation of the isomers was achieved by gas chromatography. **2-Methoxymethyl-2-propanol** was prepared by addition of methoxymethylmagnesium bromide to acetone.

Hydrolysis of bis(2-methylthioethoxy-1,1-*d*₂)methane was conducted in a medium consisting of 1 part by volume of concentrated sulfuric acid to 9 parts by volume of water by heating for 18 h at 60 and at 80 °C. The hydrolysis product and any unreacted starting material were recovered by ether extraction. The NMR spectrum of the residue after evaporation of the ether was recorded, and the ratio of methylthioethanol-1,1-*d*₂ by methylthioethanol-2,2-*d*₂ was determined from the relative signal areas of the methylene protons at δ 2.60 (for $\text{CH}_3\text{SCH}_2\text{CD}_2\text{OH}$) and 3.15 (for $\text{CH}_3\text{SCD}_2\text{CH}_2\text{OH}$) which appear as broad singlets. The starting material also gave a signal for the SCH_2 group at δ 2.60, and it was necessary to correct for the intensity of the signal at δ 2.60 for the amount of residual starting material in the product. The results indicated the presence of 14% of $\text{CH}_3\text{SCD}_2\text{CH}_2\text{OH}$ after hydrolysis at 60 °C, and 36% after hydrolysis at 80 °C. The label scrambling is believed to occur by rearrangement of the alcohol after acetal hydrolysis because heating methylthioethanol-1,1-*d*₂ with a 1:9 mixture of sulfuric acid and water at 80 °C for 18 h gave 40% methylthioethanol-2,2-*d*₂.

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