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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Abstract: An ion cyclotron resonance study of the low-pressure gas-phase reactions of methoxymethyl cations $CH_3OCH_2^+$ 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, $ROCH_2^+$, $RSCH_2^+$, and $R_2NCH_2^+$ dissociated by elimination of $CH_2==0$ (or $CH_2==NR$) 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 $CH_3OCH_2CH_2SCH_2^+$ and $CH_3OCH_2CH_2NHCH_2^+$, dissociation of $CH_2==0$ 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.

Alkoxymethyl cations have long been recognized as intermediates in solvolysis reactions of compounds of the type ROCH₂X such as acetals,¹ alkoxymethyl esters,² and chloromethyl ethers.³ They have been observed directly by NMR methods starting with halomethyl ethers in SbF₅-SO₂ at -60 °C,⁴ and both their spectral and chemical properties support a hybrid structure for these ions comprised of carbenium and oxonium forms, RO—CH₂⁺ \leftrightarrow RO=CH₂⁺.

In the gas phase, structurally similar ions are readily formed by electron impact fragmentation of molecules having the structural feature ROCH₂R'.⁵ Alkoxymethyl 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 alkoxymethyl 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 $CH_3OCH_2^+$ 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).

$$CH_2(OCH_3)_2 CH_3OCH_3 + CH(OCH_3)_2 (1)$$

$$CH_{3}OCH_{2} \xrightarrow{ArH} CH_{3}OH + ArCH_{2}$$
(3)

$$\begin{array}{cccc} CH_{3}XCH_{2}CH_{2}OH & CH_{3}OH + CH_{2}O + C_{3}H_{7}X^{+} & (4) \\ \hline X = 0, S & (M-17) \\ CH_{3}OCH_{2}CH_{2}SH & CH_{3}OH + CH_{2}O + C_{3}H_{7}S^{+} & (5) \\ (M-17) & (M-17) \end{array}$$

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 $C_3H_7O^+$ corresponding to the loss of 17 mass units (OH) from the parent molecule (reaction 4). This reaction, which was also observed

with 2-methylthioethanol (X = S), did not seem remarkable in the case of alcohols, but we were surprised to find that the isomeric 2-methoxyethanethiol also reacted with $CH_3OCH_2^+$ 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 CH₃O(CH₂)_nXH with X = S or O. In other cases, methyl ethers, CH₃OCH₂CH₃ or CH₃O(CH₂)_n-OCH₃, were introduced into the analyzer cell specifically as a source of CH₃OCH₂⁺.

Methoxymethyl Cations with Alcohols. Condensation of $CH_3OCH_2^+$ (*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 R₂+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.

$$\begin{array}{c} \operatorname{CH}_{3}^{18} \circ -\operatorname{CH}_{2} \longrightarrow \left[\operatorname{CH}_{3}^{18} \circ -\operatorname{CH}_{2} \atop & \downarrow & \downarrow \\ \operatorname{H} - \operatorname{OR} \end{array} \right] \longrightarrow \operatorname{CH}_{3}^{18} \circ \operatorname{OH} + \operatorname{ROCH}_{2} \qquad (6) \\ \operatorname{CH}_{3}^{-18} \circ - \operatorname{CH}_{2} \longrightarrow \left[\operatorname{CH}_{3}^{-18} \circ - \operatorname{CH}_{2} \atop & \operatorname{HO} - \operatorname{R} \right] \longrightarrow \operatorname{CH}_{3} \circ \operatorname{OH} + \operatorname{R}^{18} \circ - \operatorname{CH}_{2} \qquad (7) \\ \operatorname{HO} - \operatorname{R} \longrightarrow \left[\operatorname{CH}_{3}^{-18} \circ - \operatorname{CH}_{2} \right] \longrightarrow \operatorname{CH}_{3} \circ \operatorname{OH} + \operatorname{R}^{18} \circ - \operatorname{CH}_{2} \qquad (7)$$

Using ¹⁸O-enriched reactants we were able to determine whether the oxygen of the reactant ion was transferred as neutral methanol (route 6) or retained in the product ion (route 7). The neutral alcohol employed was 2-methoxyethanol and the reactant ions were produced by fragmentation of methoxyethane-¹⁸O. The molar ratio of alcohol to ether was 1.3:2.8, and the ether was 26% enriched in ¹⁸O. The two isotopically labeled reactant ions of interest were CH₃¹⁸OCH₂⁺ (m/e 47) and CH₃¹⁸OCHCH₃⁺ (m/e 61), which are primary fragment ions of methoxyethane. Both m/e 47 and the ordinary ¹⁶O ion m/e 45 condensed with 2-methoxyethanol to form product ions of m/e 89, while m/e 61 and the ¹⁶O ion m/e 59 gave m/e 103 (reactions 8 and 9). No product ions of m/e 91 or 105 were observed corresponding to the retention of the isotopic label. Therefore, the isotopic label of the reactant ion must have been lost as neutral methanol, consistent with the addition-elimination mechanism of route 6. (It is not possible to monitor CH₃¹⁸OH directly because the ICR experiment detects only ions-not neutrals.)

$$\begin{array}{c} \begin{array}{c} CH_{3}^{18}OCH_{2} & \underline{m}/\underline{e} & 47 \\ \hline \\ CH_{3}^{16}OCH_{2} & \underline{m}/\underline{e} & 45 \end{array} \\ \hline \\ CH_{3}^{16}OCH_{2} & \underline{m}/\underline{e} & 45 \end{array} \\ CH_{3}^{16}OCH_{2} & \underline{m}/\underline{e} & 45 \end{array}$$

$$\begin{array}{c} H_{3}^{16}OCH_{2} & \underline{m}/\underline{e} & 45 \\ \hline \\ H_{3}^{16}OCH_{2} & \underline{m}/\underline{e} & 45 \end{array} \\ \end{array}$$

$$\begin{array}{c} H_{3}^{16}OCH_{2} & \underline{m}/\underline{e} & 45 \\ \hline \\ H_{3}^{16}OCH_{2} & \underline{m}/\underline{e} & 45 \end{array} \\ \end{array}$$

$$\begin{array}{c} H_{3}^{16}OCH_{2} & \underline{m}/\underline{e} & 45 \\ \hline \\ H_{3}^{16}OCH_{2} & \underline{m}/\underline{e} & 45 \\ \hline \\ H_{3}^{16}OCH_{2} & \underline{m}/\underline{e} & 45 \\ \hline \\ H_{3}^{16}OCH_{2} & \underline{H}/\underline{e} & 45 \\ \hline \\ H$$

сн₃осн₂сн₂он

$$\begin{array}{c} \text{MW 76} & \begin{array}{c} \text{CH}_{3}^{18}\text{OCHCH}_{3} \underline{m}/\underline{e} \ 61} \\ \text{CH}_{3}^{16}\text{OCHCH}_{3} \underline{m}/\underline{e} \ 59} \\ & \begin{array}{c} \text{CH}_{3}\text{OCH}_{2}\text{CH}_{2}\text{OCHCH}_{3} + \text{CH}_{3}^{18}\text{OH} \ (9) \\ \text{CH}_{3}^{16}\text{OCHCH}_{3} \underline{m}/\underline{e} \ 59 \\ & \begin{array}{c} \text{CH}_{3}\text{OCH}_{2}\text{CH}_{2} \\ \text{CH}_{3}\text{CH}_{2} \underline{m}/\underline{e} \ 61 \\ \text{CH}_{3}\text{CH}_{2}\text{SCH}_{2} \underline{m}/\underline{e} \ 75 \\ \end{array} \end{array} \right) \\ & \begin{array}{c} \text{CH}_{3}\text{CH}_{2}\text{CH}_{2}\text{OCH}_{2}\text{CH}_{2}\text{OCH}_{2} + \text{CH}_{3}\text{SH} \ (10) \\ \text{CH}_{3}\text{CH}_{2}\text{SCH}_{2} \underline{m}/\underline{e} \ 75 \\ \end{array} \right) \\ & \begin{array}{c} \text{CH}_{3}\text{CH}_{2}\text{CH}_{2}\text{SH} \\ \end{array} \right) \\ \end{array}$$

Alkylthiomethyl cations $RSCH_2^+$ behaved like alkoxymethyl cations toward 2-methoxyethanol and gave product ions of m/e 89 (reaction 10). This result clearly means that the alcohol oxygen is retained in the product ion, as expected for an addition-elimination mechanism (route 6).

The validity of route 6 and the assignment of structure to the products of reactions 8 and 9 is strengthened further by the results of reactions with deuterium-labeled reactants. When the deuterium label was a part of the neutral alcohol, the deuterium was retained in the product ion (reactions 11-13). When the label was in the alkoxy portion of the reactant ion ROCH₂⁺ it was lost as neutral alcohol (reactions 13-14), but, when the label was part of the positive methylene group

$$CH_{3}OCH_{2}CD_{2}OH \xrightarrow{CH_{3}OCH_{2}\underline{m}/\underline{e}}_{45} CH_{3}OCH_{2}CD_{2}OCH_{2} + CH_{3}OH (11)$$

$$\underline{m}/\underline{e} 91$$

$$CD_{3}OCH_{2}CH_{2}OH \xrightarrow{CH_{3}OCH_{2}\underline{m}/\underline{e}}_{45} CD_{3}OCH_{2}CH_{2}OCH_{2} + CH_{3}OH (12)$$

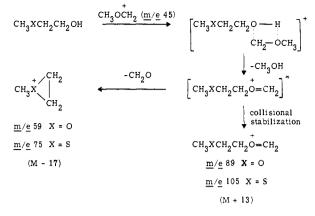
$$\underline{m}/\underline{e} 92$$
+

 $CH_{3}CD_{2}OCH_{2}CH_{2}OH \xrightarrow{CH_{3}CD_{2}OCH_{2} \underline{m/e} \ 61} CH_{3}CD_{2}OCH_{2}CH_{2}OCH_{2} + \underline{m/e} \ 105 CH_{3}CD_{2}OH$

$$CH_{3}OCH_{2}CH_{2}OH \xrightarrow{CD_{3}OCH_{2} \underline{m}/\underline{e} \ 48}_{(13)} CH_{3}OCH_{2}CH_{2}OCH_{2} + CD_{3}OH (14)$$

$$CH_{3}OCH_{2}CH_{2}OH \xrightarrow{CH_{3}OCD_{2} \underline{m}/\underline{e} 47} CH_{3}OCH_{2}CH_{2}OCD_{2} + CH_{3}OH$$
(15)
m/e 91

Scheme I



 $ROCD_2^+$, the label was retained in the product ion (reaction 15).

Effect of Alcohol Structure. Considering that 2-methoxyand 2-ethoxyethanol condensed readily with methoxymethyl, ethoxymethyl, and methylthiomethyl cations, it was somewhat unexpected to find that simple unsubstituted primary, secondary, and tertiary alcohols did not show a comparable reaction with ROCH₂⁺. These and related results are summarized in Table I. Evidently, for reaction 2 to occur at a detectable rate in the ICR experiment, a substitutent is necessary in the alkyl side chain of the alcohol. The results of Table 1 can be summarized as follows. Condensation of alcohols of structure $X(CH_2)_nOH$ with $CH_3OCH_2^+$ (m/e 45) to give $X(CH_2)_n^ OCH_2^+$ (m/e (M + 13)), and methanol was observed for n =2 and for $X = OCH_3$, SCH₃, NH₂, and NHCH₃, but not for X = H, Br, and Cl. As the chain length n was varied from n =2 to 4, condensation remained a significant reaction for X =OCH₃ and SCH₃. By n = 5 the condensation reaction was insignificant and the ion chemistry was dominated by proton-transfer reactions to give (M + 1) ions. Provided that the neutral alcohol has a β -methoxy substituent, it does not appear to matter whether the alcohol is primary or secondary as condensations of m/e 45 to give (M + 13) ions were observed for 1-methoxy-2-propanol, as well as for 2-methoxyethanol and 2-methoxy-1-propanol. A minor (M + 13) ion was detected from the reaction of the tertiary alcohol 1-methoxy-2methyl-2-propanol with CH₃OCH₂⁺, although indirect evidence suggests that it fragments as it forms (see next section).

Reactant ions besides methoxymethyl cations were employed, with similar results. They included ethoxymethyl $(CH_3CH_2OCH_2^+)$, 1-methoxyethyl $(CH_3OCHCH_3^+)$, methylthiomethyl $(CH_3SCH_2^+)$, and ethylthiomethyl $(CH_3CH_2SCH_2^+)$ cations. All condensed readily with 2methoxyethanol (Table 1).

Elimination of Formaldehyde from ROCH₂⁺. As previously mentioned, 2-methoxyethanol and 2-methylthioethanol form ions of composition $C_3H_7X^+$ (X = O, S) corresponding to the loss of -OH from the neutral—that is (M - 17). There are two routes to ions of this composition; one route involves proton transfer to the alcohol from an acidic fragment ion followed by dissociation of water from the protonated alcohol;¹⁰ the second route involves the methoxymethyl cation. This ion is not acidic and does not transfer a proton to the parent alcohol. Instead, it transfers methylene by condensation (reactions 11-15) and the product ions dissociate by loss of formaldehyde. The reaction sequence is best described by Scheme 1 and is supported by double resonance and isotopic labeling results. Thus, double resonance confirmed that $CH_3OCH_2^+$ (*m/e* 45) is a precursor ion to both (M + 13) and (M - 17) ions. Also, an endothermic double resonance response was obtained on irradiation of (M + 13) while observing (M - 17), indicating

$CH_3OCH_2^+ + ROH \xrightarrow{-CH_3OH} ROCH_2^+ \xrightarrow{-CH_2O} R^+$					
Reactant ion (<i>m/e</i>) ^a	Neutral alcohol	Condensation ion (m/e) , M + 13	Elimination ion (m/e) , M – 17		
$CH_3O = CH_2^+ (45)$					
	$CH_{3}CH_{2}OH$ $CH_{3}CH_{2}CH_{2}OH$ $CH_{3}CH_{2}CH_{2}CH_{2}OH$ $(CH_{3})_{2}CHOH$ $CH_{3}CH_{2}CH(OH)CH_{3}$ $(CH_{3})_{3}COH$	b			
CD ₃ OCH ₂ + (48) ^c CH ₃ OCD ₂ + (47) ^d CH ₃ ¹⁸ OCH ₂ + (47) ^e	$CH_3OCH_2CH_2OH$ $CD_3OCH_2CH_2OH$ $CH_3OCH_2CD_2OH$ $CH_3OCH_2CD_2OH$ $CH_3OCH_2CH_2OH$ $CH_3OCH_2CH_2OH$ $CH_3OCH_2CH_2OH$ $CD_3SCH_2CH_2OH$ $H_2NCH_2CH_2OH$ $CH_3NHCH_2CH_2OH$ $CH_3NHCH_2CH_2OH$	$CH_{3}OCH_{2}CH_{2}O=CH_{2}^{+}(89) \\ CD_{3}OCH_{2}CH_{2}O=CH_{2}^{+}(92) \\ CH_{3}OCH_{2}CD_{2}O=CH_{2}^{+}(91) \\ CH_{3}OCH_{2}CH_{2}O=CH_{2}^{+}(89) \\ CH_{3}OCH_{2}CH_{2}O=CH_{2}^{+}(89) \\ CH_{3}OCH_{2}CH_{2}O=CH_{2}^{+}(89) \\ CH_{3}SCH_{2}CH_{2}O=CH_{2}^{+}(105) \\ CD_{3}SCH_{2}CH_{2}O=CH_{2}^{+}(108) \\ H_{2}NCH_{2}CH_{2}O=CH_{2}^{+}(74) \\ CH_{3}NHCH_{2}CH_{2}O=CH_{2}(88) \\ \end{array}$	$CH_{3}OC_{2}H_{4}^{+}(59)$ $CD_{3}OC_{2}H_{4}^{+}(62)$ $CH_{3}OC_{2}H_{2}D_{2}^{+}(61)$ $CH_{3}OC_{2}H_{4}^{+}(59)$ $CH_{3}OC_{2}H_{4}^{+}(59)$ $CH_{3}OC_{2}H_{4}^{+}(59)$ $CH_{3}SC_{2}H_{4}^{+}(75)$ $CD_{3}SC_{2}H_{4}^{+}(78)$		
	BrCH ₂ CH ₂ OH CH ₃ CH ₂ OCH ₂ CH ₂ OH CH ₃ CH ₂ SCH ₂ CH ₂ OH CH ₃ OCH ₂ CH(CH ₃)OH CH ₃ OCH ₂ C(CH ₃) ₂ OH CH ₃ OCH(CH ₃)CH ₂ OH CH ₃ OCH(CH ₃)CH ₂ OH CH ₃ OCH ₂ CH ₂ CH ₂ OH CH ₃ SCH ₂ CH ₂ CH ₂ OH CH ₃ OCH ₂ CH ₂ CH ₂ CH ₂ OH		$\begin{array}{c} CH_{3}CH_{2}OC_{2}H_{4}^{+}\ (73)\\ CH_{3}CH_{2}SC_{2}H_{4}^{+}\ (89)\\ CH_{3}OC_{3}H_{6}^{+}\ (73)\\ CH_{3}OC_{4}H_{8}^{+}\ (87)\\ CH_{3}OC_{3}H_{6}^{+}\ (73)\\ CH_{3}OC_{3}H_{6}^{+}\ (73)\\ CH_{3}SC_{3}H_{6}^{+}\ (89)\\ CH_{3}OC_{4}H_{8}^{+}\ (87)\end{array}$		
CH ₃ O=CHCH ₃ (59) CH ₃ CH ₂ O=CH ₂ ⁺ (59) CH ₃ S ⁺ =CH ₂ ⁺ (61) CH ₃ CH ₂ S ⁺ =CH ₂ ⁺ (75)	CH ₃ OCH ₂ CH ₂ OH CH ₃ OCH ₂ CH ₂ OH CH ₃ OCH ₂ CH ₂ OH O CH ₃ OCH ₂ CH ₂ OH	CH ₃ OCH ₂ CH ₂ O==CHCH ₃ + (103) CH ₃ OCH ₂ CH ₂ O==CH ₂ + (89) CH ₃ OCH ₂ CH ₂ O==CH ₂ + (89) CH ₃ OCH ₂ CH ₂ O==CH ₂ + (89)	CH ₃ OC ₂ H ₄ + (59)		

^{*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 *re*-tained in the product (M - 17) ion. These results are summarized in Table 1. Entirely comparable results were obtained from the reaction of CH₃SCH₂CH₂OH with CH₃OCH₂⁺.

The structures of the product ions in Scheme I 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 $CH_3O(CH_2)_nOH$ 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 $(CH_3)_2C = OH^+$ (m/e 59). On providing a source of $CH_3OCH_2^+$ 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 $CH_3OCH_2^+$. 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 $CH_3OCH_2^+$ or $CH_3SCH_2^+$ to give (M + 13) ions that did *not* dissociate by loss of formaldehyde. 2-Aminoethanol and 2-(N-methylamino)ethanol are examples (see Table 1). When the reactant ion was either $CH_3OCHCH_3^+$ or $RSCH_2^+$, 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 $RO^+ = CH_2$ is sufficiently exothermic to support dissociation to R^+ and $CH_2 = O$. The exothermicity of condensation with $RSCH_2^+$ is evidently insufficient to cause dissociation.

Methoxymethyl Cations with Thiols. There are some interesting differences between thiols and alcohols in their reactions with $CH_3OCH_2^+$. 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 1 and 11). Also, product ions of structure $RSCH_2^+$ did *not* dissociate by loss

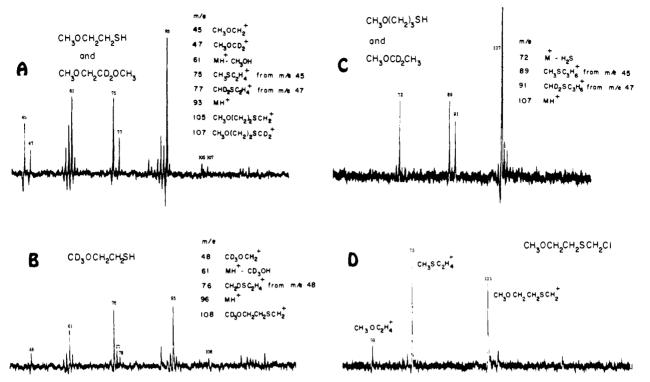


Figure 1. Single resonance mass spectrum of (a) $CH_3OCH_2CH_2SH$ (mol wt 92) at 2.5 × 10⁻⁶ Torr with $CH_3OCH_2CD_2OCH_3$ (mol wt 92) after 30-ms reaction time, (b) $CD_3OCH_2CH_2SH$ (mol wt 95) at 2.0 × 10⁻⁶ Torr and 40-ms reaction time, (c) $CH_3O(CH_2)_3SH$ (mol wt 106) at 1.2 × 10⁻⁶ Torr with $CH_3OCD_2CH_3$ (mol wt 62) at 1.1 × 10⁻⁶ Torr and 150-ms reaction time, (d) $CH_3OCH_2CH_2SCH_2CI$ at 1.4 × 10⁻⁶ Torr and 170-ms reaction time.

Table II. Condensation and Elimination Reactions of Thiols with Methoxymethyl Cations and Related lons

Reactant ion $(m/e)^a$	Neutral thiol	Condensation ion (m/e)	Elimination ion (m/e)
$CH_{3}OCH_{2}^{+}(45)$	CH ₃ CH ₂ SH	$CH_{3}CH_{2}S=CH_{2}^{+}(75)$	b
	(CH ₃) ₂ CHSH	$(CH_3)_2CHS = CH_2^+ (89)$	Ь
	CH ₃ OCH ₂ CH ₂ SH	$CH_3OCH_2CH_2S^+ = CH_2^+ (105)$	$CH_3SC_2H_4^+$ (75)
	CD ₃ OCH ₂ CH ₂ SH	$CD_3OCH_2CH_2S==CH_2^+$ (108)	$CH_2DSC_2H_4^+$ (76)
$CD_3OCH_2^+$ (48) ^c	CH ₃ OCH ₂ CH ₂ SH	$CH_{3}OCH_{2}CH_{2}SCH_{2}^{+}(105)$	$CH_3SC_2H_4^+(75)$
$CH_3OCD_2^+ (47)^d$	CH ₃ OCH ₂ CH ₂ SH	$CH_{3}OCH_{2}CH_{2}SCD_{2}^{+}(107)$	$CHD_{2}SC_{2}H_{4}(77)$
$CH_{3}CH_{2}OCH_{2}^{+}(59)$	CH ₃ CH ₂ OCH ₂ CH ₂ SH	$CH_{3}CH_{2}OCH_{2}CH_{2}S = CH_{2}^{+}(119)$	$CH_3SC_2H_4^+$ (75)
	CH ₃ OCH ₂ CH ₂ CH ₂ SH	$CH_{3}OCH_{2}CH_{2}CH_{2}S=CH_{2}^{+}(119)$	$CH_3SC_3H_6^+(89)$
	CH ₃ OCH ₂ CH ₂ CH ₂ CH ₂ SH	$CH_3OCH_2CH_2CH_2CH_2S=CH_2^+(133)$	$CH_3SC_4H_8^+$ (103)
	CH ₃ OCH ₂ CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ SH	b	b
$CH_{3}O = CHCH_{3}^{+}(59)$	CH ₃ OCH ₂ CH ₂ SH	$CH_{3}OCH_{2}CH_{2}S=CHCH_{3}^{+}(119)$	Ь
$CH_3S^+ = CH_2^+ (61)$	CH ₃ OCH ₂ CH ₂ SH	$CH_{3}OCH_{2}CH_{2}S=CH_{2}^{+}(105)$	Ь

a-d See corresponding footnotes in Table 1.

Scheme II

$$CH_{3}O(CH_{2})_{\underline{n}}SH + CH_{3}\overset{+}{\Theta}=CH_{2}$$

$$\begin{bmatrix}CH_{3}O(CH_{2})_{\underline{n}}S^{-}-H\\CH_{2} & O(CH_{2})_{\underline{n}}S^{-}-H\\CH_{2} & O(CH_{3})\end{bmatrix}$$

$$\downarrow -CH_{3}OH$$

$$CH_{3}O(CH_{2})_{\underline{n}}\overset{+}{S}=CH_{2} \quad (M + 13)$$

$$\downarrow hydride \ transfer$$

$$\begin{bmatrix}CH_{2}=O(CH_{2})_{\underline{n}}SCH_{3}\\\downarrow -CH_{2}=O\\CH_{3}S(CH_{2})_{\underline{n}}^{+} \quad (M - 17)\end{bmatrix}$$

of thioformaldehyde (reaction 17). However, with 2methoxyethanethiol and $CH_3OCH_2^+$ the reaction was unexpectedly different. A minor condensation ion (M + 13) of presumed structure $CH_3OCH_2CH_2SCH_2^+$ (*m/e* 105) was observed, but the major product ion was (M - 17) of composition $C_3H_7S^+$ (*m/e* 75) corresponding to the loss of *formal-dehyde* from $CH_3OCH_2CH_2SCH_2^+$ (*m/e* 105) (reaction 18).

The course of this reaction, which is not obvious from reaction 18, was elucidated using deuterium-labeled reactants. As shown in Table II, unlabeled 2-methoxyethanethiol with $CD_3OCH_2^+$ (m/e 48) gave $C_3H_7S^+$ (m/e 75) containing no deuterium, and with $CH_3OCD_2^+$ (m/e 47) gave $C_3H_5D_2S^+$ (m/e 77) retaining both deuteriums (see Figure 1a). For labeled 2-methoxyethanethiol ($CD_3OCH_2CH_2SH$) and either m/e 45, or 48, the product had composition $C_3H_6DS^+$ (m/e 76) retaining only one deuterium (see also Figure 1b). These results can be explained by the reaction sequence of Scheme 11.

Table III. Condensation and	Elimination Reactions of	Amines with Methoxy	ymethyl Cations

Reactant ion $(m/e)^a$	Neutral amine	Condensation ion (m/e)	Elimination ion (m/e)
$CH_{3}O = CH_{2}^{+}(45)$	CH ₃ CH ₂ NH ₂	$CH_3CH_2NH = CH_2(58)$	b
	(CH ₃ CH ₂) ₂ NH	$(CH_{3}CH_{2})_{2}N=CH_{2}+(86)$	Ь
	CH ₃ OCH ₂ CH ₂ NH ₂	$CH_3OCH_2CH_2NH=CH_2(88)$	$CH_{3}NHC_{2}H_{4}^{+}(58)$
	CD ₃ OCH ₂ CH ₂ NH ₂	$CD_{3}OCH_{2}CH_{2}NH^{+}=CH_{2}^{+}(91)$	$CH_2DNHC_2H_4^+$ (59)
	CH ₃ SCH ₂ CH ₂ NH ₂	$CH_3SCH_2CH_2NH^+=CH_2^+(104)$	$CH_{3}SC_{2}H_{4}+(75)$
	HSCH ₂ CH ₂ NH ₂	$HSCH_2CH_2NH=-CH_2^+$ (90)	b
	CH ₃ OCH ₂ CH ₂ CH ₂ NH ₂	b	Ь

^{*a,b*} See corresponding footnotes in Table 1.

The crucial step here is a hydride transfer from the O-methyl group of the (M + 13) ion to the terminal positive carbon. This rearrangement effectively transfers the positive charge from a sulfur-stabilized carbon to an oxygen-stabilized carbon, that is, sulfonium to oxonium, or sulfocarbenium to oxocarbenium. However, it is questionable whether the rearranged ion ${}^{+}CH_2OCH_2CH_2SCH_3$ has a finite existence as it is possible that rearrangement is accompanied by expulsion of formal-dehyde. Neither is it known whether the stabilized (M + 13) ion has the sulfonium or oxonium structure.

It is doubtful that the hydride transfer in Scheme II is readily reversible because little or no label scrambling was detected in the elimination products. That is to say, variously labeled ions CH₃OCH₂CH₂SCD₂⁺, CD₃SCH₂CH₂OCH₂⁺, and $CH_3SCH_2CH_2OCD_2^+$ gave, respectively, m/e 77, 78, and 75 on elimination of formaldehyde with negligible contributions from isotopic variants. Some label scrambling by reversible hydride transfer cannot be excluded completely in the dissociation of CD₃OCH₂CH₂SCH₂⁺ because product ions m/e 77 and 78 are visible (Figure 1b). Nevertheless, the observed relative abundance of m/e 76:77:78 = 55:15:10 is far different from the calculated ratio of 30:60:10 for complete scrambling of the label between the two terminal carbons. Then again, if hydride transfer were reversible. m/e 76 should be visible in the single resonance mass spectrum of CH₃OCH₂CH₂SH with CH₃OCH₂CD₂OCH₃ (Figure 1a). Instead, only m/e 75 and 77 appear and are derived respectively from the rearrangement and dissociation of $CH_3OCH_2CH_2SCH_2^+$ and $CH_3OCH_2CH_2SCD_2^+$. When 2-ethoxyethanethiol was used as a neutral reactant, the major product ion was again $C_3H_7S^+$ (*m/e* 75) which must be formed in a reaction sequence analogous to Scheme II, the only differences being the structure of the reactant ion $(CH_3CH_2OCH_2^+ (m/e 59))$ and the elimination of acetaldehyde rather than formaldehyde (reaction 19).

$$\begin{array}{c} \operatorname{CH}_{3}\operatorname{CH}_{2}\operatorname{OCH}_{2}\operatorname{CH}_{2}\operatorname{SH} & \xrightarrow{\operatorname{CH}_{3}\operatorname{CH}_{2}\operatorname{OCH}_{2}}^{+} \operatorname{CH}_{3}\operatorname{CH}_{2}\operatorname{OCH}_{2}\operatorname{CH}_{2}\operatorname{SCH}_{2} \xrightarrow{+} \\ & \xrightarrow{\operatorname{CH}_{3}\operatorname{CH}_{2}\operatorname{OH}} & \xrightarrow{\operatorname{M}/\underline{e}} 119 \\ \\ \operatorname{CH}_{3}\operatorname{SC}_{2}\operatorname{H}_{4}^{+} & \xrightarrow{\operatorname{-CH}_{3}\operatorname{CH}=\operatorname{O}} & \operatorname{CH}_{3}^{+}\operatorname{CH}\operatorname{-OCH}_{2}\operatorname{CH}_{2}\operatorname{SCH}_{3} & (19) \\ \\ & \xrightarrow{\operatorname{M}/\underline{e}} 75 & & & & & & \\ \end{array}$$

To see if the observed rearrangement was dependent on the chain length of the starting thiol, we examined the ion chemistry of a series of thiols of structure $CH_3O(CH_2)_nSH$ from n = 2 to 5. All except n = 5 showed a condensation-rearrangement-fragmentation sequence consistent with Scheme 11. For example, when the labeled reactant ion $CH_3OCD_2^+$ was introduced, each of the thiols from n = 2 to 4 gave a product ion of composition $CD_2HS(CH_2)_n^+$ derived solely from $CH_3OCD_2^+$ (*m/e* 47) (see Figure 1c).

$$\begin{array}{c} \operatorname{CH}_{3}\operatorname{O}(\operatorname{CH}_{2})_{\underline{n}}\operatorname{SH} & \xrightarrow{\operatorname{CH}_{3}\operatorname{OCD}_{2} \underline{m}/\underline{e} \ 47} & \operatorname{CD}_{2}\operatorname{HS}(\operatorname{CH}_{2})_{\underline{n}}^{+} \\ \xrightarrow{\operatorname{-CH}_{3}\operatorname{OH}} & \underbrace{m/\underline{e} \ 77 \ \underline{n} = 2} \\ \xrightarrow{\operatorname{CH}_{2} = O} & \underline{m}/\underline{e} \ 91 \ \underline{n} = 3 \\ \underline{m}/\underline{e} \ 105 \ \underline{n} = 4 \end{array}$$

The observed hydride transfers are remarkable in certain respects. They appear to be 1,6-, 1,7-, and 1,8-hydride shifts by way of seven-, eight-, and nine-membered cyclic transition states. Long-range hydride transfers of this order are not



common in the solution chemistry of acyclic carbocations although they are well documented in medium rings. We shall comment further on this point later.

Methoxymethyl Cations with Amines. The reactions of amines with $CH_3OCH_2^+$ followed the same paths as thiols. Simple alkylamines as well as substituted amines $CH_3XCH_2CH_2NH_2$ (X = O. S) condensed with methoxymethyl cations to give (M + 13) as minor product ions (reactions 20-23). However, only in the reactions of substituted ethylamines was condensation accompanied by elimination. With 2-methoxyethylamine, formaldehyde was eliminated. With 2-methylthioethylamine, methylenimine was eliminated (see also Table 111).

$$\xrightarrow{CH_3CH_2NH_2} CH_3CH_2NH = CH_2$$

$$\xrightarrow{-CH_3OH} m/e 58$$
(20)

$$(CH_3CH_2)_2NH \rightarrow (CH_3CH_2)_2N=CH_2 \qquad (21)$$

$$\underbrace{\overset{m/e}{=} \overset{45}{\longrightarrow} \overset{CH_3OCH_2CH_2NH}{\xrightarrow{-CH_3OH} CH_3OCH_2CH_2NH=CH_2} \xrightarrow{-CH_2O} \overset{-CH_2O}{\xrightarrow{-CH_2O}} C_3H_8^{+} (22)}_{m/e = 88}$$

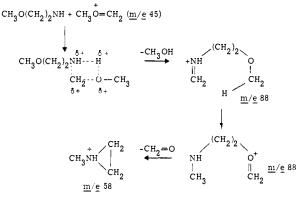
$$\underbrace{CH_3SCH_2CH_2NH_2}_{-CH_3OH} \xrightarrow{+} CH_3SCH_2CH_2NH=CH_2 \xrightarrow{-CH_2=NH}_{-CH_2OH} C_3H_7S (23)$$

$$\underline{m/e = 104} \qquad \underline{m/e 75}$$

The deuterium-labeled amine $CD_3OCH_2CH_2NH_2$ was prepared in order to follow the reaction course, and the results are comparable with the corresponding thiol reactions (Scheme 11). Only *one* of the three deuterium labels in the neutral amine was retained in the product ion $C_3H_7DN^+$ (*m/e* 59). Both of the deuterium labels in CH₃OCD₂⁺ as reactant ion were retained in the product. These results imply that the (M + 13) ion rearranges by a 1,6-hydride shift to convert an immonium ion to an oxonium ion—with expulsion of CH₂==O (Scheme III).

There are some distinctions of note between the thiol and amine reactions. The reactions of Scheme 111 account for only a minor part of the ion chemistry of amines, which is dominated for the most part by the formation of (M + 1) ions. The reverse is the case for thiols. Although condensation-elimination was observed for 2-methoxyethylamine and CH₃OCH₂⁺, no such reactions were detected for 3-methoxypropylamine. With 2aminoethanethiol. H₂NCH₂CH₂SH, which carries labile hydrogen at both ends, condensation with CH₃OCH₂⁺ took

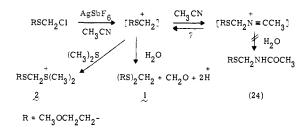
Scheme III



place but the (M + 13) ion was stable and did not eliminate either CH₂=S or CH₂=NH. In fact, elimination of CH₂=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 CH₂=O > CH₂=NH > CH₂=S.

Formation and Behavior of CH₃OCH₂CH₂SCH₂⁺ in Solution. The 1,6-, 1,7- and 1,8-hydride transfers implicated in the rearrangement and dissociation of gaseous ions of structure $CH_3O(CH_2)_nSCH_2^+$ (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 FSO₃H-SO₂, 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 $CH_3O(CH_2)_nSCH_2^+$ 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 RSCH₂Cl react by an S_Nl mechanism under solvolytic conditions.³ We therefore attempted to generate CH₃OCH₂CH₂SCH₂⁺ by reaction of the chloride CH₃OCH₂CH₂SCH₂Cl with AgSbF₆ 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(2methoxyethylthio)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 $CH_3OCH_2CH_2SCH_2CI$ was dominated by a chloride-abstraction reaction involving the fragment ion $CH_3OCH_2^+$ (*m*/*e* 45) to give $CH_3OCH_2CH_2SCH_2^+$ (*m*/*e* 105) or its oxonium isomer that dissociated to give $CH_3SC_2H_4^+$ (*m/e* 75) (see reaction 25 and Figure 1d).

$$\begin{array}{c} CH_{3}OCH_{2}CH_{2}SCH_{2}CI \\ CH_{3}SCH_{2}CH_{2}SCH_{2}CI \\ CH_{3}SCH_{2}CH_{2}OCH_{3} \\ CH_{3}SCH_{2}CH_{2}CH_{2}OCH_{3} \\ CH_{2}CH_{2}CH_{2}CH_{2}CH_{2}SCH_{3}(\underline{m}/\underline{e}\ 105) \\ \underline{m}/\underline{e}\ 75 \end{array}$$

Using another approach, we reasoned that acid-catalyzed formation or hydrolysis of the thioacetal 1 might proceed by way of $CH_3OCH_2CH_2SCH_2^+$, 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.

$$\begin{array}{c} \mathsf{CH}_3\mathsf{OCH}_2\mathsf{CH}_2\mathsf{SH} \xrightarrow{(\mathsf{CH}_2\mathsf{O})\mathsf{n}}_{\mathsf{HCI}} [\mathsf{CH}_3\mathsf{OCH}_2\mathsf{CH}_2\mathsf{SCH}_2] \xrightarrow{\mathsf{CH}_3\mathsf{OCH}_2\mathsf{CH}_2\mathsf{SH}}_{-\mathsf{H}^+} \\ & (\mathsf{CH}_3\mathsf{OCH}_2\mathsf{CH}_2\mathsf{S})_2\mathsf{CH}_2 \\ & \downarrow \\ \end{array}$$

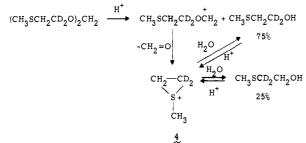
Thioacetals are difficult to hydrolyze by the acidic conditions effective for acetals,¹⁸ and they usually require metal halide catalysis¹⁹ or powerfully electrophilic alkylating agents.²⁰ Therefore, we reacted **1** with Meerwein's reagent, $(CH_3)_3O^+BF_4^-$, to labilize the S-C-S bonding. NMR analysis 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 CH₃OCH₂CH₂SCH₂⁺ was a reaction intermediate, it did not rearrange (reaction 26).

$$(RS)_{2}CH_{2} \xrightarrow{(CH_{3})_{3}O^{+}}_{CH_{2}CH_{2}} \xrightarrow{(CH_{3})_{3}O^{+}}_{RSCH_{2}SR} \xrightarrow{RSCH_{3} + [RSCH_{2}]}_{RSCH_{2}CH_{2}CH_{2}} \xrightarrow{H_{2}O^{+}}_{RSH + CH_{2}O} \xrightarrow{H_{2}O^{+}}_{(26)}$$

A powerful electrophile that rapidly cleaves thioacetals is methylthiodimethylsulfonium fluoroborate $(CH_3)_2$ -SSCH₃+BF₄-.^{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 CH₃OCH₂CH₂SCH₂+. However the only products isolated from this reaction besides methyl sulfide were disulfides RSSR and RSSCH₃, where 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 CH₃OCH₂CH₂SCH₂+.

$$\begin{array}{c} (CH_3)_2 SSCH_3 \\ (CH_3)_2 SSCH_3 \\ (CH_3)_2 S \\ \downarrow \\ R = CH_3 OCH_2 CH_2 - \\ RSCH_2 + RSSCH_3 \\ R = CH_3 OCH_2 CH_2 - \\ RSCH_2 + RSSCH_3 \\ R = CH_2 \\ R = CH_2 \\ CH_3 CH_2 + RSSCH_3 \\ R = CH_2 \\ CH_3 CH_2 + RSSCH_3 \\ R = CH_2 \\ CH_3 CH_2 + RSSCH_3 \\ R = CH_2 \\ CH_3 CH_2 + RSSCH_3 \\ R = CH_2 \\ CH_3 CH_2 + RSSCH_3 \\ R = CH_2 \\ CH_3 CH_2 + RSSCH_3 \\ R = CH_2 \\ CH_3 CH_2 + RSSCH_3 \\ R = CH_2 \\ CH_3 CH_2 + RSSCH_3 \\ R = CH_2 \\ CH_3 CH_2 + RSSCH_3 \\ R = CH_2 \\ CH_3 CH_2 + RSSCH_3 \\ R = CH_3 CH_2 \\ CH_3 CH_2 + RSSCH_3 \\ R = CH_3 CH_2 \\ CH_3 CH_2 \\ CH_3 \\ C$$

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 alkoxymethyl cations by a neighboring group is not a common circumstance in solution. To explore the possibility of dissociation of solvated CH₃SCH₂CH₂OCH₂⁺ ions, we investigated the acid-catalyzed hydrolysis of bis(2-methylthioethoxy- $1, 1-d_2$) methane ((CH₃SCH₂CD₂O)₂CH₂) in sulfuric acid solution. Assuming that acid hydrolysis proceeds by an A-1 mechanism, ions of structure CH₃SCH₂CD₂OCH₂⁺ will be formed as intermediates and, if they dissociate by loss of CH₂O, would almost certainly result in the formation of the cyclic sulfonium ion 4. The symmetry of 4 would then lead to scrambling of the CD₂ label in the product 2-methylthioethanol. Exclusive reaction by this route (Scheme IV) would lead to a product distribution of 75% CH₃SCH₂CD₂OH and 25% $CH_3SCD_2CH_2OH$. 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% CH₃SCD₂CH₂OH 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 CH₃SCH₂CH₂OCH₂⁺ 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 CH₃SCH₂CD₂OH 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.

$$\operatorname{CH}_{3}\operatorname{SCH}_{2}\operatorname{CD}_{2}\operatorname{och}_{2} \xrightarrow{+} \operatorname{CH}_{2} \operatorname{CH}_{3}\operatorname{SCH}_{2}\operatorname{CD}_{2}\operatorname{och}_{2} \xrightarrow{+} \operatorname{cH}_{2} \xrightarrow{-} \operatorname{CH}_{2} \xrightarrow{-} \operatorname{CH}_{3}\operatorname{SCH}_{2}\operatorname{CD}_{2}\operatorname{OH}$$

Summary and Conclusions

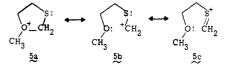
The observation that alcohols ROH react with gaseous methoxymethyl cations only when substituted with alkoxy, alkylthio, and amino substitutents implies that the substituent influences the energetics of reaction. This is so for the initial condensation to give $ROCH_2^+$ (M + 13) ions as well as for the subsequent dissociation of formaldehyde to give R⁺ (M - 17) ions. The evidence is negative that a similar dissociation of alkoxymethyl 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 $CH_3O(CH_2)_nSCH_2^+$ (n = 2-4) and CH_3O -

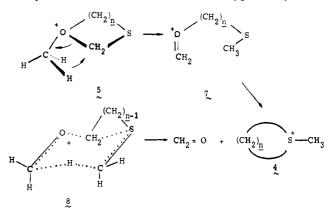
 $(CH_2)_n NHCH_2^+$ are observed in the gas phase only. We are led to the conclusion that the gaseous ions are not strictly comparable in structure to the solvated ions, and that it is an oversimplification to represent them as ROCH₂⁺ and the like.²⁵ In solution, ionic intermediates described as alkoxymethyl 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, alkoxymethyl 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 CH₃CD₂OCH₂CH₂OH 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 $CH_3OCH_2CH_2SCH_2^+$, may be better described as a hybrid of three-valence-bond structures **5a-c**.



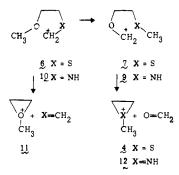
By describing **5** as a cyclic structure, it becomes easier to visualize how hydride shifts from *O*-methyl to give *S*-methyl could be facile because the cyclic structure brings the *O*-CH₃ group in a position to transfer hydride to the ring methylene. However, transfer by way of a four-center transition 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 CH_2 ==O are concurrent events by way of a transition state such as **8**.

An important point regarding hydride transfer from Omethyl 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., $8 \rightarrow CH_2O + 4$) 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 $CH_2=O$ and a sulfonium ion 4; the energetically less favorable pathway via 6 would give $CH_2=S$ 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 $CH_2=O + 4$ is more stable than $CH_2=S +$ 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 (O—CH₂ and ammonium ion 12) than those from 10 (H₂C=NH and oxonium ion 11).³³

In the case of the sulfur analogue $CH_3SCH_2CH_2NHCH_2^+$, no hydride transfer is indicated and the products of dissociation, CH_2 =NH and sulfonium ion **4**, are presumably a more stable combination than the alternative products, CH_2 =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 $C_3H_7S^+$ and $C_3H_7O^+$ 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-d₆)ethane (prepared by methylation of the monosodium salt of 1,2-ethanediol with methyl-d₃ iodide followed by a second

methylation step using methyl- d_3 iodide and silver oxide in dimethylformamide). **1,2-dimethoxyethane-1,1-d2** (prepared by lithium aluminum deuteride reduction of methyl methoxyacetate or methoxyacetyl chloride³⁹ followed by CH₃I-Ag₂O methylation in dimethylformamide), and **methoxyethane-1,1-d2** (prepared by the reduction of methyl acetate with lithium aluminum deuteride followed by methylation of ethanol-1,1-d₂). Conversion of ethanol-1,1-d₂ to iodoethane-1,1-d₂ with phosphorus and iodine followed by treatment with 1,2-ethanediol and silver oxide in dimethylformamide gave **2**- (ethoxy-1,1-d₂)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 (CCl₄, unlabeled product) δ 2.09 (singlet 6-H of two SCH₃), 2.60 (triplet, J = 7 Hz, 4 H of two SCH₂), 3.66 (triplet, J = 7 Hz, 4 H of two SCH₂), 3.66 (triplet, J = 7 Hz, 4 H of two SCH₂). 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 (CCl₄) δ 2.74 (triplet, J = 7 Hz, 4 H of two SCH₂), 3.30 (singlet, 6 H of two OCH₃), 3.53 (triplet, J = 7 Hz, 4 H of two OCH₂), 3.70 (singlet, CH₂).

2-Methoxyethanethiol,⁴² 2-methylthioethanol,⁴³ 3-methylthiopropanol,⁴⁴ 2-(*N*-methylamino)ethanol,⁴⁵ 2-methylthioethylamine,⁴⁶ and 2-mercaptoethylamine⁴⁷ were prepared by literature procedures. 2-(Methoxy-d₃)ethylamine was prepared from the picrate of aziridine by refluxing the salt with methanol-d₃ 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 2methoxyethanethiol, paraformaldehyde, and dry hydrogen chloride gas in dichloromethane solution at $-20 \,^{\circ}\text{C}^{.49}$ The product was obtained in 63% yield and had bp 54-56 °C (4 mm) and ¹H NMR (CCl₄) δ 2.89 (triplet, J = 7 Hz, SCH₂), 3.33 (singlet, OCH₃), 3.63 (triplet, J = 7 Hz, OCH₂), 4.76 (singlet, CH₂Cl).

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**, **4methoxybutanethiol**, 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 CH₃SCH₂CD₂OH) and 3.15 (for CH₃SCD₂CH₂OH) which appear as broad singlets. The starting material also gave a signal for the SCH₂ 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 CH₃SCD₂CH₂OH 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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