

Gas-phase Reactions of $\text{CH}_3\text{OCH}_2^+$ with Alcohols

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As a result of an extensive delocalization of charge and a unique covalent structure, the $\text{CH}_3\text{OCH}_2^+$ cation has, in effect, the character of an ambident electrophile. This cation can, on the one hand, be considered to be a classical electrophile. On the other hand, it may be considered to be a facile methyl cation donor. The former character predominates when this cation reacts with alcohols, as is shown in this work. In both the chemical ionization (CI) source of a conventional mass spectrometer and also via low-pressure bimolecular reactions in a Fourier transform ion cyclotron resonance (ICR) cell, the dominant reaction between alkoxyethyl cations and alcohols is the very exothermic formation of a C—O bond to give a covalent adduct having the structure of a protonated dialkoxyethane. A 1,3-hydrogen transfer is observed for the covalent adducts. In the case of those generated in the ICR cell this process is a slow unimolecular reaction. However, the rapid 1,3-hydrogen transfer observed in the CI source is a bimolecular reaction catalysed by a second molecule of alcohol. This is a new example of catalysed isomerization in the gas phase. In competition with the 1,3-hydrogen transfer, the covalent adducts may either undergo simple bond cleavage or may isomerize to proton-bound dimer adducts of ether and aldehyde (or ketone) via a hydride transfer mechanism. This mechanism either may involve an electrostatic complex intermediate or may be an asynchronous concerted process. Since the proton affinities of the ethers involved in these proton-bound dimer intermediates are greater than those of the aldehydes derived from primary alcohols, such dimers dissociate to yield protonated ether and aldehyde. Conversely, those dimers resulting from secondary alcohols involve ketones whose proton affinities are greater than those of the partner ethers and these dimers dissociate to yield protonated ketone and ether. In summary, the reactions of $\text{CH}_3\text{OCH}_2^+$ with alcohols occur via several successive and specific steps. © 1997 by John Wiley & Sons, Ltd.

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INTRODUCTION

Bimolecular processes involving gaseous ions offer a remarkably facile method of preparation of reaction intermediates *in situ*, including a wide variety of isotopically labelled species, and, for this reason, are also a uniquely powerful means for probing the details of reaction mechanisms. In this regard, the methoxymethyl cation $\text{CH}_3\text{OCH}_2^+$, is an ion of particular interest and its chemistry has been the focus of attention of many investigations.^{1–6} As a result of an extensive delocalization of charge and a unique covalent structure, this cation has, in effect, the character of an ambident electrophile. *Ab initio* calculations by Random and co-workers² revealed that the species is in fact best regarded as methyl cationized formaldehyde, since the methylene to oxygen bond length is essentially that of a normal carbonyl double bond (1.23 Å), while the methyl to oxygen bond distance is unusually long for a C—O single bond at 1.52 Å. This cation can, on the one hand, be considered to be a classical electrophile consistent with the roughly one-third positive charge found on the methylene carbon. However, on the other hand, it may

be considered to be a facile methyl cation donor, a character which is consistent with the greater than one quarter positive charge found on each of the methyl hydrogens. This dual reactivity is effectively revealed in the reactions observed with NH_3 , where two exothermic ion–molecule reaction products are observed.³ The first, CH_2NH_2^+ , is feasible via a classical electrophilic attack intermediate $[\text{CH}_3\text{OCH}_2\text{NH}_3^+]$ while the second, CH_3NH_3^+ , presumably requires an intermediate which allows transfer of CH_3^+ from CH_2O to NH_3 . If this ambident character is intrinsic to the methoxymethyl cation it should also be evident in its reactions with oxygen-containing neutrals. However, which of these characters dominates will probably depend on the nature and structure of the compound. Thus, as demonstrated elsewhere,⁴ in its reactions with ketones the $\text{CH}_3\text{OCH}_2^+$ cation primarily plays the role of a methyl cation donor. In contrast, as will be shown here, reactions in which the classical electrophilic character predominates are the norm when methoxymethyl cation reacts with alcohols.^{5,6}

The reactions with methanol, ethanol and propanols were studied in this work. It will be shown that the reaction occurs via several successive and specific steps, which depend on the thermochemistry of the system. Furthermore, a new example of catalysed isomerization in the gas phase is presented.

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EXPERIMENTAL

Metastable ion experiments

Adducts of $\text{CH}_3\text{OCH}_2^+$ (as well as several other alkoxyethyl cations) with alcohols were produced in the chemical ionization (CI) source of a reverse-geometry double-focusing mass spectrometer (VG Instruments ZAB-2F) by the introduction of an equimolar mixture of the cationic precursor, the alcohol of interest and H_2O . Protonation of the cationic precursor by H_3O^+ yields $\text{CH}_3\text{OCH}_2^+$. Several suitable cationic precursors were used, such as the dimethyl or diethyl acetals of formaldehyde and ethylene glycol dimethyl ether. For labelled methoxymethyl cations and adducts, a variety of custom-synthesized labelled alkyl methyl ethers and commercially available alcohols were also used. In each case production of the desired methoxymethyl cation and its adduct was abundant. The adducts thus generated in the source were magnetically mass selected and their subsequent metastable dissociations in the second field-free region (FFR) examined by electrostatic energy analysis (mass analysed ion kinetic energy spectrometry (MIKES))

Fourier transform ion cyclotron resonance (FT-ICR) experiments

The unimolecular reactions of transient adducts of methoxymethyl cation and alcohols were also inferred from the study of low-pressure bimolecular reactions in a Bruker CMS-47X FT-ICR spectrometer. In brief, the alkoxyethyl cation was generated from a suitable precursor in the external ion source of the FT-ICR spectrometer and subsequently transferred to the ICR cell where it was trapped for a variable period of time in the presence of a controlled pressure of the alcohol. Typically a 10–50-fold excess of inert gas (either CH_4 or Ar) was also present to ensure thermalization of the reactant ions.

The absolute pressure of each of the alcohols used was determined by following the kinetics of a reaction for which the rate constant was well established. In a few cases, where no well documented rate constant was available, the kinetics of very exothermic proton transfer, such as from CH_5^+ , to the alcohols of interest were followed. Pressures determined in this way are expected to be accurate to within the accuracy of the literature

rate constant value, which may be estimated conservatively to be of the order of $\pm 20\%$.

Thermochemistry

Qualitative potential energy profiles were constructed using thermochemical data from the NIST Ion Energetics Database.⁷ In cases where the desired data were not available, two alternative approaches were attempted. The first involved proton affinity measurements of the appropriate methoxy alkyl ether using FT-ICR proton transfer equilibrium techniques. However, in the case of linear longer chain alcohols, this method proved to be inoperable owing to competing reactions and the relevant proton affinities were estimated from those of cyclic analogues such as 1,3-dioxane and dioxolane.⁸

The second method, due to Larson and McMahon,⁹ served to provide energetics for proton-bound dimer species which, as described below, were deemed to be logical intermediates on the potential energy surface.

RESULTS

The unimolecular reaction products formed from the metastable dissociations of the adducts of methoxymethyl and ethoxymethyl cations with various alcohols are summarized in Table 1. It is of interest to compare the dissociation products of parent ions formed in association reactions in the chemical ionization source with those of the same composition resulting from protonation of stable covalent molecules. In addition, the bimolecular reaction products at low pressure in an FT-ICR spectrometer formed in collision of the same reaction partners used to generate the adducts in the chemical ionization source might be presumed to result from the unimolecular dissociation of a transient adduct of the same structure but with a higher internal energy content. A comparison of the three types of data thus permits a synthesis of general features of the potential energy surface for the reaction of interest.

Reaction of $\text{CH}_3\text{OCH}_2^+$ with CH_3OH

The metastable dissociation of the $\text{CH}_3\text{OCH}_2^+$ - CH_3OH adduct, **1**, gives exclusively m/z 45, $\text{CH}_3\text{OCH}_2^+$, with a very small kinetic energy release (1

Table 1. MIKE spectra of adduct ions 1–5

	$\text{R}_1\text{OH} + ^+\text{CH}_2\text{OR}_2$	R_2OCH_2^+			$\text{R}_2\text{OHCH}_3^+$			R_1OCH_2^+			$[\text{R}_1 - \text{H}]^+$			Others		
		m/z	%	T	m/z	%	T	m/z	%	T	m/z	%	T			
1	$\text{CD}_3\text{OH} + ^+\text{CH}_2\text{OCH}_3$	45	42	1	—	—	—	48	58	1	—	—	—	—	—	
2	$\text{C}_2\text{H}_5\text{OH} + ^+\text{CH}_2\text{OCH}_3$	45	8	2.8	47	37.6	16.4	59	54.4	4.3	—	—	—	—	—	
3	$\text{C}_2\text{H}_5\text{OH} + ^+\text{CH}_2\text{OCH}_2\text{CH}_3$	59	38.3	4.6	61	61.7	15.8	—	—	—	—	—	—	—	—	
4	$n\text{-C}_3\text{H}_7\text{OH} + ^+\text{CH}_2\text{OCH}_3$	45	2.1	7	47	43	14.8	73	49.8	6.3	59	5	17.9	—	—	
5	$i\text{-C}_3\text{H}_7\text{OH} + ^+\text{CH}_2\text{OCH}_3$	45	2	7	47	0.5	—	73	36.5	4.7	59	38.5	25	63	5.5	33.5
														87	17	21.6

meV). The behaviour of the ion derived from protonation of dimethoxymethane, CH₃OCH₂O(H)CH₃⁺, is identical. The deuterated analogue of the adduct ion, CH₃OCH₂⁺-CD₃OH, gives two metastable fragments: *m/z* 45 (CH₃OCH₂⁺), 35%, and *m/z* 48 (CD₃OCH₂⁺), 65%. The relative abundance of these two fragments varies only very slightly when the lifetime of the metastable adduct sampled, and therefore its internal energy, are lowered (Table 2). Reaction with CD₃OD reveals that no H-D exchange occurs prior to dissociation.

The bimolecular reaction of *m/z* 45, CH₃OCH₂⁺, with CD₃OD in the FT-ICR cell (Fig. 1) proceeds, without H-D exchange, to two reaction products. The first of these, reaction (1), involves 1,3-hydrogen transfer giving *m/z* 48, CD₃OCH₂⁺, with a rate constant of 7.5×10^{-13} cm³ molecule⁻¹ s⁻¹. The analogous reaction with CD₃OH, is slightly slower with a rate constant of 4×10^{-13} cm³ molecule⁻¹ s⁻¹. The second reaction channel, reaction (2), involves a methyl cation transfer from the methoxymethyl cation to the alcohol to yield *m/z* 51, CD₃O(D)CH₃⁺, with a rate constant of 2.5×10^{-13} cm³ molecule⁻¹ s⁻¹. The *m/z* 48 ion, initially formed, can also be observed to transfer a CD₃⁺ to the alcohol to give *m/z* 54, (CD₃)₂OD⁺, with equal facility. All reactions were found to have rate constants independent of the pressure of the alcohol and the pressure of an inert third body. These methyl cation transfer reactions have no observable counterparts in the metastable dissociations of the adduct ions.

Table 2. Products formed by unimolecular reaction of the [CH₃OCH₂⁺ + CD₃OH] adduct ion depending on the lifetime

B/E (kV)	<i>m/z</i>	
	45	48
	36	64
8	35	65
6	35	65
4	32	68
3	30	70
2	27	73

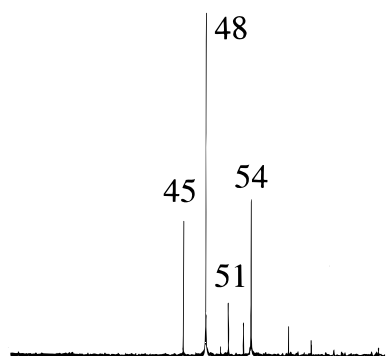
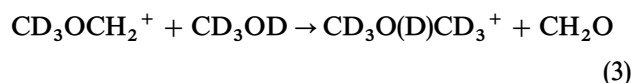
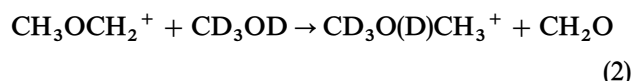
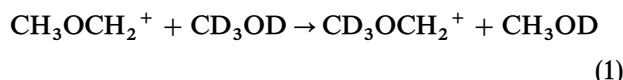


Figure 1. ICR reaction of CH₃OCH₂⁺ with CD₃OD (pressure = 10⁻⁸ mbar, reaction time = 45 s).



Reaction of CH₃OCH₂⁺ with CH₃CH₂OH

The unimolecular reaction of adduct 2 (CH₃OCH₂⁺-C₂H₅OH) yields three products: *m/z* 45 (CH₃OCH₂⁺), 8%, *m/z* 59 (C₂H₅OCH₂⁺), 54% and *m/z* 47, 38%. The MIKE collision-induced dissociation spectrum of the latter formed in the 1st FFR shows that its structure corresponds to CH₃OHCH₃⁺. Deuterium labelling reveals that this protonated ether fragment arises from transfer of both a hydride of the α-carbon and the hydroxylic hydrogen of the alcohol to the cationic reactant (Fig. 2, Table 3). The same processes are observed in the ICR cell in reaction of methoxymethyl cation with ethanol. The reactions are slow ($k = 10^{-11}$ cm³ molecule⁻¹ s⁻¹).

Reaction of CH₃CH₂OCH₂⁺ with CH₃CH₂OH

The unimolecular fragmentation of the adduct ion 3, CH₃CH₂OCH₂⁺-CH₃CH₂OH, as well as the ion derived from protonation of formaldehyde diethylacetal, gives only two products: *m/z* 59 (CH₃CH₂OCH₂⁺), 38%, and *m/z* 61 (CH₃CH₂O(H)CH₃⁺), 62%. In this case also the protonated ether fragment, *m/z* 61, arises from transfer of both a hydride from the α-carbon and the hydroxylic hydrogen of the alcohol to the cationic reactant and significant isotope effects are observed (Fig. 3, Table 4).

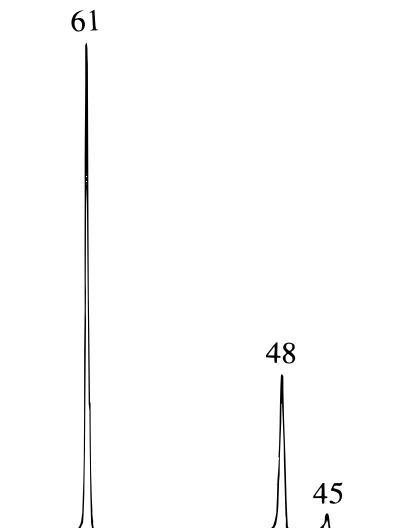


Figure 2. MIKE spectrum of the adduct [CH₃OCH₂⁺ + CH₃CD₂OH].

Table 3. MIKE spectra of labelled adducts 2

Adduct	No.	<i>m/z</i>							
		45	46	47	48	59	60	61	62
CH ₃ CH ₂ OH-CH ₂ OCH ₃	2	8	—	37.6	—	54.4	—	—	—
CH ₃ CH ₂ OD-CH ₂ OCH ₃	2a	5.1	0.5	0.3	41.1	52.5	0.5	—	—
CH ₃ CD ₂ OH-CH ₂ OCH ₃	2b	2.7	0.3	0.4	23.3	—	—	73.1	—
CH ₃ CDHOH-CH ₂ OCH ₃	2c	4.9	1.8	22.1	10.7	—	60.5	—	—
CD ₃ CH ₂ OH-CH ₂ OCH ₃	2d	2.2	—	36.4	1.1	—	—	—	60.3

The same products of bimolecular reaction are observed in the ICR cell in reaction of the ethoxyethyl cation with ethanol as those found in the above unimolecular fragmentations. The reactions are slow ($k = 10^{-11}$ cm³ molecule⁻¹ s⁻¹). Experiments with CH₃CD₂OCH₂⁺ + CH₃CD₂OH confirm the results of the labelling experiments in Table 4.

Reaction of CH₃OCH₂⁺ with *n*-C₃H₇OH and *i*-C₃H₇OH

The adduct ion 4 (CH₃OCH₂⁺-*n*-C₃H₇OH) behaves very much like the corresponding ethanol adduct ion 2 (Table 1). In addition to the expected products, *m/z* 45

(CH₃OCH₂⁺), *m/z* 47 ((CH₃)₂OH⁺) and *m/z* 71 (*n*-C₃H₇OCH₂⁺), there is a significant abundance of a product corresponding to protonated propionaldehyde, *m/z* 59 (*n*-CH₃CH₂CHOH⁺). The structure of this latter product was confirmed by reaction with CH₃CH₂CD₂OH.

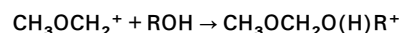
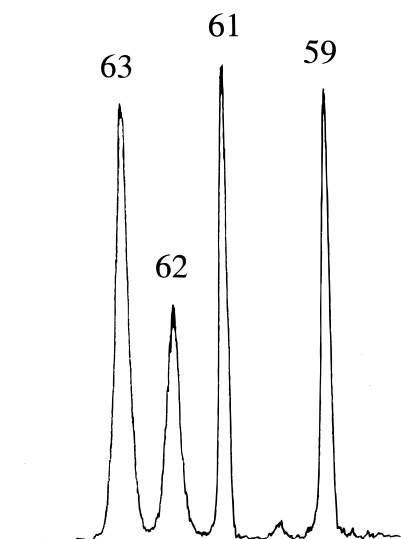
The adduct ion 5 (CH₃OCH₂⁺-*i*-C₃H₇OH) has a significantly different behaviour such that the protonated dimethyl ether product is no longer important but a protonated acetone product is the single abundant fragmentation.

DISCUSSION

C—O bond formation

The adduct 1 between methoxymethyl cation and methanol exhibits metastable dissociation behaviour identical with that of the ion derived from protonation of dimethoxymethane. Similarly, the adducts 2, 3 and 4 each show the same unimolecular dissociations as their protonated dialkoxymethane counterparts. Since the latter ions possess a covalent structure with a C—O single bond from the outset, this suggests very strongly that the reaction between alkoxyethyl cations and alcohols begins by formation of a covalent C—O bond (Scheme 1).

This hypothesis is supported by the thermochemistry of the covalent product ion formation which allows an estimate of the exothermicity of the association reaction of 25–30 kcal mol⁻¹ (1 kcal = 4.184 kJ). In addition,

**Scheme 1****Figure 3.** Mike spectrum of the adduct [CH₃CH₂OCH₂⁺ + CH₃CD₂OH].**Table 4. MIKE spectra of labelled adducts 3**

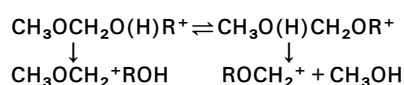
No.	Adduct	<i>m/z</i>						
		59	60	61	62	63	64	
3	CH ₃ CH ₂ OH-CH ₃ CH ₂ OCH ₂ ⁺	38.3 ^a	—	61.7	—	—	—	
3a	CH ₃ CH ₂ OD-CH ₃ CH ₂ OCH ₂ ⁺	38.4 ^a	—	61.6	—	—	—	
3b	CH ₃ CHDOH-CH ₃ CH ₂ OCH ₂ ⁺	23.3 ^a	21 ^a	16.2	39.5	—	—	
3c	CH ₃ CHDOH-CH ₃ CHDOCH ₂ ⁺	—	48 ^a	—	31	21	—	
3d	CH ₃ CD ₂ OH-CH ₃ CH ₂ OCH ₂ ⁺	28.2 ^a	—	25.8 ^a	14.1	31.9	—	
3e	CH ₃ CD ₂ OH-CH ₃ CD ₂ OCH ₂ ⁺	—	—	71.4 ^a	—	2.3	26.3	
3f	CD ₃ CH ₂ OH-CH ₃ CH ₂ OCH ₂ ⁺	21 ^a	—	23.5	32 ^a	23.5	—	
3g	CD ₃ CH ₂ OH-CD ₃ CH ₂ OCH ₂ ⁺	—	—	—	54.2 ^a	—	45.8	

^a Corresponds to ROCH₂⁺m fragment ions.

the probable absence of any significant barrier to this bond formation and the fact that this structure is expected to be more stable than all other isomers leads to the conclusion that the separated reactants should readily come together into this deep well on the potential energy surface (Fig. 4). Whether formed in the CI source of the ZAB or in the FT-ICR cell, these covalent species subsequently react via a competition between two pathways. As shown in Scheme 2, the adduct either undergoes simple bond cleavage to yield the initial reactants or, following a 1,3-intramolecular hydrogen transfer, C—O bond cleavage yields a new alkoxyethyl cation and methanol.

As is evident from the data in Table 2, when the internal energy of the adduct is greater the simple bond cleavage is favoured.

The observation of the methyl cation transfer process in the ICR studies of reactions of $\text{CH}_3\text{OCH}_2^+$ with methanol and ethanol may be presumed to occur via a methyl cation-bound intermediate, $[\text{CH}_2=\text{OCH}_3^+\cdots\text{O}(\text{H})\text{CH}_3]$, as has been shown pre-



Scheme 2

viously in the reactions of $\text{CH}_3\text{OCH}_2^+$ with aldehydes and ketones.⁴ *Ab initio* Mulliken population analysis shows that the methyl group of the methoxymethyl cation bears a substantial positive charge which gives rise to a favourable electrostatic interaction between this site and the oxygen lone pair of the alcohol reactant. Even though the transfer of CH_3^+ from formaldehyde to the alcohol is exothermic, the internal barrier to methyl cation transfer is sufficient to render this reaction very slow. As shown in the reactions with aldehydes and ketones, as the methyl cation affinity of the neutral substrate increases, so too does the rate constant for methyl cation transfer. The very slow rate constant for methyl cation transfer to methanol observed here and the absence of this reaction channel from the MIKE spectra are thus not unexpected. Since the methyl cation transfer channel plays such a minor role in both bimolecular and unimolecular processes, the methyl cation-bound intermediate has been ignored for the purposes of most of the discussion which follows.

1,3-Hydrogen transfer from oxygen to oxygen

The bulk of the experimental data show that the covalent adduct ion resulting from C—O bond formation

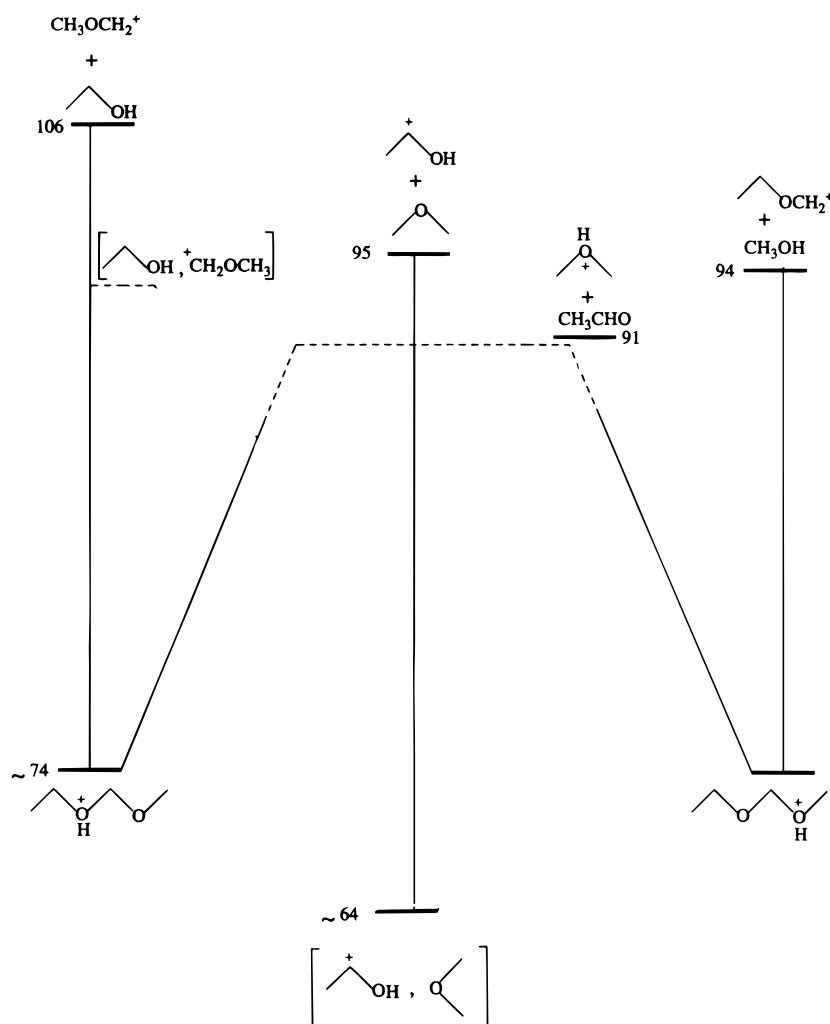


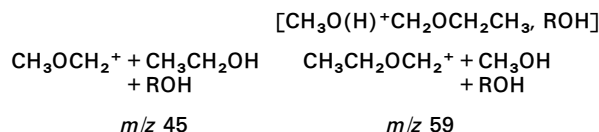
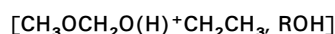
Figure 4. Potential profile for the reaction of $\text{CH}_3\text{OCH}_2^+$ with $\text{CH}_3\text{CH}_2\text{OH}$.

reacts subsequently either by simple cleavage of the newly formed bond or by a 1,3-hydrogen transfer. However, the very slow rate observed for this latter process in the FT-ICR leaves the question open of whether this is a true unimolecular process or a bimolecular process in which the initially formed transient adduct collides with another molecule of alcohol to effect what is, in essence, a catalysed bimolecular 1,3-hydrogen transfer process. In the best case, in the ICR studies, the 1,3-hydrogen transfer corresponds to an occurrence of one collision in 100 whereas in the worst case, that of reaction with methanol, the reaction appears to proceed with less than one collision in 1000.

For reactions of this low efficiency, the possibility must be considered that the transient adduct has a lifetime which is sufficiently long to permit some fraction to undergo a third-body collision with another molecule of alcohol and, in this way, to effect 1,3-hydrogen transfer by proton transfer to the alcohols from the adduct ion followed by proton transfer from the alcohol to the adduct. Since it is a termolecular process, it should then have an apparent rate constant which is dependent on the pressure of the alcohol. However, in ICR experiments in which the alcohol pressure was varied by a factor of ten, no change in apparent rate constant was observed. Hence 1,3-hydrogen transfer observed in the ICR experiments is a true unimolecular reaction of the chemically activated adduct ion. Also in support of the unimolecular nature of the reaction is the significant kinetic isotope effect observed in the reactions of $\text{CH}_3\text{OCH}_2^+$ with CD_3OH and CD_3OD . The difference in rate constants for these two reactions indicates that there is indeed a barrier to 1,3-hydrogen transfer within the adduct and the fact that the transfer is extremely slow implicates a barrier which lies only slightly below the energy of separated reactants. This is consistent with *ab initio* calculations at the MP2 level,¹⁰ which show that such a 1,3-hydrogen transfer requires 20 kcal mol⁻¹ but that its symmetric transition state lies in energy below the energy of the reactants. Similarly, in the reaction of $\text{CH}_3\text{OCH}_2^+$ with NH_3 , Okada *et al.*³ have shown at a lower level of calculation that the transition state for 1,3-hydrogen transfer is below that for C—N bond rupture.

While the evidence for a true unimolecular 1,3-hydrogen transfer in the ICR experiments is ample, it is considerably less so for the ions undergoing metastable dissociation in the 2nd FFR of the reverse geometry spectrometer. That the relative abundances of *m/z* 45 and 48 derived from adduct 1 ($\text{CH}_3\text{OCH}_2^+ - \text{CD}_3\text{OH}$) are insensitive to the ion internal energy (Table 2) is in direct contradiction to the behaviour expected when a process as entropically unfavourable as the 1,3-hydrogen transfer is competing with a simple bond cleavage. Rather, this behaviour would seem simply to reflect a secondary isotope effect which varies slightly with ion internal energy.

Even more revealing is the striking similarity between metastable fragment abundances and their evolution with lifetime for the adducts of $\text{CH}_3\text{OCH}_2^+ - \text{CH}_3\text{CH}_2\text{OH}$ (2) and $\text{CH}_3\text{CH}_2\text{OCH}_2^+ - \text{CH}_3\text{OH}$ (2'). For this to be the case, the 1,3-transfer must take place in the ion source, which is inconsistent with the slow unimolecular reaction observed in the ICR. These



Scheme 3

results thus strongly suggest that a bimolecular, alcohol-catalysed 1,3-hydrogen transfer is taking place in the CI source in intermediates formed between the initially formed adduct and another molecule of alcohol. This has recently been demonstrated for a similar system.¹⁰ As such, this is an example of proton transfer-catalysed isomerization first demonstrated by Bohme¹¹ (Scheme 3).

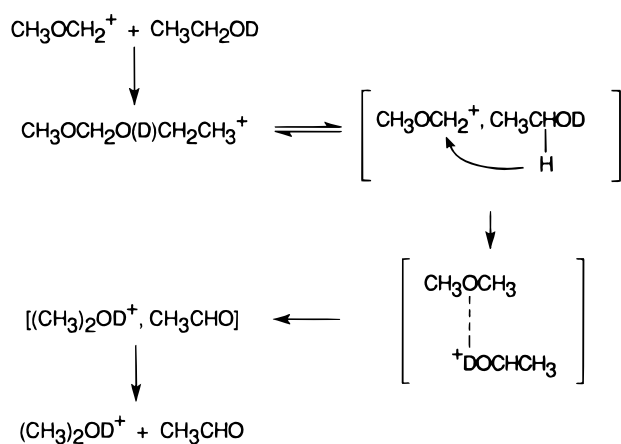
Hydride abstraction

The unimolecular dissociations of the adducts 2–5, both labelled and unlabelled, exhibit a further type of reaction parallel to the simple bond cleavage, with or without 1,3-hydrogen transfer, discussed above. This concurrent mechanistic pathway apparently has its origin in an ion–neutral complex intermediate between the alkoxymethyl cation and the neutral alcohol, $[\text{ROCH}_2^+, \text{R}'\text{OH}]$, in which hydride abstraction by the cation from the alcohol occurs, followed by formation of a proton-bound dimer which then dissociates with the proton remaining with the more basic partner. The existence of this reaction channel as well as the mechanistic ramifications depend strongly upon the nature of the alcohol involved.

In the case of an alcohol with only primary hydrogens (methanol), hydride transfer is not observed. There is no evidence that such a process occurs in adducts 1, or either 2 or 2'. In effect, the isomerization of the covalently bound adducts, $[\text{ROCH}_2\text{O}(\text{H})\text{CH}_3^+]$, to proton-bound dimers, $[\text{RO}(\text{H})\text{CH}_3^+, \text{CH}_2\text{O}]$, does not occur, largely owing to the very low proton affinity of formaldehyde which renders the energy of the proton-bound dimer too high to be accessible.

For alcohols with secondary hydrogens, such as ethanol and propanol which produce the adducts 2, 3 and 4, the adducts formed dissociate to yield a protonated ether and a neutral aldehyde. For example, the adduct formed between methoxymethyl cation and ethanol-*O-d* yields deuterated dimethyl ether and acetaldehyde, presumably via the mechanistic pathway outlined in Scheme 4.

The hydride abstraction is completely selective (Figs 2 and 3, Tables 3 and 4), irreversible and accompanied by significant deuterium isotope effects. For example, the data in Table 4 show that deuterium substitution in an ethyl group, either of the ionic or neutral reactant, such as in adducts 3 ($\text{CH}_3\text{CH}_2\text{OCH}_2^+ - \text{CH}_3\text{CH}_2\text{OH}$), favours simple bond cleavage over hydride abstraction to yield protonated ether. In addition, for the asymmetric adduct 3d the ratio of fragments *m/z* 63:62 allows a total isotope effect (primary + secondary) for a CD_2 group of 2.26 to be calculated. The symmetric adduct 3c, again from the *m/z* 63:62 ratio, gives a primary CD_2



Scheme 4

isotope effect of 1.47, which further permits a determination of a sizable secondary isotope effect of 1.54. The existence and magnitude of these isotope effects imply that in general the barrier to hydride abstraction, although considerable, is lower in energy than the products, $\text{CH}_3\text{CH}_2\text{OCH}_2^+ + \text{CH}_3\text{OH}$. More specifically, the magnitude of the secondary isotope effects demonstrates that the CO bond lengthening is an energetically costly step in the hydride abstraction. This is reminiscent of the situation encountered in the loss of CH_4 from protonated dimethyl ether in that the hydride abstraction takes place either via an ion-neutral complex intermediate, $[\text{CH}_3^+, \text{CH}_3\text{OH}]$, or via a highly asynchronous concerted mechanism in which the transition state energy lies close to that of such a complex.¹²

The decomposition of the adduct 2, in the hydride abstraction channel must therefore proceed via the initially formed proton-bound dimer of dimethyl ether and

acetaldehyde, $[(\text{CH}_3)_2\text{O}, \text{CH}_3\text{CHOH}^+]$ (Fig. 4), while that of adduct 3 goes via a proton-bound dimer of methyl ethyl ether and acetaldehyde $[\text{CH}_3\text{CH}_2\text{OCH}_3, \text{CH}_3\text{CHOH}^+]$. However, in each case, since the proton affinity of the ether is greater than that of acetaldehyde, a barrierless intramolecular proton transfer occurs to give the more stable protonated ether-acetaldehyde adduct which is stabilized by $\sim 30 \text{ kcal mol}^{-1}$ relative to the separated products. It is also important to note that, in contrast to the very small kinetic energy release which accompanies the simple bond cleavage reaction, the hydride abstraction channel exhibits a significant kinetic energy release which is essentially the same for 2, 3 and 4. Hence the transition state for the slow step of the hydride abstraction channel must lie below the energy of the reactants but several kcal mol^{-1} above that of the protonated ether product.

Finally, when the alcohol reactant bears a tertiary hydrogen, as in the case of the adduct 5, the hydride abstraction leads to a proton-bound dimer of an ether and a ketone. Since the proton affinity of the ketone is greater than that of the ether, the hydrogen initially on the alcohol oxygen remains there to yield a protonated ketone ionic product (Fig. 5).

CONCLUSION

Both in the CI source of a conventional mass spectrometer and via low-pressure bimolecular reaction in an FT-ICR cell, the dominant reaction between alkoxy-methyl cations and alcohols is the very exothermic formation of a C—O bond to give a covalent adduct having the structure of a protonated dialkoxy methane.

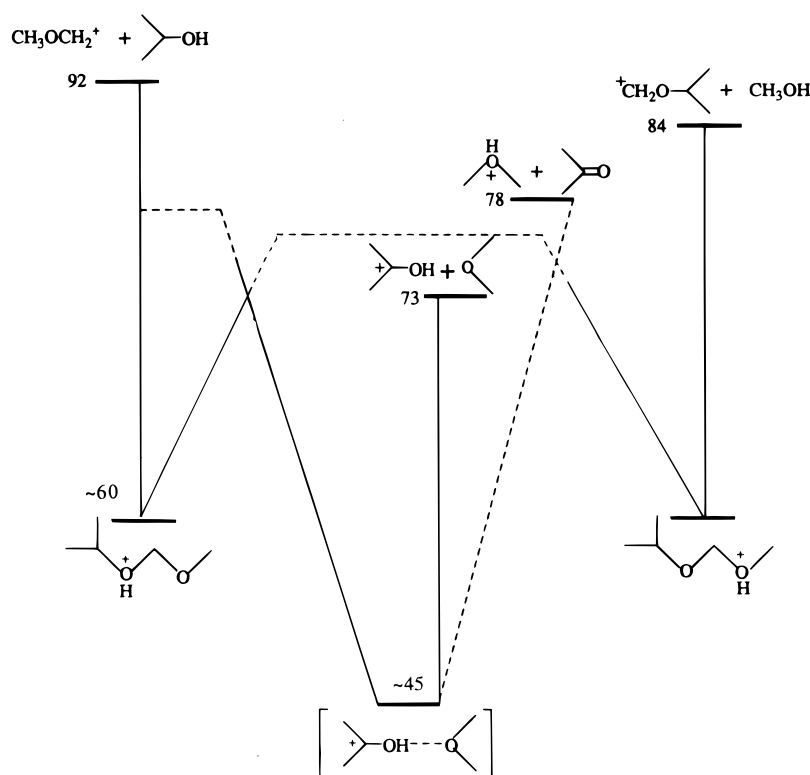


Figure 5. Potential profile for the reaction of $\text{CH}_3\text{OCH}_2^+$ with $(\text{CH}_3)_3\text{CHOH}$.

The possibility of the formation of electrostatic ion-neutral complexes of the form $[\text{CH}_3\text{OCH}_2^+, \text{ROH}]$ cannot be dismissed but no compelling evidence for their existence was found. As a result of the very low methyl cation affinity of alcohols, such complexes, in contrast to the situation found in the reaction of methoxymethyl cation with aldehydes and ketones, lead to an almost insignificant extent of methylation of the alcohol.

A 1,3-hydrogen transfer is observed for the covalent adducts. In the case of those generated in the ICR cell this process is a slow unimolecular reaction. However, the rapid 1,3-hydrogen transfer observed in the CI source is a bimolecular reaction catalysed by a second molecule of alcohol. This is a new example of catalysed isomerization in the gas phase.

In competition with the 1,3-hydrogen transfer, the covalent adducts may either undergo simple bond

cleavage or may isomerize to proton-bound dimer adducts of ether and aldehyde or ketone via a hydride transfer mechanism. This mechanism either may involve an electrostatic complex intermediate or may be an asynchronous concerted process.

Since the proton affinities of the ethers involved in these proton-bound dimer intermediates are greater than those of the aldehydes derived from primary alcohols, such dimers dissociate to yield protonated ether and aldehyde. Conversely, those dimers resulting from secondary alcohols involve ketones whose proton affinities are greater than those of the partner ethers and these dimers dissociate to yield protonated ketone and ether.

In summary, the reactions of $\text{CH}_3\text{OCH}_2^+$ with alcohols occur via several successive and specific steps as shown in Schemes 2 and 3 and in Figs 4 and 5.

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