

symmetry about the relative velocity vector and that both are centered around the center of mass. These data indicate that the reaction proceeds by way of a long-lived complex, as would be expected in view of the strong coulombic attraction between the products.

In summary, SbF_5 and its polymers have a complicated and varied chemistry which may be useful in the gas phase, as it is

in solution, for the preparation of carbonium ions for spectroscopic and kinetic studies. It also offers the chemical dynamicist the opportunity to study a class of reactions quite different from those ordinarily encountered.

Acknowledgment. Research support from the National Science Foundation is gratefully acknowledged.

Gas-Phase Elimination Reactions of Ethers Induced by Amide and Hydroxide Ions

C. H. DePuy* and Veronica M. Bierbaum*

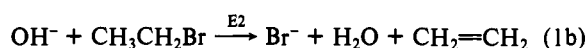
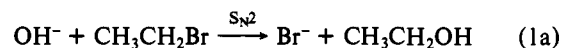
Contribution from the Department of Chemistry, University of Colorado, Boulder, Colorado 80309. Received December 22, 1980

Abstract: The flowing afterglow technique has been employed to study the gas-phase reactions of a series of dialkyl ethers with amide and hydroxide ions. Ethers with β -hydrogens react rapidly by elimination rather than substitution mechanisms, and they demonstrate considerable specificity in the direction of elimination. With amide ion elimination proceeds primarily by removal of the most acidic hydrogen with little or no evidence of alkoxide stability playing a role. With hydroxide ion as the base the stability of the leaving groups appears to be of some importance, and cluster ions between water and the alkoxide ions are the major products. Evidence is presented for a long-lived complex of reaction products which can react further before separating.

When bimolecular elimination (E2) reactions are carried out in solution, reaction rates, product distributions, and even reaction stereochemistry can be profoundly influenced by substituent and leaving-group effects in the substrate or by variations in the attacking base. It has become increasingly feasible to observe such fundamental organic processes in the gas phase and hence in the complete absence of solvent, and it is, of course, important to determine if relationships so well documented in solution will also be found under these new conditions. Two versatile techniques are most commonly used for such studies of gas-phase ion-molecule reactions. Beauchamp and his co-workers¹ used ion cyclotron resonance (ICR) spectroscopy² to examine elimination reactions of fluorinated ethanes and ethylenes induced by methoxide ion and other bases. These studies delineated the general features of gas-phase E2 reactions and examined effects of the highly polar fluorine substituents. In this paper, we report studies of E2 reactions³ using the flowing afterglow (FA) technique⁴ in which we have examined effects of alkyl substitution and, to some extent, base strength and leaving-group effects.

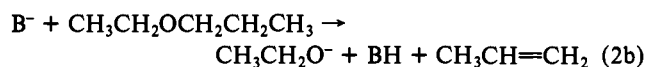
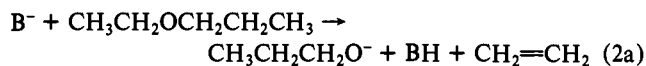
Although studies of ionic organic reaction mechanisms in the gas phase are generally more direct and less complicated than similar studies in solution, there are several limitations. In the gas phase, one is usually limited to the detection of the ionic products of the reactions.⁵ In a typical E2 reaction, the alkene which is formed is not detected and only the (charged) leaving group is seen. Indeed, it is not even known in such a fundamental reaction as that between ethyl bromide and hydroxide ion whether the product is that expected from an $\text{S}_{\text{N}}2$ (ethyl alcohol) or from

an E2 (ethylene) reaction (eq 1). All that has been measured is the loss of the OH^- signal and the appearance of Br^- .



Gas-phase ion-molecule rate constants, which can generally be measured rather easily, are of less use for mechanistic studies than might be anticipated. In the gas phase, ions and neutrals are attracted to one another by ion-induced-dipole and ion-permanent-dipole forces of up to about 20 kcal mol⁻¹ at typical reaction distances. Thus many reactions which might be slow in solution occur rapidly and without apparent activation energy in the gas phase. For example, methyl and neopentyl chloride react with fluoride ion in the gas phase at nearly the same exceedingly fast overall rate, even though there is a steric barrier to displacement at a neopentyl carbon.

To circumvent both of these problems, we chose to investigate reactions of alkyl ethers with strong bases in the gas phase. In such a reaction the nature of the ionic product (the alkoxide ion) would allow us to deduce the effect of substituents on the direction of elimination (eq 2). By varying the alkyl groups in dialkyl



ethers, we hoped to determine how alkyl substitution would affect the relative production of the two alkoxide ions. We have measured a few absolute rate constants for typical eliminations of ethers, but in general we need only measure relative rates, i.e., competition between two internal reaction channels within a single ion-dipole complex.

Experimental Section

These studies were performed with a flowing afterglow system which has been described previously.⁶ Briefly the apparatus consists of a

(1) (a) Ridge, D. P.; Beauchamp, J. L. *J. Am. Chem. Soc.* **1974**, *96*, 3595-3602. (b) Sullivan, S. A.; Beauchamp, J. L. *Ibid.* **1976**, *98*, 1160-1165. (c) Sullivan, S. A.; Beauchamp, J. L. *Ibid.* **1977**, *99*, 5017-5022.

(2) Beauchamp, J. L. *Annu. Rev. Phys. Chem.* **1971**, *22*, 527-561.

(3) Bierbaum, V. M.; DePuy, C. H.; Shapiro, R. H., preliminary results presented at the 25th Annual Conference on Mass Spectrometry and Allied Topics, Washington, D.C., May 29-June 3, 1977.

(4) Ferguson, E. E.; Fehsenfeld, F. C.; Schmeltekopf, A. L. *Adv. At. Mol. Phys.* **1969**, *5*, 1-56.

(5) Rapid progress is however being made in determining neutral reaction products. See, for example: (a) Attina, M.; Cacace, F.; Ciranni, G.; Giacomello, P. *J. Am. Chem. Soc.* **1977**, *99*, 5022-5026. (b) Lieder, C. A.; Brauman, J. I. *Ibid.* **1974**, *96*, 4028-4030. (c) Marinelli, W. J.; Morton, T. H. *Ibid.* **1978**, *100*, 3536-3539. (d) Smith, M. A.; Barkley, R. M.; Ellison, G. B. *Ibid.* **1980**, *102*, 6851-6852.

(6) Bierbaum, V. M.; DePuy, C. H.; Shapiro, R. H.; Stewart, J. H. *J. Am. Chem. Soc.* **1976**, *98*, 4229-4235.

system for handling, purifying, and measuring gas flows, a flow tube in which ion production and reaction occur, a differentially pumped mass spectrometer/electron multiplier section for ion analysis and detection, and a large capacity Roots/backing pump combination for maintaining gas flows.

Purified helium buffer gas is pumped through the stainless-steel flow tube (7.6-cm id \times 100 cm) at a velocity of ~ 8000 cm s⁻¹ and a pressure of ~ 0.3 torr, corresponding to a flow rate of ~ 130 STP cm³ s⁻¹. The helium pressure is measured with a capacitance manometer, and the flow rate is regulated and measured with an electronic mass flow controller. Small flows (≤ 1 STP cm³ s⁻¹) of other gases are added at the upstream end where electron-impact and subsequent chemical reaction generate the reactant ion. For example, OH⁻ is formed by electron impact on nitrous oxide to give O⁻, followed by rapid hydrogen atom abstraction from methane, and NH₂⁻ is produced by dissociative electron attachment to ammonia. The strongly basic amide ion is rapidly converted to hydroxide ion by trace amounts of oxygen or water vapor. However with a helium-leak-tested system, passage of helium buffer gas through a molecular sieve trap immersed in liquid nitrogen and use of high purity ammonia, an amide/hydroxide ratio of 10 could be obtained.

The reactant ion-helium mixture is allowed to flow at least 35 cm before introduction of the neutral reactant to allow collisional relaxation of the ions and development of well-defined flow and diffusion characteristics. The ethers are added through a fixed inlet 40 cm upstream of the sampling orifice and ionic product distributions are measured with 10% of the ionic reactants remaining; secondary reactions are usually negligible. Alternatively, for the kinetic studies, the ether is added through the movable inlet which is continuously variable between positions 15 and 65 cm upstream of the sampling orifice; rate constants are measured by monitoring reactant ion intensity versus reaction distance; ether-flow rates are measured by determining the pressure increase in a calibrated volume system.

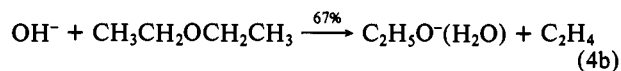
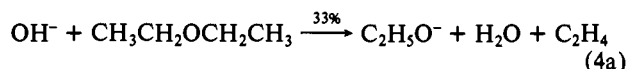
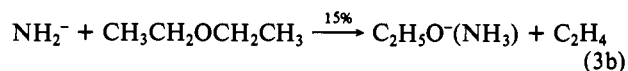
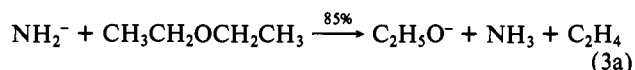
Most of the reaction mixture is exhausted through the large Roots pumping system. The ions are sampled through an orifice in a molybdenum nose cone, focussed by a series of three lens elements and mass analyzed with a quadrupole mass filter. The mass-selected ions are detected by a continuous channel ceramic electron multiplier and pulse-counting electronics. Total mass spectra are recorded on a signal averager, and ion intensities are monitored on an analog ratemeter.

All gases were obtained from commercial suppliers and were of the following purities: He (99.995%), N₂O (99.0%), CH₄ (99.0%), NH₃ (99.999%), CH₃OCH₃ (99.87%) and CH₂=CHOCH₃ (99.5%). Methyl vinyl ether was distilled before use to remove highly reactive acetylene impurity. The remaining ethers were purchased from commercial sources or prepared by reaction of the sodium or potassium salt of the alcohol with the appropriate alkyl halide followed by careful distillation. All liquid ethers were distilled from lithium aluminum hydride directly into the flowing afterglow system.

Deuterated Compounds. Diethyl-*d*₁₀ ether (99% D) and tetrahydrofuran-*d*₈ (99% D) were obtained from Merck and Co., Inc. The 2,2,5,5-tetradeuteriotetrahydrofuran was prepared by the reduction of diethyl succinate with LiAlD₄ and subsequent cyclization of the 1,4-butanediol by distillation from pyridine hydrochloride.⁷ CH₂=CDOCH₃ was prepared by reaction of methyl vinyl ether with *tert*-butyllithium and neutralization with D₂O.⁸

Results

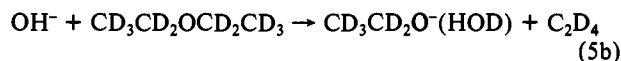
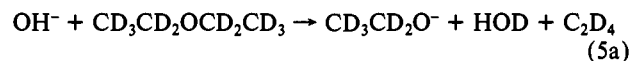
Ethyl Ether. Both hydroxide and amide ions react rapidly with ethyl ether (eq 3 and 4). Of course, the neutral product, ethylene,



is inferred and not directly observed. However, when the cluster ions are produced, ethylene is the only product thermochemically

accessible. On this evidence alone at least two-thirds of the reactions with OH⁻ must proceed by E2 rather than S_N2 reaction. Other experiments described below indicate that all of the reactions are, in fact, E2.

In order to demonstrate that the cluster ion C₂H₅O⁻(H₂O) was produced directly in the elimination and not by association of initially formed ethoxide with adventitious water, we studied the products of the elimination from completely deuterated ethyl ether (eq 5). The cluster ion appeared at *m/z* 69 showing exclusive

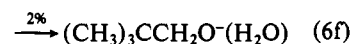
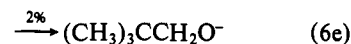
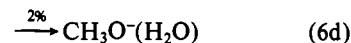
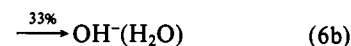
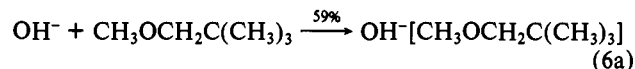


clustering with HOD as predicted. Van Doorn and Jennings⁹ have recently discussed the bimolecular formation of solvated anions in similar experiments using an ICR.

Bimolecular rate constants for these two reactions were measured by varying the reaction distance and hence the time of reaction. For reaction of ethyl ether with NH₂⁻ the experimental rate constant $k_{\text{exptl}} = 4.1 \times 10^{-10}$ cm³ molecule⁻¹ s⁻¹. Since ions and neutrals are attracted to one another by forces which depend upon their dipole moments and polarizabilities, this experimental value must be compared to a calculated value corresponding to the encounter rate. With use of the average dipole orientation (ADO) method¹⁰ $k_{\text{ADO}} = 2.3 \times 10^{-9}$ cm³ molecule⁻¹ s⁻¹ and $k_{\text{exptl}}/k_{\text{ADO}} = 0.2$. For reaction of ethyl ether with OH⁻ $k_{\text{exptl}} = 6.1 \times 10^{-10}$, $k_{\text{ADO}} = 2.2 \times 10^{-9}$, and $k_{\text{exptl}}/k_{\text{ADO}} = 0.3$. Thus, hydroxide ion reacts with ethyl ether both more rapidly and on a larger fraction of collisions than does amide ion. The experimental rate constants have total estimated errors of $\pm 25\%$.

Methyl Ether. Beta elimination is impossible for methyl ether, and α -elimination is highly endoergic. Thus substitution, which is highly exoergic, is the only pathway open for reaction. Both amide and hydroxide ions react exceedingly slowly with methyl ether, $k_{\text{exptl}} \leq 3 \times 10^{-13}$. Since methyl ether should be more reactive than ethyl ether in an S_N2 reaction, it is clear that, in ethers, E2 is strongly favored over S_N2. Based in part on these results, we believe that ethyl ether reacts exclusively by an E2 mechanism.

Methyl Neopentyl Ether. Methyl neopentyl ether, like methyl ether, cannot undergo an E2 reaction. We examined its reaction with base to determine if larger alkoxides make better leaving groups in S_N2 reactions since the neopentoxide ion should be a substantially weaker base than methoxide ion. However, this ether was also quite unreactive. A cluster ion between the ether and OH⁻ is formed slowly as well as a OH⁻(H₂O) cluster. Methoxide and neopentoxide ions and their water clusters are produced only slowly and in small amounts (eq 6). The OH⁻(H₂O) cluster is



presumably a secondary reaction product resulting from the facile bimolecular switching reaction of OH⁻[CH₃OCH₂C(CH₃)₃] with

(7) Egyed, J.; Demerseman, P.; Royer, R. *Bull. Soc. Chim. Fr.* **1973**, 3014-3017.

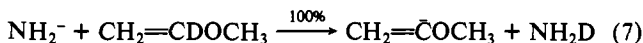
(8) Baldwin, J. E.; Höfle, G. A.; Lever, O. W., Jr. *J. Am. Chem. Soc.* **1974**, 96, 7125-7127.

(9) Van Doorn, R.; Jennings, K. R., presented at the 28th Annual Conference on Mass Spectrometry and Allied Topics, New York, N.Y., May 25-30, 1980.

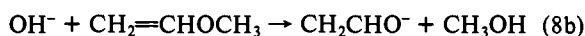
(10) Su, T.; Bowers, M. T. *Int. J. Mass Spectrom. Ion Phys.* **1973**, 12, 347-356.

traces of water impurity. Thus greater than 90% of the initial reaction product of OH⁻ with methyl neopentyl ether proceeds by direct clustering.

Methyl Vinyl Ether. Although methyl vinyl ether contains a potentially excellent leaving group for an S_N2 process, reaction with amide proceeds exclusively by proton abstraction. The acidic site was unambiguously identified by deuterium labeling experiments (Eq 7). Reaction of OH⁻ with methyl vinyl ether occurs

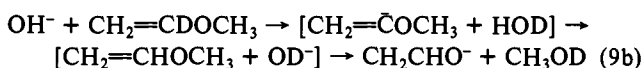
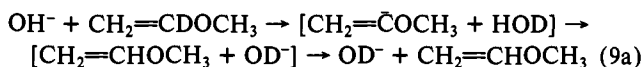


at a moderately slow rate and generates two major products, an adduct (*m/z* 75) and CH₂CHO⁻ (*m/z* 43).

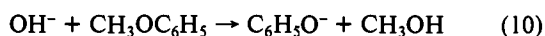


Since both proton abstraction and elimination reactions are now endothermic, a moderately slow nucleophilic substitution reaction forming a relatively stable anion is observed. The ion at *m/z* 75 may be a simple adduct, [OH⁻(CH₂=CHOCH₃)], or it may correspond to a species in which substitution has occurred but the products remain associated [CH₂CHO⁻(CH₃OH)].

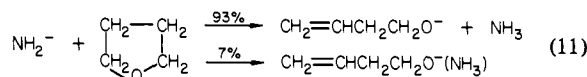
Reaction of OH⁻ with CH₂=CDOCH₃ gave intriguing results; in addition to the expected products, CH₂CDO⁻ and CH₂CD⁻O(CH₃OH), two other species were generated, OD⁻ and CH₂-CHO⁻. These probably arise by hydrogen-deuterium exchange^{11,12} within the ion-dipole complex followed by fragmentation or further reaction.



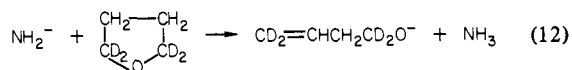
Olmstead and Brauman¹³ and Kleingeld and Nibbering¹⁴ have also reported the occurrence of slow nucleophilic substitution reactions in ethers when there is a good leaving group and the elimination mechanism is unfavorable (eq 10).



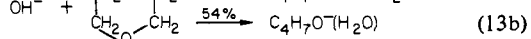
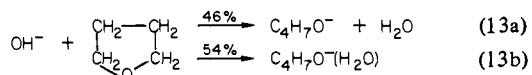
Tetrahydrofuran. Tetrahydrofuran represents one of the most definitive examples of β-elimination of ethers since the "leaving group" remains with the anion (eq 11). Amide reacts with THF



at a moderate rate to generate the M - 1 anion as 93% of the product spectrum. E2 elimination rather than proton abstraction from the α position is confirmed by the results of reaction with 2,2,5,5-tetrauteriotetrahydrofuran which loses exclusively (>98.5%) a β-hydrogen (eq 12).



Hydroxide ion reacts with THF at a moderately slow rate to produce approximately equal quantities of the M - 1 product (*m/z* 71) (eq 13a) and an ion of *m/z* 89 which by analogy with previous results we formulate as the clustered alkoxide (eq 13b).



(11) Stewart, J. H.; Shapiro, R. H.; DePuy, C. H.; Bierbaum, V. M. *J. Am. Chem. Soc.* **1977**, *99*, 7650-7653.

(12) DePuy, C. H.; Bierbaum, V. M.; King, G. K.; Shapiro, R. H. *J. Am. Chem. Soc.* **1978**, *100*, 2921-2922.

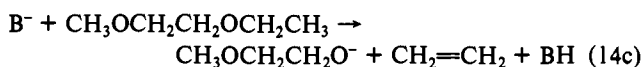
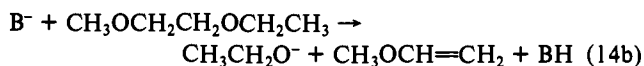
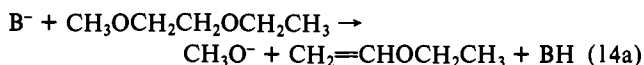
(13) Olmstead, W. N.; Brauman, J. I. *J. Am. Chem. Soc.* **1977**, *99*, 4219-4228.

(14) Kleingeld, J. C.; Nibbering, N. M. M. *Tetrahedron Lett.* **1980**, *21*, 1687-1690.

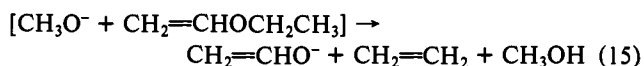
Mixed Dialkyl Ethers. In an attempt to determine the effect of alkyl substituents on the direction of E2 eliminations we studied the products from the reaction of the eight mixed ethers given in Table I with both amide and hydroxide ions. There were four products from each reaction, the two alkoxide ions and the clusters of these ions with ammonia or water. All of these reactions proceed rapidly.

Ethylene Glycol Dialkyl Ethers. Ethylene glycol dimethyl ether (CH₃OCH₂CH₂OCH₃) reacts rapidly with both amide and hydroxide ions to produce methoxide ion and the methoxide-ammonia or methoxide-water complexes. Small amounts of products corresponding to clusters of the parent ether with methoxide ion are also seen. These may arise from switching reactions or from clustering of methoxide with the ether.

The methyl ethyl ether of ethylene glycol can eliminate in three ways, and each of the three alkoxide ions can be observed (eq 14)



as can their cluster ions with the parent ether or with ammonia or water. In addition the acetaldehyde enolate ion is produced. This may arise from a further E2 reaction between methoxide ion and the ethyl vinyl ether (eq 14a) *within the initially formed ion-dipole complex* (eq 15).



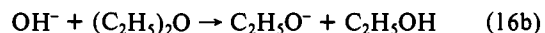
A similar set of product ions is formed when the methyl *n*-propyl ether of ethylene glycol is allowed to react with NH₂⁻ or OH⁻. This experiment eliminates the possibility that CH₂CHO⁻ is formed by decomposition of vibrationally excited CH₃CH₂O⁻, since the acetaldehyde enolate ion (but not ethoxide ion) is a product of the reaction of CH₃OCH₂CH₂OCH₂CH₂CH₃. The products obtained from these glycol ethers are summarized in Table II.

Discussion

E2 vs. S_N2 Reactions. Perhaps the most striking result of these studies is the demonstration of the very large extent by which E2 reactions predominate over S_N2 reactions, despite the similar exoergicity of these processes for most ethers. For example, standard heats of formation¹⁵ show that for ethyl ether reacting with hydroxide ion the E2 pathway is slightly endothermic and the S_N2 pathway highly exothermic. However the large increase in entropy associated with the elimination reaction makes the free energy change for the two processes approximately equal.



$$\Delta H = +1.9 \text{ kcal mol}^{-1} \quad \Delta G = -9.3 \text{ kcal mol}^{-1}$$



$$\Delta H = -9.0 \text{ kcal mol}^{-1} \quad \Delta G = -11.2 \text{ kcal mol}^{-1}$$

The corresponding values for reaction with NH₂⁻ are ΔH = -11.1 kcal mol⁻¹ and ΔG = -21.5 kcal mol⁻¹ for the E2 reaction and ΔH = -23.6 kcal mol⁻¹ and ΔG = -24.9 kcal mol⁻¹ for the S_N2 reaction. Nevertheless, the reactions are highly selective for the slightly less exoergic elimination channels.

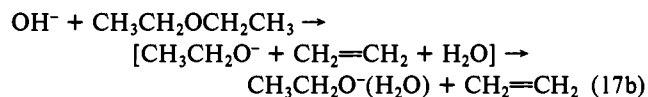
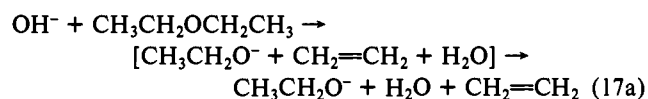
This selectivity is shown by the exclusive loss of β-protons from tetrahydrofuran, by the comparative slowness of the reactions of dimethyl ether and of methyl neopentyl ether relative to ethers with β-hydrogens, and by the formation of large amounts of

(15) (a) Bartmess, J. E.; McIver, R. T., Jr. In "Gas Phase Ion Chemistry"; Bowers, M. T., Ed.; Academic Press: New York, 1979; Vol. 2, pp 87-121. (b) Stull, D. R.; Westrum, E. F., Jr.; Sinke, G. C. "The Chemical Thermodynamics of Organic Compounds"; Wiley: New York, 1969.

alkoxide-water clusters from reactions of ethers with OH^- , products which can only arise from E2 reactions. It remains to be demonstrated whether a similar preference for E2 over $\text{S}_{\text{N}}2$ will be observed in reactions of compounds with better leaving groups. We predict that it will, and that even ethyl bromide will react with OH^- to form ethylene in addition to ethyl alcohol.

Such a preference for an E2 over an $\text{S}_{\text{N}}2$ mechanism must have its origin in the dynamics of gas phase ion-molecule collisions. An $\text{S}_{\text{N}}2$ process may well require a much more ordered transition state than an E2 reaction, which is more closely related to proton transfer.¹⁶

Long-Lived Complexes in Ion-Molecule Reactions. We have emphasized in previous publications^{11,12,17} the importance of relatively long-lived complexes in ion-molecule reactions. Not only do the initial reactants often show great selectivity in choosing among reaction channels but also the products of ion-molecule reactions do not always separate immediately. Instead they can remain together for sufficient time to allow secondary reactions to occur. For example, reaction of diethyl ether with OH^- produces a complex consisting of water, ethylene, and ethoxide ion. Such a complex can come apart in two ways, breaking up into its three components or losing only ethylene to form the ethoxide-water complex (eq 17). Formation of the water complex



is, of course, the more thermodynamically favorable pathway. In reaction of amide ion with diethyl ether much less of the ethoxide-ammonia complex is formed; this occurs because hydrogen bonding of negative ions to ammonia is energetically less favorable¹⁸ than hydrogen bonding to water and because the overall reaction is strongly exothermic so there may be a shorter ion-dipole complex lifetime in which to effect the necessary rearrangement.

The eliminations from the methyl ethyl and methyl *n*-propyl ethers of ethylene glycol provide dramatic evidence for long-lived complexes. In each case a product ion of *m/z* 43 corresponding to $\text{CH}_2=\text{CHO}^-$ is formed. This ion is most reasonably interpreted as resulting from initially formed methoxide ion inducing a second elimination at the other end of the molecule (eq 15). The conditions of the experiment are such that this secondary elimination must occur within the initial complex; if ethyl or *n*-propyl vinyl ether were to separate from the methoxide ion, it would never encounter another anion during its residence in the reaction tube.

When hydroxide ion is used as the base, about half of the methoxide ion formed induces a second elimination within the complex. When amide is the base, less than 20% reacts further. These results support the interpretation that complexes have shorter lifetimes (and hence less time for secondary reactions) if the overall reaction is more exothermic.

It is reasonable to expect that these ion-neutral intermediates exist sufficiently long for secondary reactions to occur. Spears and Ferguson¹⁹ have deduced that complex lifetimes of at least 10^{-7} s occur for termolecular association reactions. Recently, Bartmess and Caldwell²⁰ have discussed bimolecular clustering of alcohols with alkoxide ions at very low pressure, presumably by radiative stabilization; this process implies lifetimes in the millisecond range. However even lifetimes as short as 10^{-10} s would

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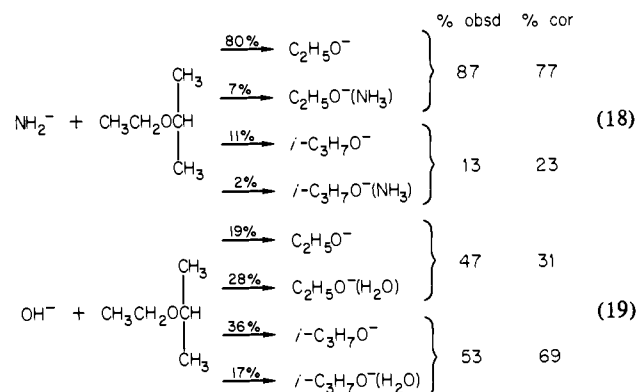
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Scheme I



allow for hundreds of vibrations. We therefore view these anion-ether reactions as proceeding through relatively long-lived complexes which allow for extensive but very specific bond reorganizations.

Direction of Elimination in Mixed Ethers. The reaction of ethyl isopropyl ether may serve as an example of the method of analysis of the data. The experimental intensities of the four ionic products are given in Scheme I. In order to minimize mass discrimination in the quadrupole mass filter, we carried out the analysis at relatively low resolution. Even so the exact values for the percentages of each reaction channel are slightly dependent upon resolution and upon the specific settings of the ion sampling and focussing potentials. However all measurements were made at the same resolution and detection system voltages and are reproducible within a few percent.

In order to make valid comparisons, we must correct the raw data by a statistical factor since there are twice as many β -hydrogens on the isopropyl group as on the ethyl group. After this correction is made, it is evident that amide ion is three times more likely to attack one of the β -hydrogens of the isopropyl group, forming ethoxide ion and propylene, than to attack one of the β -hydrogens of the ethyl group to form isopropoxide ion and ethylene. When hydroxide ion is the base, the results are nearly the opposite, with attack on the ethyl β -hydrogens being preferred over attack on the isopropyl β -hydrogens by nearly as large a factor. Clearly these E2 reactions are highly selective despite the fact that they occur rapidly.

The relative rates per β -hydrogen atom for the eight simple mixed ethers are given for both NH_2^- and OH^- in Table I. In every case amide ion prefers to abstract a proton from the larger of the two alkyl groups, forming the smaller alkoxide ion. The result is most dramatic in ethyl *tert*-butyl ether where only a trace of *tert*-butoxide ion is formed. If we compare the ethyl propyl ethers with the ethyl butyl ethers, we again see a greater tendency for attack on the larger (butyl) group as compared to the smaller (propyl). In the case of the two propyl butyl ethers the results are at least qualitatively consistent in that attack by NH_2^- occurs on the larger of the two groups as it does in all other ethers.

These results for reactions of amide ion with ethers are in the direction one might expect for an elimination reaction proceeding through an intermediate carbanion (E1cb) in which the breaking of the carbon-hydrogen bond is most important, and relative carbanion stabilities play a decisive role. Although relative gas-phase stabilities of alkyl anions are not yet known, it is known that branched alkyl groups stabilize oxy anions (for example *tert*-butoxide ion is less basic than ethoxide ion¹⁵). Proton abstraction from the *tert*-butyl group would generate a carbanion (II) of structure similar to that of the *tert*-butoxide ion as compared to abstraction from the ethyl group (I). In the gas-phase

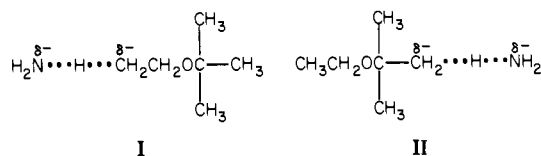


Table I. Reactions of NH_2^- and OH^- with Dialkyl Ethers

reactant neutral	product ions	product distributions ^a for B ⁻			
		NH_2^-		OH^-	
		% obsd	% cor ^b	% obsd	% cor ^b
$\text{C}_2\text{H}_5\text{O}-n\text{-C}_3\text{H}_7$	$\text{C}_2\text{H}_5\text{O}^-$	40	55	10	
	$\text{C}_2\text{H}_5\text{O}^-$ (BH)	5		4	20
	$n\text{-C}_3\text{H}_7\text{O}^-$	47	45	45	80
	$n\text{-C}_3\text{H}_7\text{O}^-$ (BH)	8		41	
$\text{C}_2\text{H}_5\text{O}-i\text{-C}_3\text{H}_7$	$\text{C}_2\text{H}_5\text{O}^-$	80	77	19	31
	$\text{C}_2\text{H}_5\text{O}^-$ (BH)	7		28	
	$i\text{-C}_3\text{H}_7\text{O}^-$	11	23	36	69
	$i\text{-C}_3\text{H}_7\text{O}^-$ (BH)	2		17	
$\text{C}_2\text{H}_5\text{O}-n\text{-C}_4\text{H}_9$	$\text{C}_2\text{H}_5\text{O}^-$	73	84	21	49
	$\text{C}_2\text{H}_5\text{O}^-$ (BH)	5		18	
	$n\text{-C}_4\text{H}_9\text{O}^-$	19	16	34	51
	$n\text{-C}_4\text{H}_9\text{O}^-$ (BH)	3		27	
$\text{C}_2\text{H}_5\text{O}-i\text{-C}_4\text{H}_9$	$\text{C}_2\text{H}_5\text{O}^-$	50	79	3	14
	$\text{C}_2\text{H}_5\text{O}^-$ (BH)	5		2	
	$i\text{-C}_4\text{H}_9\text{O}^-$	40	21	60	86
	$i\text{-C}_4\text{H}_9\text{O}^-$ (BH)	5		35	
$\text{C}_2\text{H}_5\text{O}-s\text{-C}_4\text{H}_9$	$\text{C}_2\text{H}_5\text{O}^-$	84	83	14	27
	$\text{C}_2\text{H}_5\text{O}^-$ (BH)	5		24	
	$s\text{-C}_4\text{H}_9\text{O}^-$	11	17	48	73
	$s\text{-C}_4\text{H}_9\text{O}^-$ (BH)	0		14	
$\text{C}_2\text{H}_5\text{O}-t\text{-C}_4\text{H}_9$	$\text{C}_2\text{H}_5\text{O}^-$	93	97	42	97
	$\text{C}_2\text{H}_5\text{O}^-$ (BH)	6		57	
	$t\text{-C}_4\text{H}_9\text{O}^-$	1	3	1	3
	$t\text{-C}_4\text{H}_9\text{O}^-$ (BH)	0		0	
$i\text{-C}_3\text{H}_7\text{O}-n\text{-C}_4\text{H}_9$	$i\text{-C}_3\text{H}_7\text{O}^-$	32	59	22	60
	$i\text{-C}_3\text{H}_7\text{O}^-$ (BH)	0		11	
	$n\text{-C}_4\text{H}_9\text{O}^-$	60	41	24	40
	$n\text{-C}_4\text{H}_9\text{O}^-$ (BH)	8		43	
$i\text{-C}_3\text{H}_7\text{O}-i\text{-C}_4\text{H}_9$	$i\text{-C}_3\text{H}_7\text{O}^-$	22	63	≤9	≤57
	$i\text{-C}_3\text{H}_7\text{O}^-$ (BH)	0		≤9	
	$i\text{-C}_4\text{H}_9\text{O}^-$	62	37	≥37	≥43
	$i\text{-C}_4\text{H}_9\text{O}^-$ (BH)	16		≥45	

^a Product distributions were measured under conditions where mass discrimination is minimized but probably not completely eliminated. ^b Raw data have been adjusted by a statistical factor which corrects for the different number of β -hydrogen atoms in the two alkyl moieties of the unsymmetrical ethers.

methane is only 13 kcal/mol weaker an acid than ammonia,¹⁵ and neopentane should be appreciably more acidic than methane. We are dealing here, then, with a very strong base inducing an elimination on a compound with a poor leaving group in an exothermic reaction. All these factors tend to favor an E1cb-type elimination with removal of the most acidic hydrogen.

We also studied elimination by NH_2^- from two mixed ethers of ethylene glycol. The attempt in these experiments was to separate the effects of leaving groups from those of olefin stability. For example, in the elimination of ethyl *n*-propyl ether attack on the propyl group forms the stronger base (ethoxide ion) along with the more stable olefin (propylene) while attack on the ethyl group generates the weaker base (*n*-propoxide ion) together with the less stable olefin (ethylene). The roughly equal amounts of attack on the two groups could be the result of large compensating effects due to relative olefin and alkoxide stabilities.

The results for the ethylene glycol ethers indicate that there are no large effects of leaving group. In the case of methyl ethyl and methyl *n*-propyl ethylene glycol one would expect the stability of the two vinyl ether products to be the same, as would the relative stabilities of the two carbanions resulting from proton abstraction. The only difference in the two major pathways is that one produces methoxide, the other ethoxide or *n*-propoxide. The stronger base,

Table II. Reactions of NH_2^- and OH^- with Ethylene Glycol Dialkyl Ethers

reactant neutral	product ions ^b	obsd product distributions ^a for B ⁻ , %	
		NH_2^-	OH^-
$\text{CH}_3\text{OCH}_2\text{CH}_2\text{OCH}_3$	CH_3O^-	100	100
$\text{CH}_3\text{OCH}_2\text{CH}_2\text{OC}_2\text{H}_5$	CH_3O^-	41	4
	CH_2CHO^-	7	4
	$\text{CH}_3\text{OCH}_2\text{CH}_2\text{O}^-$	14	82
	$\text{C}_2\text{H}_5\text{O}^-$	38	10
$\text{CH}_3\text{OCH}_2\text{CH}_2\text{O}-n\text{-C}_3\text{H}_7$	CH_3O^-	43	11
	CH_2CHO^-	7	11
	$\text{CH}_3\text{OCH}_2\text{CH}_2\text{O}^-$	7	41
	$n\text{-C}_3\text{H}_7\text{O}^-$	43	37

^a Product distributions were measured under conditions where mass discrimination is minimized but probably not completely eliminated. ^b Clusters of these ions with NH_3 or H_2O and with the parent ether were observed; for simplicity, these ion intensities are included with those of the unclustered product ion.

methoxide, is formed in slightly greater amounts than the weaker bases. Only a small amount of product results from base attack on the ethyl group; again this is consistent with an E1cb-like transition state.

In contrast, hydroxide ion reacts with ethers in a fundamentally different way than does amide ion. No overall consistent pattern emerges which allows prediction of the product distribution. For example, consider the four ethyl butyl ethers: base attack is mainly on the butyl group for the *tert*-butyl ether, mainly on the ethyl group for the isobutyl and *sec*-butyl ethers, and approximately evenly divided for the *n*-butyl case. However, in every example hydroxide attacks the ethyl group to an equal or greater extent than does amide. It appears that the stability of the alkoxide ion which is forming is exerting an influence, but this factor is not controlling the reaction. In the ethylene glycols there is a slight preference for loss of the more stable anion, but the biggest change is the predominance of reaction at the ethyl group or *n*-propyl group. One factor which may seriously complicate the recognition of any consistent trend in the reaction of hydroxide is the high percentage of clustered product, $\text{RO}^-(\text{H}_2\text{O})$, which is formed. This observation introduces a host of new considerations including differential solvation enthalpies of the alkoxide ions, differing steric barriers in the ion-dipole complex to migration of the newly formed H_2O to the incipient alkoxide etc. The superposition of a variety of subtle but important effects could preclude any straightforward trend.

Conclusions

Cyclic and acyclic ethers with β -hydrogens react rapidly in the gas phase with both amide and hydroxide ions by elimination rather than substitution pathways. Despite the rapidity of these reactions, they are also quite selective. Ethers without β -hydrogens are relatively unreactive under the same conditions. Using mixed ethers as substrates, it has been possible to measure the effect of alkyl groups on the direction of elimination. Amide-induced eliminations occur mainly by abstraction of the most acidic hydrogen of the ether. For hydroxide ion reactions the direction of elimination is less predictable; it appears that the stability of the resulting alkoxy anion exerts an effect. Long-lived reaction complexes play a role with both bases but are more important for hydroxide ion. In several cases initial products react further before decomposition of the ion-dipole complex.

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