Cavity-Size-Dependent Dissociation of Crown Ether/ Ammonium Ion Complexes in the Gas Phase

Simin Maleknia[†] and Jennifer Brodbelt[*]

Contribution from the Department of Chemistry and Biochemistry, University of Texas, Austin, Texas 78712-1167

Received March 18, 1992

Abstract: Ion complexes of crown ethers and amine substrates were generated by liquid secondary ion mass spectrometry (LSIMS). The ammonium ions were produced from the precursors: ammonium chloride, methylammonium and hydrazinium hydrochlorides, methylhydrazine sulfate, and tosylhydrazine. The effective hydrogen bonds between the ammonium ions and multi-oxygen receptors are the predominant binding interactions in the complex formation. Results of collision-induced dissociation (CID) of the ion complexes at 7 and 0.4 keV show two strikingly different types of fragmentation pathways. At the lower collision energy, the dominant dissociation pathways involve decomplexation in conjunction with losses of ethylene oxide units from the resulting protonated ether molecules, which are the fragmentation processes previously observed for dissociation of protonated crown ethers. In addition, metastable ions corresponding to decomplexation of neutral amines from the polyether/ammonium ion complexes by intramolecular proton transfer are also observed. Higher collision energy activation and dissociation of the ion complexes proceed by intramolecular ring-opening reactions which result in odd-electron, acyclic product ion structures. These ring-opening reactions are significantly favored over the simple eliminations of ethylene oxide units as the cavity sizes of the crown ethers increase and the strengths of hydrogen-bonding interactions increase. Hydrazinium and methylhydrazinium ion complexes dissociate via macrocyclic ring-opening pathways that result in the loss of hydroxymethylene radical. This ring-opening reaction is the dominant dissociation pathway when the host cavity is large enough to encapsulate the hydrazinium ion, such as for 18-crown-6 and 21-crown-7. In contrast, ion complexes of crown ethers with tosylhydrazines dissociate by covalent bond cleavage of the nitrogen–sulfur bond of the guest substrate. These results suggest that the association energy for the multiple hydrogen-bonding interactions of the crown ether/ammonium ion complex is on the same order of the covalent macrocyclic or nitrogen–sulfur bonds.

Introduction

The specific site recognition and complexation between macrocycles and substrates is a complex process which requires size and conformational compatibilities of the host and guest molecules.[1] Molecular recognition of amines by macrocycles has been demonstrated and is of great interest because of its similarity to important biological processes, such as transport of amino acids and drugs across membranes or enzyme/substrate interactions.[1,2] Structural characterizations of several amine/macrocycle complexes have revealed the importance of multiple hydrogen-bonding interactions.[1,2] The chemical consequences of these interactions have been demonstrated in the case of the enhanced rates of intramolecular thiolysis when glycylglycine *p*-nitrophenyl ester ions form complexes to macrocycles.[3] There have been few reports of the use of model compounds for formation of complexes by hydrogen bonding in nonpolar solvents in which selective solvation effects would be expected to be minimized; however, gas-phase reactions provide optimum conditions for the evaluation of the *intrinsic* role of hydrogen-bonding effects and other electrostatic interactions in molecular recognition processes. For example, recent mass spectrometric results showed the selectivity of crown ethers for alkali metal ion complexation in the gas phase.[4]

Crown ether macrocycles serve as simple receptor models and are well-suited as hosts because of their conformational flexibility and the presence of multiple binding sites. These characteristics provide capabilities for metal ion encapsulation[1a,5] and the formation of inclusion complexes with protonated amines[2] in solution. Structural characterizations of crown ether/amine ion complexes have been investigated by crystallographic techniques[6] and molecular modeling studies.[7] These results suggest that the stability and formation of these types of host/guest complexes are greatly influenced by hydrogen-bonding interactions and solvation effects. For example, comparison of the cavity sizes (Table I) of the crown ethers and the diameter of the ammonium ion of 2.86 Å[8] reveals that the best fit is possible with 18-crown-6 or 21-crown-7. In fact, although complexes of the ammonium ion with 21-crown-7, 18-crown-6, or 15-crown-5 have been isolated in aqueous solution,[9] complexes of 12-crown-4 with the ammonium ion were not observed. The formation constants measured by calorimetric titration in water showed the stability of the 15-crown-5 ion complex favored over the 18-crown-6 with log *K*

---

[*] Address correspondence to: Prof. Jennifer Brodbelt, Department of Chemistry and Biochemistry, University of Texas at Austin, Austin, TX 78712-1167. Tel. (512)471-0028. Fax (512)471-8696.

[†] Present address: Department of Chemistry, Massachusetts Institute of Technology, Cambridge, MA 02139.

(1) (a) Vogtle, F., Weber, E., Eds. *Host Guest Complex Chemistry: Macrocycles*; Springer-Verlag: New York, 1985. (b) Atwood, J. L., Ed. *Inclusion Phenomena and Molecular Recognition*; Plenum Press: New York, 1988.

(2) (a) Cram, D. J. In *Applications of Biochemical Systems in Organic Chemistry* (Techniques of Chemistry Series, Vol. 10, Part 11); Jones, J. B., Sih, C. J., Perlman, D., Eds.; John Wiley: New York, 1976. (b) Reinhoudt, D. N. *J. Coord. Chem.* **1988**, *18*, 21–43.

(3) Lehn, J.-M.; Sirlin, C. *J. Chem. Soc., Chem. Commun.* **1978**, 949–951.

(4) (a) Maleknia, S.; Brodbelt, J. *J. Am. Chem. Soc.* **1992**, *114*, 4295. (b) Liou, C.-C.; Brodbelt, J. *J. Am. Soc. Mass Spectrom.* **1992**, *3*, 543–548. (c) Zhang, H.; Chu, I.-H.; Leming, S.; Dearden, D. V. *J. Am. Chem. Soc.* **1991**, *113*, 7415–7417.

(5) Izatt, R. M., Christensen, J. J., Eds. *Synthetic Multidentate Macrocyclic Compounds*; Academic Press: New York, 1978.

(6) (a) Trueblood, K. N.; Knobler, C. B.; Lawrence, D. S.; Stevens, R. V. *J. Am. Chem. Soc.* **1982**, *104*, 1355–1362. (b) Nagano, O.; Kobayashi, A.; Yukiyoshi, S. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 790–793.

(7) (a) Howard, A. E.; Singh, U. C.; Billeter, M.; Kollman, P. A. *J. Am. Chem. Soc.* **1988**, *110*, 6984–6991. (b) Gehin, D.; Kollman, P. A.; Wipff, G. *J. Am. Chem. Soc.* **1989**, *111*, 3011–3023.

(8) Frensdorff, H. K. *J. Am. Chem. Soc.*, **1971**, *93*, 600–606.

(9) Wang, W. J.; Chantooni, M. K.; Kolthoff, I. M. *J. Coord. Chem.* **1990**, *22*, 43–52.

0002-7863/93/1515-2837$04.00/0

Table I. Relative Cavity Sizes of Crown Ethers[5]

polyether ring	cavity size, Å
12-crown-4	1.2–1.5
15-crown-5	1.7–2.2
18-crown-6	2.6–3.2
21-crown-7	3.4–4.3

values of 1.71 and 1.23,[10] respectively. In contrast, the order of binding constants measured potentiometrically in anhydrous methanol for the ammonium ion is 18-crown-6 > 21-crown-7 > 15-crown-5 > 12-crown-4.[11] Moreover, in anhydrous methanol, 18-crown-6 shows equal binding affinities for the ammonium and methylammonium ions,[12] whereas in chloroform[13a] or water[13b] 18-crown-6 binds more effectively to the ammonium ion than the methylammonium ion. These data show the importance of solvation energy effects which direct the complexation equilibrium and make the extraction of intrinsic thermodynamic or kinetic parameters difficult.

In the gas phase, the hydrogen bonds between the amine donors and oxygen receptor sites dominate the stability of crown/amine inclusion complexes. The capability for hydrogen-bond formation also determines the gas-phase basicities[14] of polyethers, and it has been shown that primary amines form the most stable complexes with crown ethers. Higher order effects of multiple hydrogen bonding increase with the increasing cavity size of crown ethers, and an association energy as great as 46 kcal/mol was estimated for the ion complex involving 18-crown-6 bound to c-$C_6H_{11}NH_3^+$ based on proton-transfer experiments in a high-pressure mass spectrometer.[15]

The goal of the present study is to evaluate the nature of gas-phase intramolecular interactions of primary amines with crown ethers of different cavity sizes by tandem mass spectrometry. Two types of experiments were performed to address this question. First, collision-induced dissociation (CID) results of the ammonium ion complexes are compared to CID spectra of simple protonated crown ethers to determine new dissociation reactions which arise from intramolecular interactions of the amines and polyethers. Second, complexes with hydrazines are examined with the aim of comparing preferential covalent bond activation of nitrogen–nitrogen or nitrogen–sulfur bonds within the guest molecule that have bond strengths similar to the association energies of the multiple hydrogen-bonding interactions which bind the hydrazine guest to the macrocyclic host. Ion complexes of hexaethylene glycol, an acyclic analogue of 21-crown-7, are examined to account for the differences in complexation between cyclic and acyclic ethers, a phenomenon termed the "macrocyclic effect".[2a,5]

Experimental Section

Ion complexes of crown ethers with the amine substrates were generated by the liquid secondary ion mass spectrometry (LSIMS) technique. The primary beam of cesium ions was generated from a JEOL cesium gun operating at 26 kV and 1.8 A. The complexes were formed from ionization of a solution of the polyether and amine. The matrix used was *O*-benzylglycerol; however, 21-crown-7 and hexaethylene glycol samples were analyzed without the matrix. Crown ethers of 15-crown-5, 18-crown-6, and 21-crown-7 were used to provide a host series with increasing cavity sizes (Table I).[5] However, 12-crown-4 was excluded since the effective hydrogen-bonding interactions were predicted to be minimum with this ether because of its small cavity size. For this reason and due to its high volatility, ion complexes of 12-crown-4 were formed in low abundances in the source and are not reported in this study.

A JEOL HX110/HX110 tandem mass spectrometer[16] in E_1B_1/E_2B_2 configuration equipped with a variable-voltage floating collision cell in the third field-free region was operated at an accelerating voltage of 10 kV. The resolution of both mass spectrometers was 1:1000. Collision-induced dissociation (CID) experiments were performed with the collision cell floated at 3 or 9.6 kV above ground. The resulting collision energy in the laboratory frame was 7 or 0.4 keV, respectively. Helium was used as the collision gas at a pressure to attenuate the main beam by 30%. This approaches near-single collision conditions. Maximum energy available for dissociation of complexes is calculated by converting the laboratory energy (E_{lab}) to the center-of-mass energy (E_{cm}) when $E_{cm} = (E_{lab}M_{helium})/(M_{complex} + M_{helium})$. For example, E_{cm} values for ammonium ion complexes of 15-crown-5 and 21-crown-7 at a laboratory energy of 7 keV are 58 and 43 eV, whereas a 0.4-keV laboratory energy corresponds to 3.3 and 2.4 eV in the center-of-mass frame, respectively. The results of CID experiments at the two voltage settings of the collision cell show distinctive dissociation pathways, and the voltage of the collision cell is continuously variable. However, the energy bracketing technique was not used. Determination of the absolute threshold dissociation energy and partitioning of energy into various internal modes of the complexes is beyond the main focus of this study. The results of CID experiments are discussed *qualitatively* to show how the interactions of primary amines and crown ethers can alter the dissociation channels of the ethers. The observed change in the fragmentation behavior is thus attributed to different cavity sizes of the host which promote different numbers and strengths of binding interactions.

Materials. The commercial source for ethers of 15-crown-5, 18-crown-6, and hexaethylene glycol was Aldrich Chemical Co. (Milwaukee, WI), and 21-crown-7 was purchased from Parish Chemical Co. (Vineyard, UT). ND_4Cl was purchased from Cambridge Isotope Laboratory (Cambridge, MA). Commercial sources of hydrazines were Aldrich for $N_2H_4{\cdot}HCl$, Eastman Organics (Rochester, NY) for $CH_3N_2H_4{\cdot}H_2SO_4$, and Johnson Matthey Alfa (Wardhill, MA) for 4-toluenesulfonyl (tosyl) hydrazine. Perdeuterated hydrazines were prepared by hydrogen/deuterium exchange from D_2O solutions.

Results and Discussion

Two types of primary amine substrates were selected to examine their intramolecular interactions with crown ethers. First, guest molecules, such as the ammonium or hydrazinium ions that can be *completely* encapsulated by the cavity of some of the ether molecules (Table I), were chosen to evaluate differences qualitatively in complexation behavior due to cavity size effects based on changes in fragmentation behavior of the complexes. The second type of guest molecules, such as methyl- and tosylhydrazines, can *partly* fit within the macrocycles. For these latter types of complexes, crystal structures show the geometry of the N–N bond of the guest molecules as normal to the plane of the hosts.[6] The intramolecular dissociation reactions that are promoted because of the specific site binding of crown ethers may also be related to the cavity size effect of the hosts. When the crown ether molecule anchors one portion of the guest molecule (i.e., the amine portion), the dissociation reactions from the unbound side of the guest may be altered relative to an uncomplexed guest ion. Hydrogen-bonding interactions in these types of host/guest complexes may be strong enough to withstand activation leading to covalent bond cleavages in the guest molecule. Such behavior is not unprecedented. For example, in solution, covalent bond dissociation catalyzed by intramolecular reactions of hydrogen-bonded host/guest complexes has been demonstrated in the case of thiolysis of *p*-nitrophenyl.[3] In the gas phase, dissociation of host/guest complexes, primarily stabilized by multiple hydrogen-bonding interactions, should provide information about the hydrogen-bonding energies relative to other covalent bonds of the complex (N–N, C–C, etc.).

---

[10] Izatt, R. M.; Terry, R. E.; Haymore, B. L.; Hanson, L. D.; Dalley, N. K.; Avondet, A. G.; Christensen, J. J. *J. Am. Chem. Soc.* **1976**, *98*, 7620–7626.

[11] Gokel, G. W.; Goli, D. M.; Minganti, C.; Echegoyen, L. *J. Am. Chem. Soc.* **1983**, *105*, 6786–6788.

[12] Izatt, R. M.; Izatt, N. E.; Rossiter, B. E.; Christensen, J. J.; Haymore, B. L. *Science*, **1978**, *199*, 994–996.

[13] (a) Beresford, G. D.; Stoddart, J. F. *Tetrahedron Lett.* **1980**, *21*, 867–870. (b) Naguchi, H.; Nagamatsu, M.; Yoshio, M. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 1855–1856.

[14] (a) Moet-Ner, M. *J. Am. Chem. Soc.* **1983**, *105*, 4906–4911. (b) Aue, D. H.; Bowers, M. T. In *Gas Phase Ion Chemistry*; Bowers, M. T., Ed.; Academic Press: New York, 1979; Vol. 2.

[15] Moet-Ner, M. *J. Am. Chem. Soc.* **1983**, *105*, 4912–4915.

[16] Sato, K.; Asada, T.; Ishihara, M.; Kunihiro, F.; Kammei, Y.; Kubota, E.; Costello, C. E.; Martin, S. A.; Scoble, H. A.; Biemann, K. *Anal. Chem.* **1987**, *59*, 1652–1659.

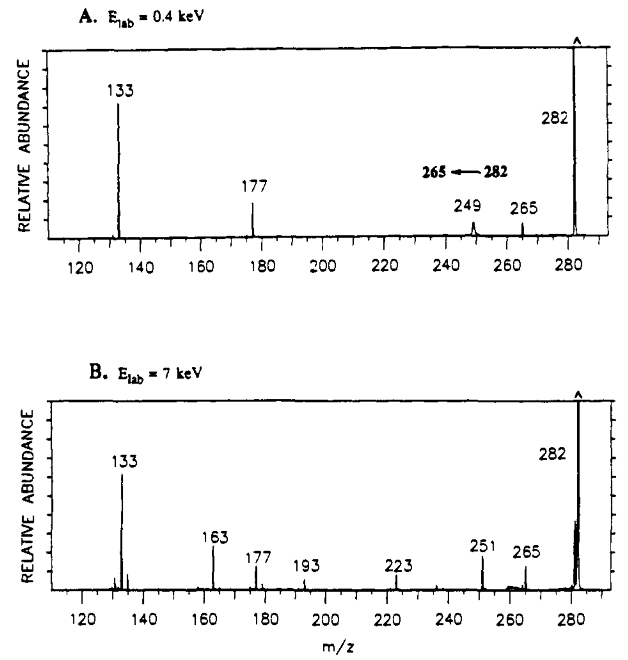

Figure 1. CID mass spectra of 18-crown-6/ammonium ion complex.

Structural Characterization by Collision-Induced Dissociation. Collision-induced dissociation of the crown ether/ammonium ion complexes at high and low collision energies was used for structure elucidation and to probe the nature of the multiple interactions between the amines and polyethers. Two distinct types of fragmentation pathways are observed after high- and low-energy collisions. At high collision energies with the collision cell voltage floated at 3 kV (7 keV collision), the center-of-mass kinetic energy of the complexes of the polyethers with ammonium, methylammonium, or hydrazinium ion was between 40 and 60 eV. As shown in the following section, this magnitude of kinetic energy, after partial conversion to internal energy, is sufficient to induce extensive rupture of the macrocyclic structure. At the lower collision energy (collision cell voltage of 9.6 kV, 0.4-keV collisions), less than 5 eV of internal energy is available for deposition into the ion complexes. This magnitude of energy predominantly causes the loss of a neutral amine guest after intramolecular proton transfer from the guest to the host, in combination with systematic cleavages of the resulting protonated macrocycle.

Low-Energy CID. Ion complexes incorporating ammonium, methylammonium, or hydrazinium ions show similar types of fragmentation pathways, and only dissociation reactions of ammonium ion complexes are discussed in detail.

Low-energy collisions occurred at the laboratory energy of 0.4 keV. As an example, Figure 1A shows the CID spectrum, of the ammonium ion adduct of 18-crown-6. The series of fragment ions observed at *m/z* 265, 221, 177, and 133 corresponds to the losses of 0, 1, 2, or 3 ethylene oxide units in conjunction with elimination of ammonia. At this low collision energy, cleavages of carbon–oxygen bonds of the macrocyclic skeleton occur. The dissociation products of the cyclic and acyclic ether ammonium ion complexes are similar to the ones observed in CID spectra of the simple protonated ethers.[17] Additionally, a metastable ion at *m/z* 249 is observed, corresponding to decomplexation of ammonia from the polyethers. The presence of metastable ions[18] in low-energy CID spectra is not unique to the dissociation of these hydrogen-bonded ion complexes of ethers. The hexaethylene glycol/ammonium complexes also dissociated by losses of ethylene oxide units in combination with the loss of ammonia. Metastable ions are also present in the CID spectra of these acyclic ion complexes. All of the other macrocyclic complexes incorporating methylammonium or hydrazinium ion guests dissociate by elimination of the neutral amine guest, resulting in simple protonated polyethers, with consecutive losses of ethylene oxide units.

The low-energy CID spectra of the ammonium ion complexes offer evidence that the macrocyclic structures are not disrupted upon initial complexation in the gas phase because the spectra are similar to those obtained for simple protonated crown ethers. Additionally, after low-energy activation, the amine substrate is never retained by any fragmented portion of the host polyether ion. Moreover, the formation of radical fragment ions by intramolecular rearrangements is not indicated. These latter two types of processes are important upon high-energy collision activation of the ammonium ion complexes, as discussed in the next section.

High-Energy CID. Polyether/NH_4^+ Complexes. In general, both electronic and vibrational excitations occur after high-energy collisional activation, resulting in higher energy deposition and access to different dissociation processes.[19] For example, shown in Figure 1B is the 7-keV CID spectrum of the 18-crown-6/ammonium ion complex. The types of fragment ions produced are typical of ones observed for the other ammonium/macrocyclic ion complexes after high-energy activation. In contrast to the low-energy CID spectra which only showed carbon–oxygen bond cleavages, high-energy activation of the ion complexes of the cyclic ethers proceeds by homolytic cleavages of carbon–carbon and carbon–oxygen bonds. For instance, in addition to the fragment ions seen in the low-energy CID spectrum in Figure 1A, typical neutral losses from CID of the ion complexes of crown ethers are 31, 59, 89, or 119 u. These identical neutral losses were also observed from high-energy collision-induced dissociation of alkali metal ion complexes of polyethers.[20]

Furthermore, when crown ether ion complexes involving ND_4^+ were examined, the neutral losses of 31, 59, 89, ... remained unchanged which indicates that all of the atoms of the ND_4^+ ion are completely retained by the ionic portion of the dissociating complex and are not involved in the neutral losses. The identity of these neutral losses as radicals, such as $^{\bullet}CH_2OH$ (31 amu), and not amine-containing species, such as CH_3NH_2 (31 amu), was thus confirmed by the deuterium-labeling experiments. For example, elimination of the neutral of 31 amu from $(M + ND_4)^+$ must be due to $^{\bullet}CH_2OH$ and not its amine counterpart CH_2DND_2 (which would be observed as a loss of 34 amu) because of the absence of a deuterium shift in that fragmentation pathway. The observation that the ammonium portion of the complex apparently remains a "spectator" in the dissociation processes led to proposal of mechanisms (Scheme I) similar to fragmentation pathways of the alkali metal ion adducts described previously in which extensive macrocyclic cleavage occurred without expulsion of the attached cation.[20] The mechanisms are used only to illustrate possible rational pathways for dissociation of the complexes and to suggest that the ammonium portion may remain remote from the fragmentation site, and have not been confirmed by extensive labeling studies.

Scheme I shows the proposed mechanisms of dissociation for the ammonium ion complex of 18-crown-6. After high energy activation, the crown ether complex opens, and the amine remains attached to the ether. For neutral losses of 31, 89, and 119 u, the proposed ring-opening process includes the transfer of a proton to an oxygen site. Homolytic cleavages of carbon–carbon bonds may result in the neutral losses of 31 and 119 u, as shown in Scheme I, A and B, respectively. Scheme IC shows how the homolytic cleavage of a carbon–oxygen bond in conjunction with

---

(17) Maleknia, S.; Liou, C.-C.; Brodbelt, J. *Org. Mass Spectrom.* **1991**, *26*, 997–1002.

(18) Cooks, R. G.; Beynon, J. H.; Caprioli, R. M.; Lester, G. R. *Metastable Ions*; Elsevier: New York, 1973.

(19) Bush, K. L.; Glish, G. L.; Mc Luckey, S. A. *Mass Spectrometry/Mass Spectrometry*; VCH Publishers: New York, 1988.

(20) Maleknia, S.; Brodbelt, J. *Rapid Commun. Mass Spectrom.* **1992**, *6*, 376–381.

Scheme I. Mechanisms for Dissociation Pathways of Ammonium Ion Complexes of Crown Ethers

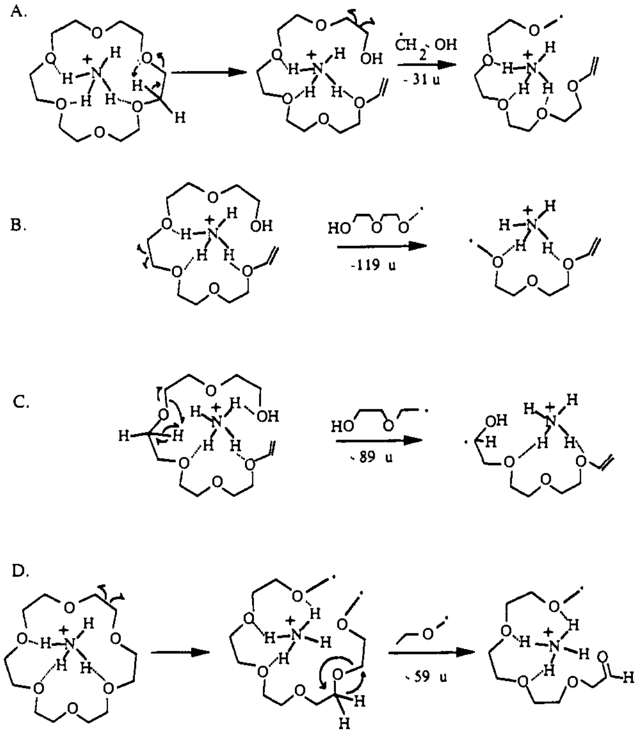

Table II. High Energy CID Results for Crown Ether Ammonium Cation Complexes

neutral loss,[a] u	fragment ions, m/z (% abundances)		
	15-crown-5/NH_4^+	18-crown-6/NH_4^+	21-crown-7/NH_4^+
17	221 (100)	265 (20)	309 (13)
31 A_0	207 (5)	251 (29)	295 (2)
46		236 (4)	280 (9)
59 D_0	179 (2)	223 (13)	267 (4)
76			250 (4)
		221 (2)	
89 C_0		193 (9)	237 (14)
D_1		179 (5)	223 (4)
	177 (4)	177 (20)	221 (2)
106			220 (4)
119 B_0		163 (38)	207 (43)
C_1			193 (3)
D_2		135 (14)	179 (29)
			177 (16)
B_1			163 (6)
C_2			149 (8)
	133 (25)	133 (100)	133 (100)

[a] The letters A to D represent fragmentation pathways shown in Scheme I, and the subscripts denote the number of ethylene oxide units in conjunction with the mechanistic schemes.

a hydrogen atom transfer results in the loss of 89 u as a radical. Alternatively, the ring may open by homolytic cleavages of a carbon–carbon bond, and the transfer of a hydride to a carbon center results in the loss of 59 u as a radical (Scheme ID). The transfer of a proton to the first or third oxygen in conjunction with heterolytic cleavages of corresponding carbon–oxygen bonds results in the neutral losses of 31 or 119 u. Note that the ions resulting from these pathways are all radical cations and, in fact, are illustrated as distonic ions.

The CID spectra of the $(M + NH_4)^+$ complexes of the other crown ethers are summarized in Table II. The intramolecular ring-opening reactions described in Scheme I are increasingly favored over net dissociation by decomplexation in conjunction with loss of multiple ethylene oxide units (formation of $(M + H)^+$ and ions of m/z 221, 177, or 133), especially as the cavity size of the crown ether increases and the number of pole–dipole interactions of the amines increase. For example, the total percentage of the fragment ion current[21] due to formation of radical-type ions is <5% for the 15-crown-5 complexes, 32% for the 18-crown-6 complexes, and 45% for the 21-crown-7 complexes.

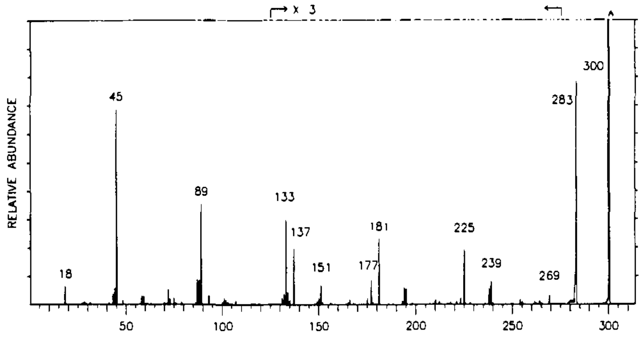

Figure 2. High-energy CID mass spectrum of hexaethylene glycol/ammonium ion complex.

The fact that extensive macrocyclic cleavage involving elimination of radicals from the polyether skeleton may compete successfully with simple decomplexation of the crown ether/ammonium ion complexes is remarkable. This result suggests that the host/guest binding interactions are collectively strong enough to permit efficient internal energy redistribution throughout the complex after collisional activation and prior to rapid decomplexation.

As an additional comparison, collision-induced dissociation of the ammonium ion complex of hexaethylene glycol (Figure 2), an acyclic analogue of 21-crown-7, was studied. Homolytic cleavages of carbon–carbon or carbon–oxygen bonds are observed. The ion series at m/z 269, 225, 181 and 137 which corresponds to neutral losses of $\cdot CH_2-(OC_2H_4)_n-OH$ (where n = 0, 1, 2, or 3) is observed. These dissociation pathways occur in conjunction with the ethylene oxide unit losses, the latter of which were observed upon high-energy CID of the protonated molecule.[17] The results from CID of ND_4^+ adducts show that the entire ammonium ion is always retained by the fragment ions formed from the neutral losses of $\cdot CH_2(OC_2H_4)_nOH$ and may interact with the ether oxygens or the hydroxy terminus. Thus, the ammonium portion of the complex is not involved in the rearrangements that lead to radical fragment ions. In general, simple decomplexation of the hexaethylene glycol/ammonium ion adduct, resulting in $(M + H)^+$ at m/z 283, and related fragmentation processes leading to the conventional glycol ions at m/z 177, 133, 89, and 45 are much more favored processes than were observed for the 21-crown-7/ammonium ion analogue. Moreover, formation of those fragment ions which proceed through the types of rearrangements illustrated in Scheme I (leading to radical cations) is less favored, and collectively represent about only 16% of the total fragment ion current. This sum is far less than the 45% total reported above for the 21-crown-7/ammonium ion complexes. A rationale for the striking differences between the preferred dissociation processes of the cyclic polyether and hexaethylene glycol ion complexes is discussed in the section on hydrazinium ion complexes.

Crown Ether/CH_3–NH_3^+ Complexes. Figure 3 shows the high-energy CID spectrum of 18-crown-6 ion complex with methylammonium, and the CID results for the other crown ethers are listed in Table III. Dissociation pathways for the 18-crown-6/methylammonium complex are similar to the ones occurring from the ammonium ion complex; for example, the neutral losses of 31, 59, and 89 u which lead to radical cation fragments are observed. These similarities support mechanisms which do not intimately involve the participation or fragmentation of the ammonium guest. The extent of the ring-opening intramolecular dissociation reactions of crown ether/methylammonium ion complexes again increases with increasing cavity size. For

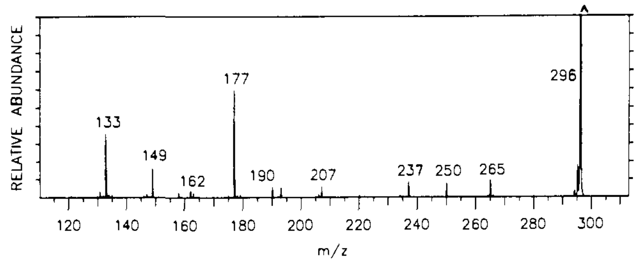

Figure 3. CID mass spectrum of 18-crown-6/methylammonium ion complex at 7 keV.

Table III. High-Energy CID Results for Crown Ether/Methylammonium Cation Complexes

	fragment ions, *m/z* (% abundances)		
neutral loss,[a] u	15-crown-5/ $CH_3NH_3^+$	18-crown-6/ $CH_3NH_3^+$	21-crown-7/ $CH_3NH_3^+$
31 A_0	221 (100)	265 (21)	309 (8)
46		250 (13)	294 (22)
59 D_0	193 (19)	237 (14)	281 (5)
76		220 (4)	264 (10)
89 C_0		207 (12)	251 (12)
D_1		193 (8)	237 (4)
106		190 (10)	234 (29)
119 B_0		177 (100)	221 (67)
D_2		149 (23)	193 (50)
B_1			177 (37)
C_2			163 (17)
			149 (18)
	133 (71)	133 (50)	133 (100)

[a] The letters A to D represent fragmentation pathways shown in Scheme I, and the subscripts denote the number of ethylene oxide units in conjunction with the mechanistic schemes.

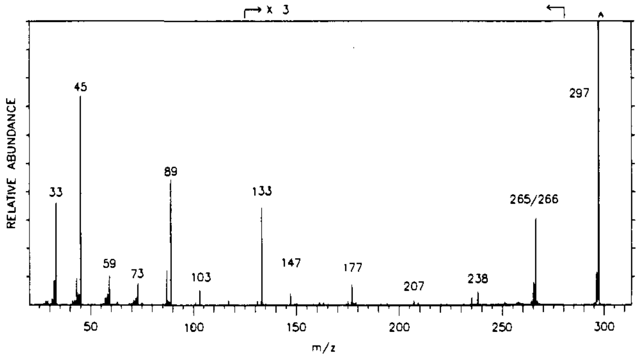

Figure 4. CID mass spectrum of 18-crown-6/hydrazinium ion complex at 7 keV.

example, the total percentage of the fragment ion[21] current attributed to formation of radical type ions for the 15-crown-5 complex is 10%, 22% for the 18-crown-6 complexes, and 28% for the 21-crown-7 complexes.

Crown Ether/Hydrazinium Complexes. The solid-state structure of the 18-crown-6 ion complex shows that hydrazinium ion lies between two upper and lower O_3 planes, and hydrogens associated with both nitrogen atoms bond to five different oxygens of the host.[6a] Thus, these complexes are expected to be especially strongly bound in the gas phase. Figure 4 shows the CID spectrum of 18-crown-6/$N_2H_5^+$ complex, and this spectrum is qualitatively representative of the CID spectra obtained for the 15-crown-5/$N_2H_5^+$ and 21-crown-7/$N_2H_5^+$ complexes. After high-energy collisional activation, the crown ether/hydrazinium complexes dissociate by three types of pathways. The complex may simply split apart to form the hydrazinium ion, *m/z* 33, or the protonated crown ether, *m/z* 265 (after intramolecular proton transfer between the hydrazinium ion and the crown ether). Additionally, the decomplexed protonated crown ether may undergo further fragmentation by losses of ethylene oxide units (resulting in the standard crown ether fragment ions at *m/z* 45, 89, 133, 177, ...). The most interesting process is the elimination of hydroxymethylene radical (31 u).

Table IV. Product Ion Ratios from High-Energy CID of Crown Ether Complexes with Hydrazine Cations[a]

	hydrazine substrates		
	NH_2–NH_3^+	$CH_3N^+H_2NH_2$	tosyl-$NHNH_3^+$
polyether	$\Sigma(C + H)^+$: $\Sigma(C + N_2H_5^+ - {}^\bullet CH_2OH)$	$\Sigma(C + H)^+$: $\Sigma(C + CH_3N_2H_4^+ - {}^\bullet CH_2OH)$	$\Sigma(C + H)^+$: $\Sigma(C + N_2H_4)^+$
15-crown-5	100:5	100:5	100:6
18-crown-6	100:11	100:19	100:13
21-crown-7	100:28	100:46	100:28

[a] C denotes the crown ether molecule. Spectra were recorded at a laboratory collision energy of 7 keV.

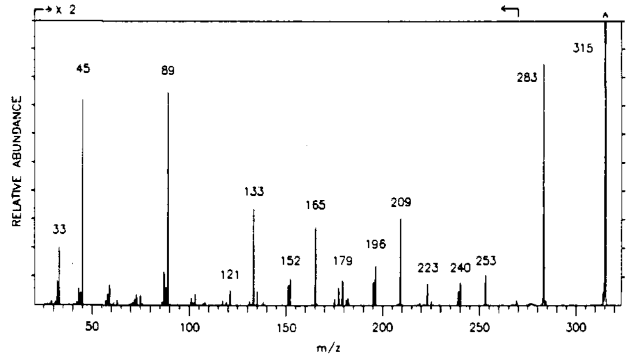

Figure 5. High-energy CID mass spectrum of hexaethylene glycol/hydrazinium ion complex.

The identity of this neutral loss as ${}^\bullet CH_2OH$ and not CH_3NH_2 was confirmed by CID experiments of the corresponding $N_2D_5^+$/crown ether ion complexes. For the deuterium-labeled complexes, the loss of 31 u incorporated no deuterium, demonstrating that the entire hydrazonium species remained associated with the crown ether, and instead the elimination of 31 amu occurred from the polyether skeleton. The extent of this ring-opening dissociation reaction is again strongly cavity-size dependent, and, in fact, it dominates over the intramolecular proton-transfer pathways for ion complexes of 18-crown-6 and 21-crown-7. Table IV summarizes the abundance of the elimination of ${}^\bullet CH_2OH$ relative to the simple decomplexation processes. As the size of the crown ether increases, the extent of loss of the hydroxymethylene radical doubles for each crown ether.

The hydrazinium ion complex of hexaethylene glycol provided an interesting comparison of the behavior of an acyclic analogue of 21-crown-7. After high-energy CID (Figure 5), the hydrazinium ion complex dissociates predominantly by loss of neutral hydrazine (~40% of the fragment ion current), resulting in protonated hexaethylene glycol at *m/z* 283. Second, fragment ions which presumably result from the loss of hydrazine in conjunction with multiple ethylene oxide units (*m/z* 239, 195, 151, 107, 63) or with water and ethylene oxide units (*m/z* 221, 177, 133, 89, 45) account for 5% and 30%, respectively, of the total ion current. Direct dehydration of the hydrazinium/hexaethylene glycol complex in conjunction with ethylene oxide units accounts for ions observed at *m/z* 253, 209, 165, and 121, which sum to 15% of the ion current. These previous processes are all standard types of dissociation pathways of glycol ions. Most interesting, however, is that the ion expected at $(M + N_2H_5^+ - {}^\bullet CH_2OH)^+$ (observed for all the crown ethers) is absent, and

---

(21) The ion currents due to related fragmentation processes were summed in order to minimize any CID differences stemming from small internal energy differences in the precursor ions that would cause some of the complexes to undergo sequential dissociation steps. Thus, the standard crown ether series attributed to elimination of ethylene oxide units and resulting in the abundant ions at *m/z* 45, 89, 133, 177, ... was considered as one type of process.

the related ion series at *m/z* 240, 196, 152 attributed to $(M + N_2H_5^+ - {}^\bullet CH_2OH - nC_2H_4O)^+$, where $n = 1, 2$, or 3, respectively, accounts for only 10% of the remaining ion current. The fact that the losses of $({}^\bullet CH_2OH + nC_2H_4O)$ are a much less abundant series of processes overall than the analogous loss of ${}^\bullet CH_2OH$ and related radical elimination pathways from the 21-crown-7/hydrazinium complexes suggests that it is particularly kinetically or energetically disfavored for the hexaethylene glycol complex. This striking difference between the dissociation processes favored by the acyclic versus cyclic ether/hydrazinium complexes may have several explanations. First, the high gas-phase basicity of hexaethylene glycol may disfavor the formation of strongly-bound hydrazinium complexes, instead resulting in protonated hexaethylene glycol molecules with loosely associated hydrazine molecules. These latter types of complexes would favor decomplexation pathways. However, the gas-phase basicity of 21-crown-7 is not expected to be substantially different from that of hexaethylene glycol, and thus this thermochemical rationalization may not be well-supported.

Secondly, the flexible nature of the hexaethylene glycol ligand may not promote as effective stabilization of the hydrazinium complex compared to a preorganized cyclic ether ligand (especially upon high-energy collisional activation), resulting in complexes which do not favor the same dissociation pathways as the cyclic complexes. Hexaethylene glycol and 21-crown-7 have similar numbers and types of vibrational modes; therefore, such a large difference in the nature of the dissociation processes would not be statistically predicted if the initial structures of the hydrazinium/ether complexes were similar. Either differences in the initial stabilities (based on the effective hydrogen-bonding interactions) or configurations (i.e., rigid cycle versus semicyclized) may play an important role.

Crown Ether/Methylhydrazine Ion Complexes. This type of complex represents a case in which the crown ether host can *partly* encapsulate the guest and likely binds only the amine portion. In addition to the same types of decomplexation reactions and crown ether fragmentation reactions described for the hydrazinium complexes (i.e., formation of $(M + H)^+$ and loss of ethylene oxide units), the intriguing loss of 31 u is again observed, indicating net retention of the methylhydrazinium species despite macrocyclic skeletal cleavage. The relative favorability of the latter reaction relative to competing decomplexation by intramolecular proton transfer is summarized in Table IV. Again, a cavity-size dependence is observed for the series of processes involving the elimination of radicals ${}^\bullet CH_2OH$, ${}^\bullet CH_2OCH_2CH_2OH$, etc., versus the series related to simple decomplexation (loss of neutral methylhydrazine in conjunction with nC_2H_4O units). As the cavity size of the ether increases, dissociation of the complex by macrocyclic skeletal cleavage increases relative to the loss of the neutral methylhydrazine guest by intramolecular proton transfer. This result supports the proposal that multiple pole–dipole interactions occur with the larger cavity sizes, and the total multiple hydrogen-bonding interaction energy is at least on the order of the macrocyclic C–O bond strength.

Crown Ether/Tosylhydrazine Ion Complexes. High-energy collisional activation of tosylhydrazine ion complexes of crown ethers results in the cleavage of the nitrogen–sulfur bond in the guest which is estimated as 59 kcal/mol.[22] The results in Table IV which show the relative abundances of the series of fragment ions related to tosylhydrazine and nC_2H_4O elimination (i.e., formation of $(M + H)^+$ and its fragments at *m/z* 45, 89, 133, ...) versus the series of fragment ions related to loss of the tosyl unit by N–S bond cleavage suggest a less pronounced cavity-size dependence for dissociation of these complexes relative to the effects observed for the methylhydrazine complexes. This observation may be related to the increased bulk and number of vibrational modes of the tosylhydrazine guest which would tend to disfavor the cleavage of the strong sulfur–nitrogen bond relative to the weaker hydrogen bonds. Other less abundant fragment ions in the high-energy CID spectra include ions attributed to cleavages within the tosylhydrazine guest and ions due to elimination of ethylene oxide units from the decomplexed protonated polyether (i.e., formation of the ion series at *m/z* 45, 89, 133, 177, as seen previously in Figure 4).

To provide a comparison of the dissociation routes of a noncomplexed guest ion, the high-energy CID spectra of protonated tosylhydrazine were examined. After collisional activation, protonated tosylhydrazine dissociates by elimination of N_2H_2 or N_2H_4, two routes which involve sulfur–nitrogen bond cleavage. The loss of N_2H_2 suggests facile transfers of hydrogens from the hydrazine moiety to the oxygen sites. In contrast, the predominant dissociation pathway of each crown ether/tosylhydrazine ion complex is the cleavage of the nitrogen–sulfur bond which results in the ion of $(\text{crown ether} + N_2H_4)^+$. The dissociation pathway by elimination of N_2H_2 for the crown ether/tosylhydrazine complexes is disfavored, possibly due to stabilizing hydrogen-bonding interactions which prevent hydrogen transfers from within the hydrazine portion of the guest molecule.

Implications of Dissociation: Kinetic and Energetic Effects. The intriguing formation of radical fragment ions from the polyether/ammonium ion complexes which are only observed after high-energy activation suggests that these types of dissociation processes have high activation barriers which are not surmounted after low-energy collisional activation. Thus, the decomplexation processes and subsequent dissociation pathways leading to crown ether-related fragmentations (*m/z* 45, 89, 133, ...) apparently have lower activation energies. More interestingly, the pathways leading to radical fragment ions are increasingly favored as the size of the crown ether increases. This trend can be rationalized on a kinetic or energetic basis. For example, the ammonium ion complexes incorporating 15-crown-5 may be sufficiently loosely bound relative to the complexes involving the larger polyethers that simple decomplexation of the 15-crown-5/ammonium ion complexes is kinetically favored over slow intramolecular rearrangements leading to radical-type fragment ions. This explanation implies that the 15-crown-5/ammonium ion complexes dissociate readily due to the low activation barrier to decomposition, and likewise that the 18-crown-6 and 21-crown-7/ammonium ion complexes have increasingly greater activation barriers to decomplexation. Because of the larger cavity sizes of 18-crown-6 and 21-crown-7, the ammonium ion complexes would be expected to be more stable.

Alternatively, it may be rationalized that the radical-type fragmentation pathways of the larger polyether complexes are especially kinetically favored because of relatively low activation and entropy barriers that are readily surmountable after high-energy activation. This latter explanation is somewhat less plausible because the larger complexes have only a few more vibrational modes which may participate in internal energy redistribution than the complexes involving 15-crown-5. Additionally, the loss of ${}^\bullet CH_2OH$ or other radicals involves essentially the same types and energies of bond cleavages in all of the polyether complexes, regardless of the size of the macrocycle.

It is more likely that the radical-type fragmentation pathways are favored for the larger crown ether/ammonium ion complexes because the greater number of oxygen donor sites in the preorganized crown ethers promotes more effect stabilization of the complex during the multistep rearrangement process. Such stabilization is particularly important in light of the fact that the ammonium portion remains a spectator and yet may depart by a relatively low-energy competing pathway. This suggestion is further supported by the low abundance of radical fragmentation routes for the hexaethylene glycol/ammonium ion complexes, in which the flexible polyether structure may not entropically favor

---

[22] Fleig, V. H.; Becke-Goehring, M. *Z. Anorg. Chem.* **1970**, *375*, 8–14.

multisite coordination of the ammonium ion after high-energy activation and thus disfavor the necessary rearrangement sequences.

Conclusions

Intramolecular dissociation reactions of the polyether/ammonium ion complexes are energy dependent, with the formation of unusual radical-type ions observed only upon high-energy activation. Low-energy CID activation promotes decomplexation of the amine guests from the polyethers by intramolecular proton transfer to the hosts. Additionally, sequential cleavages of carbon–oxygen bonds of the polyether hosts are observed. High-energy fragmentation pathways proceeded by homolytic bond cleavages of the host or guest depending on the size of the amine molecules. For ion complexes of the ammonium, methylammonium, or hydrazinium ion, rearrangements involving homolytic carbon–carbon or carbon–oxygen bonds of the polyether host occur, resulting in formation of radical ions. In contrast, ion complexes of crown ethers with methyl- and tosylhydrazine dissociate by direct covalent bond cleavages in the hosts or guests. These results suggest stronger electrostatic interactions within the host/guest complexes that adopt a nesting conformation. In addition, covalent bond activation of the guest and host molecules provide an estimation for the association energy of the multiple hydrogen-bonding complexation.

Acknowledgment. The authors thank the NIH Mass Spectrometry Facility at MIT for generous support of this research. This facility is supported by the NIH Grant No. RR00317 awarded to Professor K. Biemann. Additionally, funding from ACS-PRF (22270-G5), Welch Foundation (F-1155), and NIH (R01-GN46723-01) are gratefully acknowledged.